

**U.S. Environmental Protection Agency  
Science Advisory Board  
PFAS Review Panel**

**Summary Minutes for the Public Meeting held on  
December 16, 2021, January 4, 2022, January 6, 2022, and January 7, 2022**

**Meeting Participants:**

**SAB PFAS Review Panel Members \***

Dr. Weihsueh Chiu, Chair  
Dr. Sandeep Burman  
Dr. Aimin Chen  
Dr. Deborah Cory-Slechta  
Dr. Jamie C. DeWitt  
Dr. Jeffrey Fisher  
Dr. James K. Hammitt  
Dr. Lisa Kamendulis

Dr. David Keiser  
Dr. Loren Lipworth  
Dr. Lala Ma  
Dr. Sheila Olmstead  
Dr. Gloria Post  
Dr. Kristi Pullen-Fedinick  
Dr. David A. Savitz  
Dr. Angela L. Slitt

\*For the full SAB membership see Roster<sup>i</sup>

**Designated Federal Officer**

Dr. Suhair Shallal, Science Advisory Board Staff Office

**Other Attendees**

See Attachment A.

**Meeting Summary:**

**Thursday December 16, 2021**

**Meeting convened** (day 1)

The Science Advisory Board (SAB) PFAS Review Panel convened for a public video conference on December 16, 2021.

Dr. Suhair Shallal, Designated Federal Officer (DFO) for the Panel, convened the meeting at approximately 12:00 p.m. (eastern time) under the Federal Advisory Committee Act (FACA). Dr. Shallal opened the meeting with the review of the documents to be discussed by the Panel and listed the next meeting dates of January 4, 6 and 7, 2021, which is when the Panel will deliberate on the charge topics for the noted documents. Dr. Shallal explained that the Panel is meeting via Zoom and the video is being broadcast live on YouTube. In addition, the meeting can also be accessed via a call-in-number for those wishing to only listen to the meeting. The FACA requirements were presented by Dr. Shallal. It was noted that there is an opportunity for public comment, and that four members of the public had registered on time, with one dropping out, leaving three scheduled public commenters for later in the day's agenda<sup>ii</sup>.

Dr. Shallal provided notification of the posting of meeting materials to the meeting website. She described the membership of the Panel, stating that Panelists are special government employees (SGE), and they are subject to ethics laws. She then explained that ethics information for all Panelists had been reviewed and that it was determined that all Panel members have no conflict of interest or appearances of a lack of impartiality. Dr. Shallal announced that Dr. Kevin Boyle had withdrawn from membership on the Panel for personal reasons. Finally, she introduced Mr. Thomas Brennan, Director of the Science Advisory Board Staff Office, to present his welcoming remarks.

Mr. Brennan welcomed and thanked the Panelists for their service. In addition, he thanked the EPA Office of Water's staff and management. He turned the meeting over to Dr. Weihsueh A. Chiu, Chair of the Panel.

Dr. Chiu began the meeting by asking each Panel member to introduce themselves and elaborate on their expertise and background. Panelists did so (see published biosketches on website).

Dr. Chiu stated that the meeting objective, for December 16, 2021, is to gather information and that the Panel comments should not be interpreted as individual positions or positions of the Panel. Dr. Chiu reviewed the agenda. He indicated that EPA Office of Ground Water and Drinking Water (OGWDW) division director Mr. Eric Burneson would provide opening remarks.

Mr. Eric Burneson introduced himself and thanked the Panel for their effort. Mr. Burneson talked about the context of the documents-under-review and how they fit within the regulatory process. Mr. Burneson emphasized that one of the Administrator's key priorities is the PFAS strategic roadmap and to establish national primary drinking water regulation for PFOA and PFOS. Mr. Burneson laid out the PFAS timeline, with the goal of fall 2022 for the proposed rule and fall 2023 for the promulgated rule. He discussed the requirements to promulgate a rule, the need to establish a maximum contaminant level goal (MCLG), and explained what EPA is seeking from the Panel. Mr. Burneson concluded by telling the Panel that their input is going to be important to the EPA's process and the success of EPA's planned regulatory action.

Dr. Chiu asked if the Panel members had any questions for Mr. Burneson. Hearing none, Dr. Chiu invited Dr. Brittany Jacobs from EPA to begin her presentation on the proposed approaches for the derivation of a draft MCLG for PFOA and PFOS in drinking water.

EPA presentation on *Proposed Approaches to the Derivation of a draft Maximum Contaminant Level Goal for PFOA in Drinking Water* and *Proposed Approaches to the Derivation of a Maximum Contaminant Level Goal for PFOS in Drinking Water*

Dr. Jacobs presented an overview of the *Proposed Approaches to the Derivation of a draft Maximum Contaminant Level Goal for PFOA in Drinking Water* and *Proposed Approaches to the Derivation of a Maximum Contaminant Level Goal for PFOS in Drinking Water* documents. Utilizing the slide presentation posted to the meeting website<sup>iii</sup>, Dr. Jacobs presented the background, approach, results, and draft input values for deriving the PFOA and PFOS MCLGs. Dr. Jacobs began with the timeline for the EPA's assessment of PFOA and PFOS highlighting

that the start of EPA's effort began in 2009 and in 2016 EPA finalized health effects support documents (HESDs) and published health advisories for PFOA and PFOS. She noted that those documents served as the springboard for the updates that EPA is asking the Panel to review. Dr. Jacobs described the purpose and scope of the proposed approaches and informed the Panel that the documents themselves do not derive the MCLGs and that EPA wants input from the Panel before that step is completed. She provided details, as indicated in the slide presentation posted to the meeting website as a meeting material, regarding the two documents, results, conclusions, and implications.

#### Clarifying Questions from the Panel for EPA

Dr. Chiu asked if there were any questions from the Panel. Several Panelists had clarifying questions.

A Panelist asked if EPA considered the duration of exposure for the reference dose, wondering if this is for short-term as well as chronic exposure. Dr. Jacobs said EPA had considered exposure duration. The Panelist noted that this is not clearly stated in the document. A Panelist inquired if a systematic review approach was used only for identifying, screening, and evaluating of the individual studies or if a systematic review methodology was utilized in the evidence synthesis of the animal, human, and overall effects. Dr. Jacobs responded that a partially systematic procedure was followed in conducting the EPA review. The process involved multiple people synthesizing the data, exchanging the synthesizes, plus a tertiary review; concluding it was in a sense systematic but did not adhere to all the elements of a systematic review process. The Panelist followed-up with further clarifying questions. EPA responded with elaborating on methodologies and offering to provide additional documents for clarification. A Panelist inquired about the criteria used for inclusion and exclusion of studies. Dr. Jacobs described their strategy for including or omitting certain documents. Questions were raised by the Panel about the mechanistic studies for PFOS that are still ongoing and will not be completed until after the Panel's review. Dr. Jacobs replied that for PFOS EPA used the 2016 document as the foundation. A Panelist questioned if any consideration was given to an effect seen in multiple epidemiology and rodent studies versus something observed by a single investigator, asking if the totality of evidence was considered. Dr. Jacobs responded that if the Panel finds that such an approach/analysis is appropriate then it should be included in their recommendations or suggestions.

#### Review of charge questions for *Proposed Approaches to the Derivation of a draft Maximum Contaminant Level Goal for PFOA in Drinking Water* and *Proposed Approaches to the Derivation of a Maximum Contaminant Level Goal for PFOS in Drinking Water*

Following Panel questions regarding the EPA's overview, Dr. Chiu moved to the next agenda item, reviewing the charge questions for *Proposed Approaches to the Derivation of a draft Maximum Contaminant Level Goal for PFOA in Drinking Water* and *Proposed Approaches to the Derivation of a Maximum Contaminant Level Goal for PFOS in Drinking Water*. Dr. Jacobs reviewed each charge question found on the slides posted to the meeting website. The Panel followed most charge questions with clarifying comments.

For charge question #2 on noncancer hazard identification, a Panelist asked if EPA is asking if there is strong enough evidence for additional effects. Dr. Jacobs clarified that the question is

asking if there are additional effects and also if the Panel disagrees with any of the endpoints identified by EPA. The Panelist clarified their question, asking about the terminology used, i.e., strong versus suggestive. Dr. Jacobs responded that it would be helpful for the Panel to recommend that EPA clarify these terms.

A Panelist asked if charge question #1 is looking for comments on the process for reviewing studies or if the goal of the question was to seek additional studies. Dr. Jacobs said EPA sought additional studies, however if the Panel had suggestion to improve the process, this would be helpful as well. Dr. Jacobs informed the Panel that any additional charge questions and/or modified will be sent to the Panel through the DFO.

Following the discussion of charge questions and clarification portion of *Proposed Approaches to the Derivation of a draft Maximum Contaminant Level Goal for PFOA in Drinking Water* and *Proposed Approaches to the Derivation of a Maximum Contaminant Level Goal for PFOS in Drinking Water*, Dr. Chiu thanked Dr. Jacobs and transitioned to the next section, *EPA's draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of PFAS*.

#### EPA presentation on the draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of PFAS

Ms. Colleen Flaherty began the review of EPA's *draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of PFAS* utilizing the slides available on the meeting website<sup>iv</sup>. Ms. Flaherty provided an overview of the EPA document. She provided the background, purpose and general approach of the *Draft Framework*, dose additivity for PFAS, component-based approaches to the assess mixtures, and a summary. Dr. Justin Conley followed with a review of the dose additivity approach for predicting the effects of mixture. Then Ms. Flaherty returned to review the flow diagram for the proposed component-based approach for PFAS chemicals. Ms. Flaherty noted a correction to slide 19, where it says, "mixture total PFOA ICEC" stating it should read "PFAS ICEC."

#### Clarifying Questions from the Panel for EPA

Following the EPA presentation on *EPA's draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of PFAS*, Dr. Chiu invited the Panelists to ask clarifying questions.

A Panelist asked where this approach will be used in the context of the Safe Drinking Water Act (SDWA), and how or at what point it will be implemented. EPA responded that the framework is not written as a directive but as a practical guide for how to assess potential health risk from PFAS mixtures in any medium. EPA further elaborated that the tool is intended to be used to inform best practices. Another Panelist asked if the EPA could explain how the Benchmark Mixture Dose (BMD) could be used in a practical sense. EPA said the BMD approach is applicable only when the mixture composition is relatively stable. A Panel member asked why EPA is using mixtures and not individual chemicals. EPA responded that PFAS were always found as mixtures in drinking water, and additivity is potentially a concern. A Panelist asked if applying a mixture assessment factor earlier in the process and could change the process that one would use in evaluating PFAS mixtures by providing a safety buffer. EPA said probably not, a standard application could potentially underestimate risk.

Review of charge questions for draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of PFAS

Following Panel questions, Dr. Chiu moved to the next agenda item, reviewing the charge questions for EPA's draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of PFAS. Ms. Flaherty reviewed each charge and Panel members then asked clarifying questions. A Panelist asked whether EPA wanted input on the use of the hazard quotient as a screening tool to determine if a risk assessment is needed. EPA clarified that the question is asking if it is a reasonable methodology as a tier-one screening approach in assessing the potential risk of PFAS mixtures. EPA further clarified that it is used as a risk indicator to identify priority chemicals in a mixture. The Panelist referenced the approach examples and noted that a comparison of the same data set across the tiers was not provided and asked if such a comparison had been done. EPA replied that they evaluated PFOA and PFOS through both a hazard index and relatively potency factor approach to see how those compare.

Dr. Chiu thanked the EPA presenters.

The Panel took a 15-minute break. After the break, the Panel continued with the EPA presentations.

EPA presentation on the Analysis of Cardiovascular Disease Risk Reduction as a Result of Reduced PFOA and PFOS Exposure in Drinking Water

Ms. Morgan McCabe began the review of EPA's Analysis of Cardiovascular Disease Risk Reduction as a Result of Reduced PFOA and PFOS Exposure in Drinking Water utilizing the slides available on the meeting website<sup>v</sup>. Ms. McCabe provided an overview of the analysis. She provided the background and purpose, overview of the cardiovascular disease (CVD) risk reduction analysis, baseline and treatment scenarios, estimation of cholesterol changes, estimation of CVD risk reduction, results, and limitations and uncertainty. Ms. McCabe noted that the EPA started by looking at all health effects identified in the MCLG documents discussed earlier for potential quantification of the health risk reduction and health cost analysis for the proposed rule. She stated EPA is asking for the Panel's input on the CVD risk reduction analysis due to the complexity and novelty of this methodology and approach. Ms. McCabe reviewed the PFOA and PFOS baseline scenario, explaining that EPA is currently establishing estimates for national occurrence of PFOA and PFOS that will be used to support the health risk reduction, and in the meantime, EPA is modeling a hypothetical public water system for the national level analysis. Additionally, Ms. McCabe stated that while EPA is actively developing MCLGs and regulatory options for the proposed National Primary Drinking Water Regulation, they are using a hypothetical regulatory scenario to demonstrate the utility of the methodology.

Clarifying Questions from the Panel for EPA

Following the EPA presentation Dr. Chiu asked the Panel if they had any clarifying questions.

A Panelist asked questions regarding EPA's decision to use the 90<sup>th</sup> percentile and asked for clarification on the validation exercise. EPA emphasized the 90<sup>th</sup> percentile is based on a hypothetical scenario to illustrate the methodology and the validation exercise is detailed in the documentation. A few Panel members asked for additional information on the literature review

process, the study quality, and confounders in some of the studies. EPA offered to provide additional details for the members.

Review of charge questions for *Analysis of Cardiovascular Disease Risk Reduction as a Result of Reduced PFOA and PFOS Exposure in Drinking Water*

Following Panel questions, Dr. Chiu moved to the next agenda item, reviewing the charge questions for *Analysis of Cardiovascular Disease Risk Reduction as a Result of Reduced PFOA and PFOS Exposure in Drinking Water*. Ms. McCabe reviewed each charge question found on the slides posted to the meeting website. Dr. Chiu asked about the exclusion of HDL and if the omission was included in the uncertainty analysis. Ms. McCabe said it was not and the Panel can propose that as a recommendation. Dr. Chiu asked if a meta-analysis was conducted. Ms. McCabe referred him to the documentation. A Panelist asked for clarification on what EPA needs from the Panel noting the magnitude of additional work and time needed. Mr. Burneson responded that EPA's goal is to accomplish the Administrator's goals and reiterated the PFAS timeline.

After the Panel completed their questions, Dr. Chiu moved to the next agenda item, public comments <sup>vii</sup>.

Public comments

Dr. Shallal, DFO, provided the ground rules for public speakers and reminded the Panel that one of the four registered speakers withdrew. Each of the remaining three speakers was allocated 3-minutes to provide their comments.

Steve Risotto, from the American Chemistry Council (ACC), spoke about ACC's support of the development of PFOA and PFOS regulation but found the health endpoint that was selected was inappropriate. Michael Dourson, from Toxicology Excellence for Risk Assessment (TERA), encouraged SAB to consider the disparity in critical dose between animals and humans, noting that based on the critical dose, the half-life analysis may need to be revised. He noted that a summary of recommendations by TERA was available and was sent to EPA. Katie Pelch, from the University of North Texas, stated the documents under review are inconsistent with guidance documents developed by EPA's IRIS program and suggested that there was a general lack of transparency.

Dr. Chiu asked if there were clarifying questions from the Panel; there were none. He then asked the Panel if they had any overarching questions for EPA. Clarifying questions were asked regarding how generalizable the methods are. EPA responded that a public water system-specific approach would be expected rather than an approach that is applicable at the national level.

The Panel then asked clarifying questions about the meeting format and the role of lead discussants. To respond, Dr. Chiu reviewed next steps and expectations for the upcoming meetings.

Dr. Shallal explained that discussions among Panel members must remain limited to subgroup members only. She reminded members to include her on correspondence when discussing the responses to the charge questions. Dr. Shallal reviewed the timeline of the meetings and

requirements of lead discussants. After ascertaining that there were no further questions from Panel members, she recessed the meeting at approximately 5:00 p.m.

## **Tuesday, January 4, 2022**

### Meeting re-convened (day 2)

Dr. Shallal, Designated Federal Officer (DFO) for the Panel, re-convened the meeting at approximately 12:00 p.m. on January 4, 2022. She reviewed the documents to be discussed by the Panel over the next three days. Dr. Shallal noted that the Panel had met on December 16, 2021, and received a briefing on the documents under review. The charge questions were reviewed, and public comments were presented. She informed members of the public that the Panel will be deliberating on the charge questions for EPA's *Draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of PFAS*. Dr. Shallal reiterated to the Panel and listeners information about the FACA requirements and ethics considerations relating to the advisory activity as she noted at the first day of the meeting.

Dr. Weihsueh Chiu, Chair of the PFAS Review Panel, reviewed the agenda and the meeting format. He then turned the meeting over to EPA's Ms. Colleen Flaherty and Dr. Justin Conley to provide highlights from the mixtures document to be reviewed by the Panel.

### EPA presentation

Ms. Colleen Flaherty stated that EPA is proposing a number of approaches for assessing mixtures in the *Draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of PFAS*. These include a component-based assessment of PFAS mixtures under an assumption of dose additivity, a hazard index approach, using a relative potency factor, and a mixture benchmark dose approach. Ms. Flaherty then briefly reviewed the charge questions to be discussed by the Panel.

Dr. Chiu opened the floor to the lead discussant of charge question one, Dr. Post, to begin the deliberations.

### Panel Discussion

#### *Charge question 1*

*A. Please comment on the appropriateness of EPA's approach for a component-based mixture evaluation of PFAS under an assumption of dose additivity.*

*B. If common toxicity endpoint/health effect is not considered an optimal similarity domain for those PFAS with limited or no available MOA-type data, please provide specific alternative methodologies for integrating such chemicals into a component-based mixture evaluation(s).*

Dr. Post summarized the responses from the Panelists assigned to this charge question<sup>vi</sup> along with preliminary comments submitted by 3 additional Panel members. She noted that 6 of the 7 Panel members who provided comments agreed with the assumption of dose additivity for evaluating PFAS mixtures and 1 of the 7 did not, due to lack of information on mechanisms of action. Dr. Post also stated that 6 of 7 Panelists commented that the use of a similar health effects

rather than common mode/mechanism of action as a default of PFAS mixture evaluations was preferable.

Following Dr. Post's summary of the comments, the floor was opened to Panel members who were assigned charge question 1 to provide any additional comments or clarification. One Panel member clarified their original comment of disagreeing with dose additivity approach stating that a more robust discussion of the evidence for and against dose additivity was needed in the document. Panelists deliberated about the utility of the dose additivity approach and ultimately agreed that it is appropriate given the information currently available. Following the Panel's discussion, Dr. Chiu summarized the overarching responses to the charge questions stating that there was general agreement by the Panel that dose additivity is an appropriate assumption in the absence of data for various PFAS. He stated that the literature review should be more expansive to include studies that do not necessarily support dose additivity, or that have found more complicated interactions. Dr. Chiu concluded that the Panel overall supports dose additivity as the default approach and that there are circumstances where the notion of additivity may not apply. Dr. Post agreed with Dr. Chiu's summary and there were no objections by the Panel. Dr. Chiu moved the agenda to charge question 2.

#### *Charge question 2*

*A. Please provide specific feedback on whether the HI approach is a reasonable methodology for indicating potential risk associated with mixtures of PFAS. If not, please provide an alternative.*

*B. Please provide specific feedback on whether the proposed HI methodologies in the framework are scientifically supported for PFAS mixture risk assessment.*

Dr. Fisher, the lead discussant for charge question 2, summarized the responses to the charge from the assigned members<sup>vi</sup> and 3 additional members who submitted preliminary comments. Dr. Fisher stated that across the comments there was cautious agreement to use the hazard index approach for screening to determine if there is a potential risk associated with mixtures of PFAS. Most Panelists also commented about the challenges and sought clarification on how this approach would be implemented. The floor was opened to the rest of the Panel who discussed the use of TOSHI, the possibility of lowering the hazard index below 1, the concerns regarding implementation for states already screening PFAS, the use of NAMs as a tool for assessing mixtures, the utilization of hazard index as a screening methodology rather than performing a risk assessment, and the need for clarity on the data requirements for various approaches. The Panel also concluded that the purpose and intent of the document needs to be clarified by EPA. Dr. Chiu summarized the Panel's discussion stating that the Panel does not have any specific objections to including hazard index and TOSHI among the options for conducting mixtures assessments, but it needs to be recognized that states might use these approaches as decision making tools in regulatory actions when considering drinking water. Dr. Chiu elaborated that the Panel might recommend the approaches be presented as a menu of options with pros and cons and advantages and disadvantages associated with each approach. He further explained that this would allow individual states to decide the best approach given the data available to them. Additionally, Dr. Chiu summarized the Panel's discussion on reconsidering the idea of using health-based water concentrations for hazard index instead of RfDs, since health-based water concentrations also incorporate potentially different exposure factors in their calculations and not just toxicity data. In conclusion, Dr. Chiu's presented the proposal of using a hazard index < 1 as



a possible approach, but also noting its limitations. Dr. Chiu asked the Panel if they had any more comments, hearing none he moved onto a 15-minute break.

The Panel took a 15-minute break

*Charge question 3*

- A. Please provide specific feedback on whether the RPF approach is a reasonable methodology for estimating risk associated with mixtures of PFAS. If not, please provide an alternative.*
- B. Please provide specific feedback on whether the proposed RPF methodology in the framework is scientifically supported for PFAS mixture risk assessment.*

Following the break Dr. Chiu opened the floor to Dr. Slitt, the lead discussant of charge question 3<sup>vi</sup>, who noted that there were 9 Panel members who submitted preliminary comments. Dr. Slitt explained that there was agreement regarding the Relative Potency Factor (RPF) approach as a reasonable method for assessing mixtures of PFAS. Dr. Slitt referenced the previous discussion on the need for a pros and cons list for each of the proposed approaches, and/or creating a menu of options. There was agreement between Panel members on the expansion on the discussion on the differences between TOSHI and RPF, and the types of information needed to support each assessment exercise. There was discussion and concern that the mixtures document should provide additional discussion, rationale, and justification regarding the selection of the index chemical. The Panel thought the mixtures document would be strengthened if a flowchart was provided to describe the process used to select the index chemical. The Panel discussed the dose response curves, and the need to make sure there is congruence among the shapes of the curves. The Panel agreed that the mixtures document would benefit from greater transparency.

Dr. Chiu summarized the Panel's response to charge question 3. He said the Panel agrees that the RPF is a reasonable approach as one of the menu options. There is also a need for additional discussion and comparison of the approaches and data requirements for the index chemical selection when a similar or different result is derived using another approach. Dr. Chiu's final summary point was about the need for discussion on some alternative approaches available when the requirements for the RPF are not satisfied or when some of the assumptions are violated. Dr. Chiu asked the Panel if they had any more comments, hearing none he moved onto charge question 4.

*Charge question 4*

- A. Please provide specific feedback on whether the Mixture BMD approach is a reasonable methodology for estimating what is in essence a mixture-based point-of-departure. If not, please provide an alternative.*
- B. Please provide specific feedback on whether the proposed Mixture BMD methodology in the framework is scientifically supported for PFAS mixture risk assessment.*

Dr. Cory-Slechta, lead discussant of charge question 4, summarized the preliminary responses<sup>vi</sup>. Dr. Cory-Slechta stated that the Panel agreed the Mixtures BMD is a reasonable approach, but more clarification is needed in describing the approach, its application, and how it differs from other proposed approaches, as well as when the Mixture BMD approach would be used over others. The Panel discussed the need for a menu-based approach for delivering the various

assessment options. Dr. Chiu added that many of the comments from previous charge questions about RPF and HI approaches apply here as well. He asked if there are any overarching comments from the Panel before they move onto clarifying comments from EPA and the public. A Panel member commented on the need to possibly reorient the document, since the various approaches are weighted averages of what is available. A Panelist emphasized the need to calculate a human equivalent dose as an ideal when applying the mixture approaches, and when human equivalent dose is absent there is increased uncertainty. This recommendation was agreed upon by the Panel.

Dr. Chiu turned the meeting over to Dr. Shallal for clarifying questions.

#### Clarifying comments

Ms. Colleen Flaherty, an EPA representative, thanked the Panel for their discussion, stating it was very helpful. Ms. Flaherty commented on the mixture BMD, saying the approach is very site specific and the components in the mixture and the ultimate point of departure must be known. She recognized that this section needs more clarification. Dr. Justin Conley from EPA responded to the comment on the use of the human equivalent dose (HED), noting that HED should be used where possible, and he sees the mixtures document needs to be clearer on the importance of using the HED.

A public commenter submitted a request for a clarifying question. Mary Butow, public commenter, asked a question on similarities and differences between approaches and the need for comments on the various methods and what would cause divergences. Dr. Chiu said that in the Panel's comments they did request EPA elaborate on the similarities and differences and when certain methods should be utilized.

Dr. Chiu thanked all members and the lead discussants.

Dr. Shallal recessed the meeting at 3:34 p.m.

### **Thursday January 6, 2022.**

#### Meeting re-convened (day 3)

The meeting was reconvened by Dr. Sue Shallal at approximately 12:00 noon (eastern time). Dr. Shallal reviewed the meeting logistics and reminded everyone about the next meeting start time on Friday, January 7<sup>th</sup> would be one hour earlier at 11:00 am eastern time.

Dr. Shallal indicated the meeting today is intended to cover the *EPA's Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctanoic Acid (PFOA) (CASRN 335-67-1) in Drinking Water* and *EPA's Proposed Approaches to the Derivation of a Draft Maximum Contaminant Level Goal for Perfluorooctane Sulfonic Acid (PFOS) (CASRN 1763-23-1) in Drinking Water*.

Dr. Shallal stated that all presentations from EPA, preliminary comments from all Panelists, and all related meeting materials are available on the SAB website ([www.epa.gov/sab](http://www.epa.gov/sab)) associated with this advisory activity.

Dr. Shallal reminded members of the public that all comments should be sent to her, and she will provide them to Panelists for their consideration as they develop their advice. She further indicated that an opportunity to present oral clarifying comments is available and if any member of the public wishes to comment, please email her directly before the break in the agenda and she provided her email address ([Shallal.Suhair@epa.gov](mailto:Shallal.Suhair@epa.gov)).

Dr. Shallal reiterated that Dr Kevin Boyle had withdrawn from the Panel due to personal reasons and will no longer be participating in the review.

She further explained that the Panel consists of special government employees (SGE) and will abide by all applicable ethics laws and implementing regulations. All Panelists have submitted confidential financial disclosure forms which were reviewed, and it was determined by the Agency deputy ethics official that no appearance of, nor actual, conflicts of interest relating to this topic were identified for any Panelists.

Dr. Shallal proceeded to call roll and all members of the Panel were present. She then handed the meeting over to the Panel Chair, Dr. Chiu.

Dr. Chiu reviewed the agenda and indicated the Panel will go through the topics and charge questions in chronological order. Upon conclusion of the charge questions, there will be an opportunity for clarifying comments before recessing for the day.

Dr. Chiu invited Dr. Brittany Jacobs from the EPA Office of Water to provide some brief remarks.

#### EPA presentation

Dr. Jacobs started by thanking the Panel, and noted that the assessments have been developed in support of deriving maximum contaminant level goals (MCLGs) for national drinking water standards. The MCLG documents under review do not include the derivation of the actual MCLG but rather a description of the selection of data and factors that will be used to calculate the MCLG. She reminded the Panel that EPA is seeking advice on the adequacy and appropriateness of the science and technical details that will be used in the assessments. She mentioned the following specific considerations: literature search, systematic review, selection of critical studies, toxicokinetic models used, the cancer slope factors, selection of candidate POD and recommended RfD. Panel recommendations regarding the derivation of RfDs based on developmental immune effects in children and the proposed RSC of 20% are also being requested.

#### Panel Discussion

Dr. Chiu introduced charge question #1 for the Study Identification and Inclusion topic. He then called upon the lead discussant for this question, Dr. Kristi Pullen-Fedinick.

#### Charge Question #1- Study Identification and Inclusion

*EPA used systematic review methods consistent with the current ORD systematic review practice to ensure transparency and completeness of literature identification, sorting, and study quality evaluation. Is the process clearly described? Please identify additional peer-reviewed studies that the Panel is aware of that could inform toxicity value derivation.*

Dr. Pullen-Fedinick indicated 5 Panel members had provided preliminary comments on this question. She went on to describe areas for agreement, including the literature search strategy and the screening process description.

Dr. Pullen-Fedinick noted that according to the preliminary comments submitted, the systematic review protocol is not published, nor clearly articulated in documentation. She indicated the areas that need additional clarity or transparency, such as the criteria for study inclusion/exclusion. For example, the inclusion of epidemiological and animal studies appears to be inconsistent. Furthermore, she mentioned terms were not used consistently or defined clearly. Also, she commented that studies should not be downgraded for sensitivity or be inconsistent with other practices; for example, it appears to be out of line with ORD handbook.

Dr. Pullen-Fedinick went on to list a number of additional references that were provided by Panel members for consideration. She concluded that the five preliminary commenters didn't seem to have areas of significant disagreement, and then opened the discussion up to comments from other members of the Panel.

Dr. Chen added that the systematic review process is quite extensive and reasonable. There were some limitations and areas needing improvement. In the existing systematic review, it was difficult to know if the compilation included epidemiological studies, historic studies, etc. Multiple BMDs were given, and a clearer description of the criteria used to weight different studies is needed.

Dr. Post indicated there was some overlap with comments included in the next charge question on noncancer. She noted that the systematic review appears consistent with current EPA methods for developing toxicity values although specifics were not provided about the modifications in the fit for purpose discussion, so further elaboration is needed. She indicated that the MCLG documents should clarify that systematic review was used for identification and inclusion of individual studies, but not for synthesis and calculation of each health effect.

The rationale for not including the human studies from 2016 is not clear and may not be supportable. There is no reason to believe older studies are of lower quality than newer ones. To bolster the overall weight of evidence, it is especially important to use all the relevant data, including human studies, not just a particular study.

Dr. Post indicated that the mechanistic data and the decision process and criteria used by EPA needs to be clearly explained. She provided detailed comments on the Summary tables. She commented that EPA was not clear in a number of areas and provided examples. She also indicated she thought the evidence section is clear and appropriate, however it was not clear in the health effects synthesis and integration sections and the hazard identification sections. She

suggested EPA may not be able to make all changes, so the general approach from draft ORD IRIS handbook should be used, if this is not possible, an explanation must be provided.

Dr. Pullen-Fedinick commented that if an analysis of the overall evidence determination hasn't been completed, then this is troubling especially for the cancer endpoint. A number of Panel members reiterated their confusion about why specific studies are included and others excluded.

Dr. Chiu summarized the concern that studies from the EPA's 2016 assessment were not included for the POD determination. The concern is not that studies were overlooked but that a broader body of evidence should have been considered.

A broader discussion about the exclusion of human studies in the 2016 assessment ensued and Dr. Post noted that this was related to the lack of an available model to estimate an internal dose based on exposure. Panel members also agreed that the time period for the studies being considered should be extended to include those published before 2013 until about 6 months prior to the final assessment. Dr. Chiu and others expressed a concern about the workload involved to include every study in that time frame. Panel members concluded that EPA should focus their efforts on specific studies that are related to the key endpoints.

Dr. Chiu summarized by stating that EPA needs to provide a better transition/synthesis between the 2016 document and current literature search. This should include all studies with more transparent documentation of evidence selection and integration, including a clear separation between the hazard identification portion and the POD derivation. He added that a protocol for selecting and evaluating the studies is needed if a reevaluation were to occur, ideally *a priori*.

Finally, Dr. Chiu asked if any other Panelists wanted to comment or ask questions. None heard.

Dr. Chiu transitioned to the next topic; Noncancer Hazard Identification charge question 1: *Please comment on the health effect/outcome categories identified from the review of the available literature. Do you agree with the strong vs. suggestive evidence designations for the various health outcome categories? Do any other health systems or endpoints need to be considered for POD derivation?*

Dr. Post, lead discussant, summarized areas of agreement and disagreement among Panelists. The Panelists agreed that a strong and transparent rationale regarding conclusions and all aspects of EPA's assessment is critical and should be provided. Additionally, the draft MCLG should include confidence limits. Panelists concluded that the rationale for the POD and a consistent process for deriving the POD should be used across EPA documents. The Panel recognized that there is limited information on health effects, and they suggest EPA that use a weight of evidence approach in the integration and analysis of information. Furthermore, mixtures should be described in greater detail and considered by EPA.

The Panel discussed several additional issues including the need for a consistent approach and terms for conducting synthesis and integration. Several Panelists offered comments regarding whether or not an association between exposure and outcome may be deemed causal for an

observed endpoint noting that the rigor and reproducibility of data are important factors to consider. The Panel appeared to agree that a recommendation to focus on key health outcomes, with specific studies.

Dr Chiu then introduced the next charge question:

*Elevation of liver serum biomarkers in humans is frequently used as an indication of liver injury, although it has not been shown to be as specific as functional tests, such as histology findings and liver disease (Boone, 2005, HERO ID: 782862). However, greater than 2-fold increases in alanine aminotransferase (ALT) activity, the most sensitive test of hepatocellular injury in humans, above the upper limit of normal are considered indicative of hepatocellular injury. EPA concluded that the available data in adults show a consistent positive association between PFOA and/or PFOS exposure and increased serum ALT levels in the epidemiological literature. However, this response was not selected for dose response modeling because 1) the magnitude of the effect was not large compared to control levels, and 2) concerns about the clinical relevance of the findings and non-specificity of the biomarkers relationship to adverse liver injury and disease.*

*Does the SAB Panel agree with EPA's rationale for not considering the ALT endpoint reported in the epidemiological studies for the derivation of a POD for the liver health effects? Please provide your justification and if you suggest that EPA consider this endpoint for POD derivation, please provide your recommendations for a modeling approach.*

- i. Are you aware of additional studies that support the ALT levels as markers of adverse liver effects? Please provide citations.*
- ii. Are there other adverse liver endpoints identified in the epidemiological literature that need to be considered?*

Dr Cory-Slechta was the lead discussant and indicated there were 8 Panel members that provided preliminary comments. She indicated that the Panel did not agree with EPA regarding their rationale for not considering ALT endpoint from epidemiological studies for deriving the POD for liver health effects. She also indicated further information should be added to the discussion of ALT, liver disease, and other endpoints. She commented that several of the endpoints probably deserve greater consideration before being dismissed and cautioned that the magnitude versus severity of effects are different considerations. She added that perhaps considering approaches used by California EPA may be helpful. She then opened the discussion up to other members of the Panel.

Several members supported the EPA approach for selecting endpoints that are more quantifiable with available information. Additional discussion ensued about considerations of clinical endpoints and evaluating other information related to liver damage. The Panel agreed to provide additional references for EPA consideration. The need for additional transparency in the selection of endpoints was also a major focus for Panel members.

Dr. Chiu summarized the discussion stating that the rationale and decision-making process needs to be clearly articulated in the EPA documents. Dr Chiu then proceeded to the next charge question regarding cancer designation:

*A. PFOA: Based on new cancer studies identified since the 2016 PFOA Health Advisory (HA), EPA concludes that the available cancer data for PFOA indicate a 'likely carcinogen' categorization which is a change from 'suggestive' in the 2016 HA. Does the Panel agree with the 'likely' designation based on the new evidence? If yes, is the rationale clearly described? If no, please provide an explanation for arriving at a different conclusion.*

Dr. Lipworth was the lead discussant, and she noted a number of areas of agreement based on the preliminary comments submitted by the Panelists. The Panel agreed, in general, that the evidence for carcinogenicity of PFOA had been strengthened since the 2016 assessment. In addition, EPA provided consistent data and examples and the Panel provided additional information for consideration. The Panel determined that the designation of PFOA is consistent with California EPA conclusions and noted some differences for EPA to explore.

The Panel proceeded to deliberate on the next part of the charge question:

*B. PFOS: Based on a small number of new cancer studies identified since the 2016 PFOS HA, EPA concludes that the available cancer data for PFOS indicate a 'suggestive' categorization which is unchanged from the categorization identified in the 2016 HA. Does the Panel agree that the new studies do not change the designation? If yes, is the rationale clearly described? If no, please provide an explanation for arriving at a different conclusion.*

The Panel discussed the use of a weight-of-evidence approach. Members noted that a meta-analysis using data collected from multiple studies can be conducted rather than relying on the data from a single study. The Panel also suggested that the studies used, and conclusions reached by state regulatory agencies should be considered. The Panel concluded that any decision regarding the cancer designation should be clearly explained. Dr. Chiu declared that a more systematic approach needs to be followed, and more clearly documented.

The Panel recessed for a short break. Dr. Shallal reminded members of the public that if they wish to make comments to please email her during this break.

Dr. Chiu reconvened the meeting after the break at 2:40 Eastern Time. He introduced the next charge question regarding the topic of Cancer Slope Quantification:

*Cancer Slope Quantification: EPA used the Shearer et al., 2021 epidemiological study to quantify a cancer slope factor ~~using peak exposure~~ for PFOA. Has EPA adequately justified the use of this study ~~and peak exposure~~ for the quantification of a cancer slope factor for PFOA? If no, please describe alternate approaches that SAB recommends. Does SAB support the selection of this CSF in the derivation of a risk specific dose for PFOA (i.e., the concentration of PFOA in drinking water that would have a one-in-1-million chance of an increased cancer risk)? If not, please provide input on the strengths and weaknesses of the other candidate CSFs that EPA derived.*

Dr. Kamendulis provided a summary of the preliminary comments submitted in advance of the meeting. In general, the Panel agreed it is preferable to base the CSF derivation on human epidemiological data while acknowledging the lack of "high confidence" data for PFOA. An

extensive discussion about the Shearer *et al.* 2021 study ensued. Additional observations were made regarding consistency overall in epidemiological studies and associations between PFOA and other chemicals. The draft MCLG document did not provide a detailed rationale for choosing the Shearer study as the sole basis for the CSF and one should be provided. The Panel agreed that overall, multiple CSFs should be developed and clearly documented using a wide range of studies and study types. The Panel also discussed the mechanism of action for kidney cancer. Panelists agreed to provide further documentation for consideration by EPA.

The Panel then discussed the next topic- Toxicokinetic Modeling. The Panel offered general comments regarding the lack of transparency in the documentation for the modeling approach as it was difficult to follow in the MCLG documents. A suggestion was made to have EPA put the modeling code in an appendix and to create diagrams that specify the modeling assumptions, workflows, and where modeling fits in the calculations. In addition, estimates and evaluation of model implementation and sensitivity when using different variables is recommended to better gauge performance.

A. The Panel discussed the human toxicokinetic modeling regarding the following charge question: *For endpoints observed in adults, EPA used a steady-state approach to calculate the HED, which assumes a relatively constant exposure and clearance during adulthood. Please comment on this method of HED calculation. Are there alternative approaches that EPA should consider? If so, please describe the rationale for recommending this approach(es).*

B. *Two key parameters are the half-life and volume of distribution, which were used to calculate clearance. Half-life and volume of distribution were assumed to be constant across sex and age groups because of a lack of strong quantitative data to parametrize changes across sex and age. Please comment on the strengths and weakness of the use of this assumption and the choice of these parameters by the EPA. Please describe the rationale for alternative recommended approaches.*

The Panel addressed these questions together agreeing that in general, for adults chronic with exposure, the compartment model for adults (not lactating) is adequate for use in HED determinations. The Panel noted that additional details, specifically items regarding code, parameters, data and performance, are needed. In addition, Panelists stated that the approach appears reasonable but more information on process, application and performance are required. The Panel agreed that compartmental models are reasonable for simulating dosimetry during pregnancy and lactation. However, for the life-stage models, the Panel agreed that EPA should reconsider the Verner model, which assumes a constant dose in mg/kg-d, as to whether it was fit for purpose, and consider other models such as the Goeden model, which includes consideration of life-stage-specific exposure factors in the context of a constant drinking water concentration; additional references were provided by Panel members.

Future considerations should be given to broader more physiologically-based life-stage modeling.

C. The Panel discussed the last part of the question: *The key chemical-specific parameters that describe the transfer of the chemical from the mother to the child during gestation and*



*lactation are the maternal to fetal serum ratio and the ratio of maternal serum to milk PFOA/S concentration. These ratios were assumed to be constant during gestation and lactation, respectively. Another important parameter is the rate of milk ingestion, which is chemical-independent and varies throughout lactation. Please comment on the strengths and weaknesses of the choice of parameters for fetal to maternal partitioning and partitioning into breastmilk, as well as the choice for lactation rate. Please also comment on the choice to assume that fetal to maternal partitioning and partitioning to breastmilk did not vary in time. Please describe whether there are other methods you would recommend to account for these changes over time and across development.*

The Panel agreed that using constant ratios was reasonable given the available data. The Panel went on to discuss the Animal Toxicokinetic Model related questions. The discussion covered all subparts together.

Dr. Fisher led a discussion starting with a review and brief summary of preliminary comments from Panel members regarding the questions about the Animal Toxicokinetic Model. Dr. Slitt noted that the models are probably reasonable and provided some additional details regarding the selection of parameters and other considerations. Other Panelists agreed and indicated that perhaps additional sensitivity analysis may be warranted to evaluate the strength of the modeling results.

The Panel agreed with the selection of Wambaugh model for the calculation of dose metrics and urged EPA to provide a rationale and clearer explanations for model choices. The Panel discussed the pros and cons of the approach EPA (regarding POD from serum plasma) and suggested that data may be available.

The Panel moved on to discuss the charge question about the Epidemiological Study RfD derivation. The question: *EPA evaluated potential confounding as part of their study quality evaluation of the epidemiological studies and selected only 'medium' and 'high' quality studies for POD derivation. Have the epidemiological studies that were selected for dose-response modeling sufficiently addressed confounding? If not, are there key additional analyses that could be performed to further address the potential confounding of PFAS exposures in these studies?*

Dr. Savitz started the discussion regarding the potential for confounding due to the presence of other chemicals, like PFOS or other PFAS and how this may influence the outcomes. Panelists discussed whether cofounders should be considered if they had no impact on the disease outcome. Several examples were presented including caffeine and socioeconomic factors as a common issue of concern.

The Panel was concerned that studies were discounted due to “socioeconomic factors”. Many appeared to be rated low because of this. Specifically, the Panel discussed that drinking water (unlike for other contaminants) contamination of PFAS is not necessarily correlated with socioeconomic status (SES). Panelists concluded that determining whether SES is a potential confounder should be evaluated on a case-by-case basis related to the specific study population. It should not be a “blanket” consideration as a confounder. Panelists added that this decision can be important especially for POD considerations.

The next charge question: *Studies of developmental immune health outcomes (Grandjean et al., 2012 [HERO ID: 1248827]; Grandjean et al. 2017 [HERO ID: 3858518]; Grandjean et al., 2017 [HERO ID: 4239492]; and Budtz-Jorgensen and Grandjean, 2018 [HERO ID: 5083631]) after PFOA/S exposure identified associations with very low doses of either PFOA or PFOS with developmental immune effects. The RfD for this outcome was selected as the critical effect because it was the lowest among the candidate RfDs for PFOA or PFOS and can result in severe illness. Does the Panel agree with the selection of the critical study and critical effect for the derivation of chronic RfDs for PFOA and PFOS?*

- i. If so, please explain your justification.*
- ii. If not, please provide your rationale and detail an alternative critical study and/or critical effect you would select to support the derivation of chronic RfDs.*
- iii. Are any additional analyses or rationales needed to increase the confidence in the chronic RfDs for PFOA and PFOS?*

Overall, the Panel agreed with the selection of the critical study and the use of immune response suppression in children as the biomarker. The Panel stated that candidate RfDs should be developed for other health endpoints consistent with epidemiological studies and animal studies. Furthermore, the Panel determined that a “meta-analysis” approach should be used, or at least considered. The Panel agreed that phrase “short term” should be changed to “short term and chronic” exposure. The Panel concluded that a stronger case should be made by including more studies.

The Panel continued their deliberations. The next question is: *The health outcomes identified in the critical studies were decreased antibody response, specifically in serum anti-tetanus and anti-diphtheria, in children after vaccination (Grandjean et al., 2012 [HERO ID: 1248827]; Grandjean et al. 2017 [HERO ID: 3858518]; Grandjean et al., 2017 [HERO ID: 4239492]; and Budtz-Jorgensen and Grandjean, 2018 [HERO ID: 5083631]). This health outcome represents an increased susceptibility to a disease that can cause very severe symptoms, including lethality. Furthermore, children who are immunocompromised may mount a lower antibody response and in turn, be more susceptible to contracting the disease, if exposed than healthy children. Because this health outcome has the potential for severe illness and was assessed in children (i.e., EPA guidelines [US EPA, 1991] support a 5% BMR for developmental effects), a benchmark response (BMR) of 5% was selected for benchmark dose modeling. While some clinical findings are available, the clinical relevance of a 5% decrease in antibody response is not clear. Given the need to protect sensitive subpopulations (e.g., children, individuals with pre-existing conditions) and the available clinical data (i.e., antibody response clinical level), does the SAB support the 5% BMR selection for modeling to identify the POD? If not, please recommend the BMR level and a scientific rationale for an alternative selection.*

The Panel generally supported the use of a decrease of 5% in the BMR, however they urged the agency to provide a better justification, especially regarding a decreased antibody response versus other health outcomes. A detailed discussion ensued with additional citations from Panel members for inclusion in the document.

The Panel went on to discuss the uncertainty factors in response to the following question:

*EPA has evaluated and applied where appropriate uncertainty factors to account for intraspecies variability (UFH), interspecies differences (UFA), database limitations (UFD), duration (UFS), and LOAEL-to-NOAEL extrapolation (UFL) for PFOA and PFOS.*

*i. Has uncertainty been adequately accounted for in the derivation of the RfDs? Please describe and provide suggestions, if needed.*

*ii. Does the provided scientific rationale support the application of the selected uncertainty factors? Please explain.*

Dr. Pullen-Fedenick summarized the preliminary comments submitted by the Panelists. The Panel agreed that uncertainty factors were appropriate and justified. They stated their concerns regarding the cumulative impacts that were not being considered. The Panel agreed that EPA may not be able to include all stressors in the assessment now and suggested that they do so in the future. The Panel also supported the notion of probabilistic frameworks to characterize the risk. An extensive discussion occurred regarding the use of additional uncertainty factors and alternative approaches without any specific recommendations.

#### Clarifying comments

The meeting then turned to clarifying comments. Dr. Kevin Bromberg was the only public commenter. He asked the Panel to consider public comments regarding the notion that suppression of the immune response should not be considered an adverse outcome. He also urged the Panel to ask EPA to respond to public comments directly and publicly. His comments and all public comments are available on the SAB website.

Dr. Shallal recessed the meeting at 5:37 Eastern time.

### **Friday January 7, 2022**

#### Meeting re-convened (day 4)

Dr. Shallal reconvened the meeting and reminded the panel and members of the public that this was the fourth and final day of deliberations. Dr. Shallal indicated the meeting today is intended to complete the discussion from the previous day and to discuss the *EPA's Analysis of Cardiovascular Disease Risk Reduction as a Result of Reduced PFOA and PFOS Exposure in Drinking Water*.

Dr. Shallal stated that all presentations from EPA, preliminary comments from all Panelists, and all related meeting materials are available on the SAB website ([www.epa.gov/sab](http://www.epa.gov/sab)) associated with this advisory activity.

She explained that the Panel consists of special government employees (SGE) and will abide by all applicable ethics laws and implementing regulations. All Panelists have submitted confidential financial disclosure forms which were reviewed, and it was determined by the

Agency deputy ethics official that no appearance of, nor actual, conflicts of interest relating to this topic were identified for any Panelists. Dr. Shallal reiterated that Dr Kevin Boyle had withdrawn from the Panel due to personal reasons and will no longer be participating in the review.

Before the Panel began their deliberation, there was a short delay to rectify technical issues with the live stream of the proceedings. When these issues were addressed, the Panel began their deliberations.

Dr. Chiu opened the day's deliberations by calling on Dr. Sandeep Burman to present a summary of the response to Charge Question #6.

#### Panel deliberations

The Panel started with charge question 6 on the topic of relative source contributions: *EPA applies a Relative Source Contribution (RSC) when calculating the MCLG to provide a margin of safety that an individual's total exposure from a contaminant does not exceed the RfD. The RSC is the portion of an exposure for an individual in the general U.S. population estimated to equal the RfD that is attributed to drinking water; the remainder of the exposure equal to the RfD is allocated to other potential sources. Based on the physical properties, detected levels, and available exposure information, there are significant potential sources other than drinking water ingestion for PFOA and PFOS; however, information is not available to quantitatively characterize exposure from these different sources. EPA followed Agency guidance on how to derive an RSC (U.S. EPA, 2000; available online at: <https://www.epa.gov/sites/default/files/2018-10/documents/methodology-wqc-protection-hh-2000.pdf>) and recommends an RSC of 20 percent (0.20) for PFOA and PFOS. This RSC is the same as what was used in the 2016 HAs for PFOA and PFOS.*

- i. *Are you aware of additional relevant exposure data that EPA should consider in developing the RSCs for PFOA and PFOS? If so, please provide citations.*
- ii. *Please provide comment on whether the recommended RSC of 20 percent (0.20) for PFOA and PFOS is adequately supported and clearly described.*

Dr. Burman summarized the preliminary comments from a total of 5 Panelists. The Panel, overall, agreed on the recommendation of a RSC of 20% but it was unclear how EPA arrived at this value. The Panel urged EPA to be more explicit in the defining the RSC as stated in the EPA guidance (2000).

Dr. Chiu then opened the discussion to all Panelists to discuss any other relevant issues before concluding the deliberations of the MCLG documents. Panelists were concerned about the RSC being protective for susceptible populations. It was noted that the RSC is not used for this purpose and because the RfD was derived using a health endpoint resulting from exposure to children, it is protective. They also commented that EPA should consider using available data on non-drinking water exposures to PFOA and PFOS to support the choice of an RSC of 20%.

Dr. Chiu then transitioned to the discussion of the final document: *EPA's Analysis of Cardiovascular Disease Risk Reduction as a Result of Reduced PFOA and PFOS Exposure in Drinking Water*. He called on Morgan McCabe to present an overview of the document.

### EPA presentation

Morgan McCabe reviewed the intended timeline for completing the analysis. EPA are currently looking at all the endpoints identified, beyond CVD, in the MCLG documents to determine if any are amenable to quantification. She also noted that EPA was interested in the Panel's recommendations regarding other endpoints that may be amenable to a benefits calculation.

### Panel Discussion

*Overall Charge Question- EPA is seeking SAB evaluation on the extent to which the approach to estimating reductions in CVD risk associated with reductions in exposure to PFOA and PFOS in drinking water is scientifically supported and clearly described.*

#### **Charge Question #1- EPA's Meta-Analysis**

*Section 4.2 presents EPA's meta-analysis for the total cholesterol dose-response function.*

- i. *Please provide specific feedback on the extent to which the study selection criteria, the identified studies, and the methodological approach of the meta-analysis are complete and capture up to date scientific literature.*
- ii. *To inform the CVD risk reduction analysis for those ages 40-89 using the ASCVD risk model, EPA used a meta-analysis approach for the total cholesterol dose-response function. Please provide specific feedback on the extent to which this approach is reasonable for this application, or whether using a single dose-response study (e.g. Dong et al., 2019) selected in the analysis of cholesterol impacts in the "Proposed Approaches for Deriving Maximum Contaminant Level Goals for PFOA and PFOS in Drinking Water" would add additional strengths for the CVD risk reduction application.*

Dr. Savitz presented a summary of the comments from panel members. He noted panelists agreed that EPA should provide a clearer rationale and list the main assumptions at the outset before launching into the considerable detail that follows. The Panel recommends more discussion as to the rationale for selecting CVD for risk reduction analysis as well as considering risk reduction analyses for other endpoints. The Panel concluded that EPA should strengthen the hazard conclusion with respect to PFOA or PFOS, identify dose-response data from which to derive a dose-response function or risk-specific dose estimates, strengthen the justification and linkage between changes in biomarkers to changes in morbidity or mortality, and identify data for monetizing benefits.

The Panel stated that performing a sensitivity analysis may strengthen and provide justification for EPA conclusions. The Panel noted that the apparent discrepancy between the CVD document focus on CVD risk, and the draft MCLG documents' conclusions that the evidence of CVD was not sufficient to form the basis of a RfD was confusing. The Panel agreed that EPA should list the studies that were excluded from the meta-analysis and provide a brief description of these studies and why each was excluded.

After the discussion concluded, Dr. Chiu called on Dr. Lala Ma to provide a summary of the comments on Charge Question #2.

#### **Charge Question #2- EPA's Life Table Approach**

*Section 5.1 presents EPA's life table approach methodology.*

- i. *Please comment on the extent to which this analysis is scientifically supported and clearly described. To the extent improvements are suggested, please provide specific changes that are implementable in a U.S. national-level benefits analysis with readily available data.*

Dr. Lala Ma was the lead discussant and she summarized that in general the approach was appropriate and well described. Table 3 was found to be hard to follow. The Panel stated that EPA should describe how the current application of the life table methodology differs in the use of prevalence statistics and other key input data and assumptions from prior applications. The Panel noted that assumptions and modeling decisions in the proposed methodology, that may affect the estimates of the mortality/morbidity impact should be clearly listed. Some suggested modifications to clarify and strengthen the discussion.

Dr. Chiu summarized the discussion noting that the Panel concluded that more description is needed to understand how this approach was consistent with or deviated from previous analyses. Also, additional details on the underlying assumptions and associated uncertainties along with sensitivity analyses that can demonstrate their impact should be provided.

He then asked Dr. James Hammitt to summarize the comments from Panel member on Charge Question #3.

#### Charge Question #3- ASCVD Risk Model

*Section 5.2 presents EPA's application of the atherosclerotic cardiovascular disease (ASCVD) risk model used to estimate the probability of hard CVD events corresponding to total cholesterol changes.*

- i. *Please comment on the scientific validity of the ASCVD model application for estimating the probability of first time CVD events in various sub-populations and the extent to which it is clearly described.*
- ii. *Please comment on whether EPA's approach and assumption of a uniform first CVD event hazard distribution over the 10-year period is sufficiently robust given current data sources and literature. If additional distributional sources of information are suggested, please provide specific citations/sources for EPA's consideration.*
- iii. *Please comment on the scientific validity of using the ASCVD risk model for estimating reduced CVD risk stemming from changes in total cholesterol in response to reducing exposure to PFOA and PFOS in drinking water.*

The ASCVD pooled cohort equation (PCE) risk model is a scientifically valid approach to estimating the probability of first CVD events. A limitation is that it is estimated only for non-Hispanic white and Black populations. The accuracy of the ASCVD model seems modest, even for the populations for which it is estimated. Further discussion of the accuracy of the model predictions in sub-groups with varying levels of social deprivation is needed. The Panel noted that EPA should evaluate whether inclusion of HDL would influence the results of the modeling.

The Panel agreed that EPA's approach and assumption of a uniform first CVD event hazard distribution over the 10-year period is sufficiently robust given current data sources and literature.

Dr. Chiu then called on Dr. Sheila Olmstead to lead the discussion for Charge Question #4

Charge Question #4- Limitations and Uncertainties

*Section 7 and Appendix A describe the limitations and uncertainties of the CVD risk reduction analysis. Has EPA clearly described the individual contributions of the sources of uncertainty?*

The modeled uncertainties are clearly presented; however, Table 7 of unmodeled sources of uncertainty needs to be clearer to provide more useful information. Providing the most important sources would be helpful. Quantified uncertainty about the slope of the relationships between TC and either PFOA or PFOS should be clarified and should account for the sensitivity of the meta-analysis results to restrictions on the functional form of the included estimates.

Panelists also noted that EPA has not described ways they intend to reduce some of the uncertainties described in the document. Overall, panelists observed that, in general, all assumptions need to be clarified in EPA's documents and the justification for each assumption be included.

The Panel noted that more information was needed on other endpoints that can be quantified and potentially monetized. Beyond CVD, are there other monetizable endpoints like, decreased antibody response, liver disease, cancer, etc.? The Panel noted the importance of the decreased antibody response and the need for a more robust discussion of this adverse health effect in the document.

A panelist had a related comment about the health effects selected for calculating benefits resulting from reduced exposures. She noted that some endpoints may be more valid when considering epidemiological evidence in humans. Dr. Chiu concurred and added that the four outcomes considered by EPA are biomarkers, and not overt disease. Panelists then discussed other studies, health endpoints, biomarkers and indicators for consideration to substantiate hazard concerns and may also be amenable for a benefits assessment. Panel members agreed to provide additional studies and references for inclusion along these lines.

Clarifying comments

No additional clarifying comments from EPA or the Public were provided.

Dr. Chiu invited Panel members to discuss any other issues regarding the four EPA documents under review.

Dr. DeWitt stated she had sent a citation for a study discussing a 5% BMD for immune response.

Dr. Slitt mentioned that her review of the public comments prompted her to urge more clarity regarding the various health effects using a weight of evidence approach. She urged an agnostic process be implemented at the beginning by considering all studies and then deciding which to include, or exclude.

Dr. Chiu asked Dr. Shallal to explain the next steps. First, she noted that earlier there were technical difficulties in starting the live stream but that no deliberations were missed by the public, only introductory comments from the DFO.

She then discussed next steps and timing for the development of a consensus report from the Panel. A tentative timeline was shared with the Panel. This included the due dates for revised preliminary comments, for draft responses developed by lead discussants and the anticipated reconvening of the Panel to discuss a draft report in late April or early May 2022.

Panel members asked for the dates when documents were due. She provided this information and noted that she would follow-up with this information in an email. Panel members had no additional clarifying questions or comments.

Meeting adjourned

Dr Shallal adjourned the deliberations at 1:37 PM Eastern Time.

**Respectfully Submitted and Certified as Accurate,**

\_\_\_\_\_/s/  
Suhair Shallal, PhD  
DFO

\_\_\_\_\_/s/  
Weihsueh Chiu, PhD  
PFAS Review Panel, Chair

Date: April 5, 2022

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 to not rely on the minutes to represent final, approved, consensus advice and recommendations offered to the Agency. Such advice and recommendations may be found in the final advisories, commentaries, letters, or reports prepared and transmitted to the EPA Administrator following the public meetings.



**Attachment A: Additional meeting participants in attendance or who requested the teleconference call-in number**

	NAME	AFFILIATION
1.	Eric Burneson	US EPA
2.	Justin Conley	US EPA
3.	Colleen Flaherty	US EPA
4.	Moran McCabe	US EPA
5.	Brittany Jacobs	US EPA
6.	Thomas Brennan	US EPA
7.	Bryan Bloomer	US EPA
8.	Carolyn Kilgore	US EPA
9.	Brian Chalfant	Pennsylvania Department of Environmental Protection
10.	Lindsey Jones	Georgia-Pacific
11.	Patsy Root	None
12.	Eugene Sekiguchi	ADM
13.	Kim Nimmer	North Carolina Department of Environmental Quality
14.	Bill Keegan	None
15.	Kathryn Lynnes	U.S. Air Force
16.	Shannon Garcia	Air Force Civil Engineer Center
17.	Hilda Arellano	None
18.	Astrika Adams	SBA Office of Advocacy
19.	Tim Cansler	Cansler Consulting, LLC
20.	Michael Dobbs	Bayer
21.	Daniel Grapski	ExxonMobil
22.	Dawn Clark	Chemours
23.	Theresa M Spalletta	Water Industry
24.	Jordan B Kari	None
25.	Sam Insalaco	Arcadis
26.	Scott Kuhn	Savannah River Nuclear Solutions
27.	Gary Minsavage	ExxonMobil
28.	Nicole Shao	US EPA-ORD
29.	Bharat Chandramouli	SGS
30.	Joseph Haney	Texas Commission on Environmental Quality
31.	Kim Harris	US EPA-Region 5
32.	Lauren Weinrich	American Water
33.	Angela Perez	CTEH
34.	Esther Haugabrooks	None
35.	Zijin Guo	DAIKIN INDUSTRIES, LTD.
36.	Carl Utterback	North Carolina Department of Environmental Quality
37.	Emily Rimmel	NACWA
38.	Patrick Dube	Water Environment Federation

39.	Zach Paden	Oklahoma Department of Environmental Quality
40.	Kari Meier	DoD
41.	Natalia Vinas	DoD
42.	Elizabeth Radke	US EPA
43.	Jennifer McMullin	City of Corona
44.	Heather Lynch	Cardno ChemRisk
45.	Julie Burdey	Parsons
46.	Todd Belanger	Parsons
47.	Jaana Pietari	Ramboll
48.	Loren Lund	Jacobs
49.	Barbara Morrissey	Washington State Department of Health
50.	Kristy Richardson	CDPHE
51.	Ashley E Peppriell	ICF
52.	Jessica Vitale	Missouri Department of Natural Resources
53.	Michelle Montoya	Environmental Protection Network
54.	Dwight Flammia	Virginia Department of Health
55.	Seung-Hyun Cho	RTI International
56.	Matt Klasen	U.S. EPA
57.	Eduardo Gasca	None
58.	Maile Lono-Batura	Water Environment Federation
59.	Harrison Rennie	None
60.	Thomas B Johnson	New York State Department of Health
61.	Kaycee Cole	New York State Department of Health
62.	Cassie Berluti	New York State Department of Health
63.	Mackenzie Dalton Webber	Cadmus Group
64.	Kelly Garcia	NC DHHS
65.	Steve Risotto	American Chemistry Council
66.	John Healey	US EPA Office of Water
67.	Alex Lan	US EPA
68.	Gregory Miller	US EPA
69.	Anna Belova	ICF
70.	Rachel Gonsenhauser	US EPA
71.	Amy Delinsky	NCDEQ
72.	Tami Thomas-Burton	EPA-R4
73.	Doug Cox	Sundance Consulting Inc
74.	Deirdre White	Association of State Drinking Water Administrators
75.	Chris McMeen	Confluence Engineering
76.	Kathleen Baskin	MA Department of Environmental Protection
77.	Santhini Ramasamy	US EPA
78.	Peter D'Adamo	HDR
79.	Jennifer Sass	NRDC
80.	Alison Cullity	
81.	Bina Nayak	Pinellas County Utilities
82.	Brent Milliron	Carolina Water Service Inc of North Carolina
83.	Alan Roberson	ASDWA

84.	Stacey H	NDDEQ
85.	Michele Duggan	Pinellas County (FL) Utilities
86.	Dr. David D. Dow	None
87.	Elizabeth Behl	US EPA
88.	Anita Meyer	Army Corps Engineers
89.	Steve Via	AWWA
90.	Viktor Morozov	US EPA
91.	Gregory Garvey	GSI Environmental
92.	Keith Petka	American Petroleum Institute
93.	Jennifer Corack	Navy
94.	Kevin L Bromberg	Bromberg Regulatory Strategy, LLC
95.	Amaran Toppa	CMBG3 Law LLC
96.	John Gardella	CMBG3 Law LLC
97.	Mark Lafranconi	Environmental Resources Management
98.	Norka Paden	IDEQ
99.	Vicki Soto	US EPA/ORD/CPHEA
100.	April Kluever	OMB
101.	Rosalind Schoof	Ramboll
102.	Jeffery Sepesi	Environmental Law and Science, PLLC
103.	Mike Wright	US EPA
104.	Andrew Kraft	US EPA
105.	Laura C Green	Green Toxicology LLC
106.	John Wathen	US EPA OW
107.	Denise Keehner	Maryland Department of the Environment
108.	Pat Rizzuto	Bloomberg Environment
109.	Annie Snider	Politico
110.	Sharon Browning	Pima County Health Department
111.	Chris McMeen	Technical Service Provider
112.	Christopher Hill	AECOM
113.	Helen Goeden	MN Dept of Health
114.	Brian Pachkowski	NJDEP
115.	Lara Beaven	Inside EPA
116.	Brent Weis	Missouri DNR
117.	William Kim	None
118.	Kelsey Hendrixson	Noblis
119.	Catherine Vogel	Noblis
120.	Barry Marcel	United States Air Force
121.	Andrew Pawlisz	Trihydro
122.	Mary Butow	NH Department of Environmental Services
123.	Mark Mank	MDE
124.	Rachel Passaretti-Wu	none
125.	James Jeffrey Pletl	HRSD
126.	Bhavita Patel	US EPA R1
127.	Marie Lewis	Cadmus Group (EPA Contract Support)
128.	Susan Burden	US EPA

129.	Dana Alexandra Sargent	Cape Fear River Watch
130.	Shawn Gannon	Chemours
131.	Anita Meyer	US Army Corps Engr
132.	Katie Pelch	None
133.	Cheryl Fields	State of Connecticut Dept of Public Health
134.	Ben Montross	State of Vermont
135.	Deborah Barsotti	Triumverate Environmental
136.	Thomas B Johnson	New York State Department of Health
137.	Erick Orellana	Community Water Center
138.	Mingzhu Fang	NJDEP
139.	Kevin Carter	Broward County
140.	Connor McFayden	Nebraska Department of Environment and Energy
141.	Randy Lee	Inland Empire Utilities Agency
142.	Christina Davis	Interstate Commission on the Potomac River Basin
143.	Deborah Barsotti	Toxicologist
144.	MG	None
145.	Sarah Holt	None
146.	Giffe Johnson, PhD	NCASI
147.	Jamie Strong	US EPA ORD
148.	Janelle Wilbur	State of Vermont - DWGPD
149.	Anna Belova	ICF
150.	Mark Navarre	OHIO AGO
151.	Ellen Egen	AquaLaw
152.	Jacob Adler	Association of Clean Water Administrators
153.	Maureen C Leahy	ERM
154.	Viraj deSilva, PhD. PE, BCEE	Freese & Nichols
155.	Sarah Phillips	None
156.	Lori Blair	None
157.	Alison Cullen	Univ of Washington
158.	David Lipsky	NYCDEP
159.	Doug Brune	US EPA Region 7
160.	Nancy Yanochik	Kelley Drye
161.	Kathryn Kelly	Delta Toxicology
162.	John Backus	MD Dept of Environment
163.	Christina Piccirillo	NYSDOH
164.	Janet Anderson	GSI Environmental Inc
165.	Will Reynolds	Idaho State Government
166.	Loren Lund	Jacobs
167.	Jamin Dowdy	Steptoe & Johnson LLP
168.	Lara Beaven	Inside EPA
169.	Geary Olsen	3M
170.	Deborah Barsotti	none
171.	Abby Ulmer	Cadmus Group
172.	Mingzhu Fang	NJDEP
173.	Jane Ellen Simmons	US EPA

174.	Joseph Haney	TCEQ
175.	Bernard Gadagbui	TERA
176.	Nancy Beck	Hunton AK
177.	Steve Via	AWWA
178.	Caitlin Berretta	Evoqua Water Technologies
179.	Rosalind Schoof	Ramboll
180.	Cheryl Fields	Connecticut Dept of Public health
181.	Kevin L Bromberg	BRS
182.	Steve Risotto	American Chemistry Council
183.	Tiffany Bredfeldt	Texas Commission on Environmental Quality
184.	Mark Lafranconi	ERM
185.	Lindsey Zehr	NYSDOH
186.	Ashley Allen	US EPA
187.	Linda Birnbaum	Duke University
188.	Michele Duggan	Pinellas County Utilities
189.	Christine DeRieux	Cadmus Group
190.	June Weintraub	SFDPH
191.	Lindsay MI Boone	Enthalpy Analytical
192.	Jennifer Corack	US Navy
193.	Bobby Magill	Bloomberg Law
194.	Rachel Gonsenhauser	US EPA
195.	Anita Meyer	Army Corps of Engineers

## Materials Cited:

The following meeting materials are available on the SAB website (<http://www.epa.gov/sab>) at the page for the December 16, 2021 to January 7, 2022 meeting.

[https://sab.epa.gov/ords/sab/f?p=100:19:15942721305970:::RP,19:P19\\_ID:963](https://sab.epa.gov/ords/sab/f?p=100:19:15942721305970:::RP,19:P19_ID:963)

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<sup>i</sup> Roster

<sup>ii</sup> Agenda

<sup>iii</sup> EPA Presentation - *Proposed Approaches to the Derivation of a draft Maximum Contaminant Level Goal for PFOA in Drinking Water and Proposed Approaches to the Derivation of a Maximum Contaminant Level Goal for PFOS in Drinking Water*

<sup>iv</sup> EPA Presentation - *draft Framework for Estimating Noncancer Health Risks Associated with Mixtures of PFAS*

<sup>v</sup> EPA Presentation - *EPA's Analysis of Cardiovascular Disease Risk Reduction as a Result of Reduced PFOA and PFOS Exposure in Drinking Water*

<sup>vi</sup> Preliminary Comments from Panel

<sup>vii</sup> Public comments