

U.S. ENVIRONMENTAL PROTECTION AGENCY (EPA)

TOXIC SUBSTANCES CONTROL ACT (TSCA)

SCIENTIFIC ADVISORY COMMITTEE on CHEMICALS

(SACC)

VIRTUAL PUBLIC MEETING

DRAFT RISK EVALUATION FOR Perchloroethylene

#

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(Perchloroethylene)

TSCA SACC WEBSITE <http://www.epa.gov/tsca-peer-review>

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1 **MS. SARA WILSON:** Hello and thank you for joining
2 the meeting today. We are going to give people a couple more minutes to log in,
3 and then we will begin. Well, good morning, everyone. Welcome to this
4 meeting on the U.S. EPA Peer Review of the Draft Risk Evaluation for
5 Perchloroethylene. Battelle is an EPA contractor providing meeting support for
6 this series. This event is being recorded. Please be aware that the host may use
7 Webex chat to share announcements with all attendees, but attendees will not be
8 able to respond to the chat. I will now introduce Tamue Gibson, the Designated
9 Federal Official.

10
11 **OPENING OF MEETING**

12
13 **MS. TAMUE GIBSON:** Thank you. Thank you and
14 welcome. I am Tamue Gibson, and I will be serving as the Designated Federal
15 Official, the DFO, to the U.S. EPA Toxic Substance Control Act Science
16 Advisory Committee on Chemicals, TSCA SACC, for this meeting session. I
17 want to thank Dr. Portier for agreeing to serve as chair of the SACC for this
18 meeting.

19 I also want to thank the members of the Committee, the ad
20 hoc peer reviewers, and the public for attending this important meeting. We
21 appreciate the time and effort of the peer reviewers in preparing for this meeting,
22 taking in account to your business schedule. In addition, I want to thank EPA's
23 Office of Pollution Prevention and Toxics and my colleagues on the TSCA

1 SACC staff for their very hard work in preparing for this important review of
2 EPA's draft risk evaluation for Perchloroethylene.

3 As an added note, Dr. Todd Peterson, my colleague and
4 DFO, is on the line this week and will serve as my backup to my role as DFO.
5 Steven Knott is our Executive Secretary for TSCA SACC, and Dr. Hayley
6 Hughes is our office director. Today through Friday the SACC peer review will
7 focus on Perchloroethylene. To note, this is a virtual meeting, meaning that
8 audio is provided by telephone or over your computer and that graphics are
9 presented by the Webex online internet platform. If for any reason the Webex
10 platform or audio transmission encounters any technical difficulties, you will
11 find additional information to refer to our website, which is [www.epa.gov/tsc-](http://www.epa.gov/tsc-peer-review)
12 [peer-review](http://www.epa.gov/tsc-peer-review).

13 By way of background, the TSCA SACC is a federal
14 advisory committee that provides independent scientific peer review and advice
15 to the EPA on chemical related issues regarding impact of proposed regulatory
16 actions on human health and the environment. The TSCA SACC only provides
17 advice and recommendations to EPA. Decision making and implementation
18 authority remains with the Agency.

19 For the present meeting, there are 12 ad hoc peer
20 reviewers, and 16 of the 19 established SACC members are contributing to the
21 peer review of Perchloroethylene. As the DFO for this meeting, I serve as a
22 liaison between the TSCA SACC and the Agency. I am responsible for ensuring
23 provisions of the Federal Advisory Committee Act, FACA, are met. TSCA
24 SACC meetings are subject to all FACA requirements. This includes open

1 meetings, timely public notice of meetings, and document availability. Note,
2 documents for this meeting are located at the public docket at
3 www.regulations.gov. And of course, the docket ID number is EPA-HQ-OPPT-
4 2019-0502.

5 As the designated federal official for this meeting, a
6 critical responsibility is to work with appropriate Agency officials to ensure that
7 all appropriate ethics regulations are satisfied. In that capacity, Committee
8 members are receiving training on provisions of the federal conflict of interest
9 law. In addition, each participant has filed a standard government financial
10 disclosure report. Our deputy ethics official for the Office of Science
11 Coordination and Policy and in consultation with the Office of General Counsel
12 have reviewed these reports to ensure that all ethics requirements are met.

13 For the next four days, we have a very full agenda, and
14 meeting times are approximate. Thus, we may not keep to exact times as noted
15 due to Committee discussions and public comments. We do strive to ensure
16 adequate time for Agency presentations, public comments, and Committee
17 deliberations. We may, however, take a little extra time at various points in the
18 meeting to help with coordination and, thus, work step by step through the
19 agenda.

20 For presenters, Committee members, and public
21 commenters, please identify yourselves and speak into the telephone. This
22 meeting is being webcasted, transcribed, and recorded. One additional note, we
23 do highly recommend use of a landline for those who are speaking as a
24 Committee member, oral commenter, or Agency OPPT representative.

1 Copies of all EPA presentation materials and written
2 public comments are available in the public docket at regulations.gov. Copies of
3 presentation materials submitted this week by public commenters will be
4 available in the public docket within the next week. Members of the committee
5 are encouraged to fully consider all written and all public comments submitted
6 for this meeting. For members of the public that have not preregistered for
7 public oral comments, please notify either myself or another member of the
8 TSCA SACC staff if you're interested in making a comment. As noted before,
9 at this time the agenda is full. However, as we move through the proceedings, if
10 time allows we may be able to accommodate additional brief comments of five
11 minutes or less.

12 As I mentioned previously, there is a public docket for this
13 meeting. All background materials, questions posed to the Committee by the
14 Agency, and other documents related to this meeting are available in the docket.
15 Some documents are also available on the EPA SACC website. Please note that
16 the docket number and websites are noted on the meeting agenda.

17 For members of the press, EPA media relations staff are
18 available to answer your questions about this meeting. Please address all your
19 questions to Ken Labbe. His email address is Labbe, L-A-B-B-E.Ken, K-E-N,
20 @epa.gov.

21 At the conclusion of this meeting, the TSCA SACC will
22 prepare a report as a response to questions posed by the Agency, the background
23 materials, presentations, and public comments. This final report also serves as

1 meeting minutes. We anticipate the final report and meeting minutes will be
2 completed in approximately 60 days after the meeting.

3 Again, I would also like to say for anyone just joining us
4 this is a virtual meeting, meaning that audio is provided by telephone or over
5 your computer and that graphics are presented by the Webex online internet
6 platform. If for any reason the Webex platform or audio transmission encounters
7 any technical difficulties, you will find additional information to refer to at our
8 website at epa.gov/tsca-peer-review. And in closing, I would like to thank the
9 Committee for their participation. I now turn the meeting over to our esteemed
10 chair, Dr. Portier.

11
12 **INTRODUCTION AND IDENTIFICATION OF COMMITTEE**
13 **MEMBERS**

14 **DR. KENNETH PORTIER:** Good morning and thank
15 you, Tamue, and thank you to the Committee and EPA staff who are
16 participating and viewing today's meeting and to the general public. This is the
17 TSCA Science Advisory Committee on Chemicals' review of the draft risk
18 evaluation for Perchloroethylene, which will be referred to as PERC. At this
19 point, I'd like to introduce the members of the committee. I'll start with myself.
20 I'm Ken Portier, retired biostatistician with 40 years' experience in agriculture,
21 environmental, and public healthy areas. And I'll be chairing this week's
22 meeting. At this point, I'll call the role of the charter committee and ask them to
23 identify themselves and their expertise starting with Dr. Henry Anderson.
24

1 **DR. HENRY ANDERSON:** Hello, I'm Henry Anderson.
2 I'm a physician specializing in occupational environmental medicine and
3 epidemiology. I'm a former state health officer for the Wisconsin Department of
4 Health Services as well as now nearly 40 years as a state epidemiologist for
5 occupational and environmental health.

6 **DR. KENNETH PORTIER:** Thank you. Dr. Charles
7 Barton.

8 **DR. CHARLES BARTON:** Hello, I'm an independent
9 consultant in toxicology. And my education was in toxicology. I'm board
10 certified in toxicology. My expertise is toxicology and risk assessment. Thank
11 you.

12 **DR. KENNETH PORTIER:** Thank you. Dr. Steven
13 Bennett.

14 **DR. STEVEN BENNETT:** Good morning. I'm
15 currently working for the Household and Commercial Products Association. I'm
16 a chemist by training, and I bring expertise to consumer use and exposure to the
17 panel.

18 **DR. KENNETH PORTIER:** Thank you. Dr. Sheri
19 Blystone.

20 **DR. SHERI BLYSTONE:** Good morning. I am also a
21 chemist by training, working for over 20 years as product safety and compliance
22 professional in the chemical industry, currently with SNF Holding Company.

23 **DR. KENNETH PORTIER:** Thank you. Dr. James
24 Bruckner.

1 **DR. JAMES BRUCKNER:** Jim Bruckner, professor
2 emeritus from University of Georgia. Expertise is in pharmacokinetics and
3 toxicology, particularly focusing on volatile organic compounds like
4 Perchloroethylene.

5 **DR. KENNETH PORTIER:** Thank you. Dr. Deborah
6 Cory-Slechta. Deb, you're muted in Webex. We'll come back to her. Dr. Holly
7 Davies.

8 **DR. HOLLY DAVIES:** Hi, this is Holly Davies. I'm a
9 toxicologist at the Washington State Department of Health. My background is in
10 reproduction and development and experience with exposure to people from
11 products.

12 **DR. KENNETH PORTIER:** Thank you. Dr. Cory-
13 Slechta.

14 **DR. DEBORAH CORY-SLECHTA:** Yeah. This is
15 Deborah Cory-Slechta from the University of Rochester Medical Center. My
16 area of expertise is neurotoxicology.

17 **DR. KENNETH PORTIER:** Thank you. Dr. William
18 Doucette.

19 **DR. WILLIAM DOUCETTE:** Good morning. This is
20 Bill Doucette. I'm an environmental chemist and professor at Utah State
21 University.

22 **DR. KENNETH PORTIER:** Thank you. Dr. Kathleen
23 Gilbert.

1 **DR. KATHLEEN GILBERT:** Hello, this is Kate
2 Gilbert. I'm a retired medical school professor, and my expertise is in
3 immunotoxicology.

4 **DR. KENNETH PORTIER:** Thank you. Dr. Mark
5 Johnson.

6 **DR. MARK JOHNSON:** Hi, I'm Mark Johnson. I'm
7 Director for Toxicology at the Army's Public Health Center, and I have
8 experience in environmental toxicology and risk assessment for the last 25 years.

9 **DR. KENNETH PORTIER:** Thank you. Dr. Alan
10 Kaufman.

11 **MR. ALAN KAUFMAN:** Hi, this is Al Kaufman. I am
12 currently Senior Vice President Technical Affairs for the Toy Association,
13 biologist by training, and primary expertise is in downstream uses,
14 manufacturing processes, and consumer uses and exposure.

15 **DR. KENNETH PORTIER:** Thanks, Al. And Dr. John
16 Kissel.

17 **DR. JOHN KISSEL:** I'm John Kissel. I am professor
18 emeritus of environmental and occupational health sciences at the University of
19 Washington in Seattle. I'm an environmental engineer by training and a human
20 exposure scientist by practice.

21 **DR. KENNETH PORTIER:** Thank you. Dr. Craig
22 Rowlands. Craig, you're muted in Webex.

23 **DR. CRAIG ROWLANDS:** -- there now?

1 **DR. KENNETH PORTIER:** We'll come back to Craig.

2 Ms. Ruthann Rudel. Oh, Craig? Hello?

3 **DR. CRAIG ROWLANDS:** Okay. Sorry about that.

4 This is Craig Rowlands.

5 **DR. KENNETH PORTIER:** Oh, okay, Craig.

6 **DR. CRAIG ROWLANDS:** Do you want me to go
7 ahead? Okay. This is Craig Rowlands, the senior toxicologist at --

8 **DR. KENNETH PORTIER:** Go ahead and introduce
9 yourself.

10 **DR. CRAIG ROWLANDS:** I'm Craig Rowlands, Senior
11 Toxicologist with Underwriters Laboratories. Background is in main toxicology,
12 chemical mode of action, and chemical carcinogens.

13 **DR. KENNETH PORTIER:** Thank you, Craig. Ms.
14 Ruthann Rudel.

15 **MS. RUTHANN RUDEL:** Hi, my name is Ruthann
16 Rudel. I'm the research director at Silent Spring Institute, which is an
17 independent research institute working to understand environmental exposures
18 that affect women's health and identify opportunities for prevention. I have 30
19 years of experience as a chemist in toxicology and risk assessment and exposure
20 assessment. My expertise is in carcinogenesis and endocrine disruption.

21 **DR. KENNETH PORTIER:** Thank you. Dr. Dan
22 Schlenk.

1 **DR. DANIEL SCHLENK:** Good morning. This is Dan
2 Schlenk. I'm a professor of aquatic ecotoxicology in the Department of
3 Environmental Science at University of California Riverside.

4 **DR. KENNETH PORTIER:** Thank you. That's the --
5 those were the charter members of the SACC and now ad hoc members that
6 we've invited to add their expertise to the committee. Dr. Udayan Apte.

7 **DR. UDAYAN APTE:** Hi, I'm Udayan Apte. I'm an
8 associate professor of pharmacology, toxicology, and therapeutics at the
9 University of Kansas Medical Center. My expertise is in general toxicology,
10 specifically liver, hepatotoxicity and chemical carcinogenesis. I'm also a board-
11 certified toxicologist.

12 **DR. KENNETH PORTIER:** Thank you. Dr. George
13 Cobb. George, your phone might be muted.

14 **DR. GEORGE COBB:** I'm muted. I'm unmuted now?
15 Am I unmuted now?

16 **DR. KENNETH PORTIER:** Yes. Proceed.

17 **DR. GEORGE COBB:** So hi. I'm George Cobb. I'm a
18 professor of environmental science at Baylor University. I'm a chemist by
19 training in environmental and analytical chemistry and have experience in
20 exposure assessment as part of broader risk assessment.

21 **DR. KENNETH PORTIER:** Thank you, George. Dr.
22 Michael Daniels.

1 **DR. MICHAEL DANIELS:** Yeah. This is Mike
2 Daniels. I'm a professor and chair in the Department of Statistics at the
3 University of Florida. And my expertise is in statistical modeling.

4 **DR. KENNETH PORTIER:** Thank you. Dr. Stephen
5 Grant.

6 **DR. STEPHEN GRANT:** Hi, this is Steve Grant. I'm a
7 professor of public health at the Nova Southeastern University in Fort
8 Lauderdale. I'm a geneticist and toxicologist, and my expertise is largely in
9 environmental carcinogenesis.

10 **DR. KENNETH PORTIER:** Thank you. Dr.
11 Muhammad Hossain.

12 **DR. MUHAMMAD HOSSAIN:** Hi, good morning. I'm
13 Muhammad Hossain. I'm an assistant professor in the Department of
14 Environmental Health Sciences at Robert Stempel College of Public Health at
15 Florida International University. By training, I'm a veterinarian, and my
16 expertise are in pharmacology and molecular neuroscience.

17 **DR. KENNETH PORTIER:** Thank you. Dr. Zhoumeng
18 Lin.

19 **DR. ZHOUMENG LIN:** Hello. My name is Zhoumeng
20 Lin. I'm an assistant professor of toxicology at Kansas State University. My
21 expertise is in neurodevelopment and the application of pharmacokinetic models
22 for risk assessment. I received my PhD in toxicology from University of Serbia.
23 Now, I'm a certified toxicologist by American Board of Toxicology. I'm also

1 certified in public health by National Board of Public Health Examiners. Thank
2 you.

3 **DR. KENNETH PORTIER:** Thank you. Jaymie
4 Meliker. Dr. Meliker, you're muted in Webex.

5 **DR. JAYMIE MELIKER:** Got it. Can you hear me
6 now?

7 **DR. KENNETH PORTIER:** Yes. Proceed.

8 **DR. JAYMIE MELIKER:** Okay. So I'm Jaymie
9 Meliker. I'm a professor of public health and family population and preventative
10 medicine at Stony Brook University. And my expertise is in human exposure
11 assessment and environmental epidemiology.

12 **DR. KENNETH PORTIER:** Thank you. Dr. Michael
13 Pennell.

14 **DR. MICHAEL PENNELL:** Hi, I'm Mike Pennell. I'm
15 an associate professor of biostatistics at College of Public Health at the Ohio
16 State University. My expertise is in invasion methods and tox risk assessment.

17 **DR. KENNETH PORTIER:** Thank you. Dr. Katherine
18 Roby.

19 **DR. KATHERINE ROBY:** Good morning. This is
20 Kathy Roby. I'm at the University of Kansas Medical Center in Departments of
21 Anatomy and Cell Biology and Obstetrics and Gynecology. And my expertise is
22 fertility, infertility, and environmental impacts.

23 **DR. KENNETH PORTIER:** Thank you. Dr. Charles
24 Vorhees.

1 **DR. CHARLES VORHEES:** Hi, this is Chip Vorhees.
2 I'm professor at the University of Cincinnati in the Department of Pediatrics and
3 at Children's Hospital in the division of neurology. My training is in
4 neuroscience and neurotoxicology. Thank you.

5 **DR. KENNETH PORTIER:** Thank you and at least last
6 on my list, but not least, Dr. Calvin Willhite. Calvin?

7 **DR. CALVIN WILLHITE:** Good morning, Dr. Portier.
8 You can hear me, I assume?

9 **DR. KENNETH PORTIER:** Yes. We can hear you just
10 fine.

11 **DR. CALVIN WILLHITE:** Okay. I'm with Risk
12 Sciences International. I've been retired from the State of California for more
13 than 10 enjoyable years. Risk Sciences is a Canadian company, but I'm
14 speaking to you from here just north of the Golden Gate Bridge.

15 **DR. KENNETH PORTIER:** Thank you. Okay.
16 Tamue, did I miss anyone?

17 **DR. LAWRENCE LASH:** Yeah. You did. This is
18 Larry Lash. Hi, can you hear me?

19 **DR. KENNETH PORTIER:** Oh, Larry. How did I miss
20 you?

21 **DR. LAWRENCE LASH:** I don't know. You skipped
22 from K to M, but that's okay. Anyway. This is Larry Lash. I'm a professor in
23 the Department of Pharmacology at Wayne State University in Detroit. And I
24 guess I'm a biochemical toxicologist, worked on various assays -- primarily the

1 kidney as a target organ, also some liver, and have worked on Perchloroethylene,
2 among other things as well. So that's it.

3 **MS. TAMUE GIBSON:** Dr. Portier, thank you. Thank
4 you, Dr. Lash. Dr. Portier, at this point --

5 **DR. KENNETH PORTIER:** For some reason I had
6 checked him off but not heard from him.

7 **MS. TAMUE GIBSON:** Okay. Okay. Dr. Portier and
8 all, at this point, I have the honor of introducing Alexandra Dunn, the Assistant
9 Administrator for the Office of Chemical Safety and Pollution and Prevention.
10 Assistant Administrator Dunn, thank you for joining us today. I now turn the
11 time over to you for a few remarks.

12
13 **WELCOME**

14 **MS. ALEXANDRA DUNN:** Tamue and -- okay. Is that
15 better?
16

17 **MS. TAMUE GIBSON:** Yes.

18 **MS. ALEXANDRA DUNN:** All right. A little bit of
19 feedback.

20 **MS. TAMUE GIBSON:** Yes, we can hear you. Yes.

21 **MS. ALEXANDRA DUNN:** Okay. Great. Well, good
22 morning, everyone. I'm Alex Dunn, the Assistant Administrator of the Office of
23 Chemical Safety and Pollution Prevention. And I really do hope you and all
24 your families are doing well, particularly as we continue to navigate together

1 through the COVID-19 public health emergency. These have been challenging
2 times for all of us, and we are truly appreciative of your support and willingness
3 to participate in the draft risk evaluation peer reviews.

4 Today, we begin the ninth Science Advisory Committee
5 on Chemicals meeting and the second all virtual public meeting for the first ten
6 chemicals. In two weeks, we will conduct a third virtual public meeting, and that
7 will be on the draft risk evaluation for asbestos. That will be the --

8 **MS. TAMUE GIBSON:** Hello? I think we lost her.

9 **UNIDENTIFIED MALE:** Yeah. We're all here. I think
10 we just lost her.

11 **MS. TAMUE GIBSON:** Vincent, is she still on? Is
12 Administrator Dunn still --

13 **MR. VINCENT BROWN:** She's no longer logged in.
14 She was disconnected for some reason. We'll reach out through Hailey or
15 someone to see if she can contact back in.

16 **MS. TAMUE GIBSON:** Okay. Dr. Portier, I think I'm
17 going to turn this back over to you. And when Assistant Administrator Dunn
18 comes in, then we can stop what we're doing, and we can proceed with her
19 remaining remarks and then continue. So Dr. Portier, I'll turn the meeting over
20 to you, and I believe this is our time for the presentation, unless you have further
21 comments at this time.

22 **DR. KENNETH PORTIER:** Well, I see that Dr. Dunn
23 has logged back in again.

24 **MS. TAMUE GIBSON:** Oh, she has? Okay.

1 **DR. KENNETH PORTIER:** Alex, are you there?

2 She's trying. Oh, now I hear something.

3 **MS. ALEXANDRA DUNN:** Can you hear me now?

4 **MS. TAMUE GIBSON:** Yes.

5 **MS. ALEXANDRA DUNN:** Okay. Fantastic. Thank
6 you again, everyone, and sorry for the technical difficulties. I was just saying
7 that these virtual meetings are robust and effective, but perhaps I'm
8 demonstrating that they also have some technical issues.

9 But I wanted to say that the reason they have been
10 effective is because all of you have been willing to commit to sitting in your
11 offices and making yourselves available for extended periods of time. Your
12 commitment as SACC members and as our ad hoc expert reviewers is beyond
13 commendable. Your participation in these meetings and in writing the reports
14 and particularly your efforts to complete reports within 60 days have helped us
15 continue to meet the Lautenberg mission under incredibly tight timeframes. We
16 appreciate your consideration of working towards completing the ninth and tenth
17 reports, if you can, within 60 days. Of course, you have a full 90 days, and we
18 respect that. But we do respect and appreciate your efforts so much. You have
19 made a difference.

20 Through this meeting on Perchloroethylene and the next
21 meeting on asbestos we will have done something that the Lautenberg Act
22 challenges us to do, which was to stand up the Science Advisory Committee on
23 Chemicals and to conduct ten draft risk evaluations, to peer review them
24 publicly, to take public comment, and then we will proceed to finalize these risk

1 evaluations. We are delivering on one of the major requests of the Lautenberg
2 law. And without you, we could not have done everything that we're doing.

3 We are going to review all of your reports so that we can
4 learn how to improve the process for future peer reviews. We are committed to
5 meeting our obligations under TSCA, and we are working to thoughtfully review
6 comments from the public in peer review process. And we are, as I stated,
7 planning to finalize all ten risk evaluations this year.

8 We continue to look for ways to increase the efficiencies
9 of the SACC process. We will be reflecting -- for those of you who will be
10 joining us as continued members and for potential new members, we want to try
11 to reduce the number of meeting days so that, when we are able to travel again
12 and meet while still practicing responsible social distancing, we will be able to
13 be effective and efficient with our time. And of course, as we reach today and
14 approach the tenth risk evaluation in June, there is thought of what happens next
15 for the SACC. And I have a few times mentioned to you all that we are thinking
16 about this extensively, and we want to maintain an open and lively conversation
17 on the scientific nature of our work.

18 We are committed to peer reviewing all of our work under
19 Lautenberg, and we are committed to the SACC. The peer review committee is
20 a wonderful venue to develop our conversations. I want you all to know that, as
21 you have reviewed each of the chemicals, we have heard you loud and clear
22 about our systematic review procedures. And I wanted to reiterate that we are
23 currently contracted with the National Academies of Sciences to review our
24 approach to systematic review, and we'll be refining that approach based on the

1 comments we've heard from this very Committee and then, of course, from the
2 National Academies of Science.

3 In the future, the SACC may be a resource for us to review
4 further refinements to the systematic review protocol that brings all of our work
5 together. Additionally, through April 20th, we accepted public nominations of
6 experts to be considered for appointment to this Committee. We were pleased to
7 receive over 50 volunteers and nominees who are providing us a very robust pool
8 of experts for us to consider as we fill SACC appointments over the next year.
9 The names and biographical sketches of those interested and available nominees
10 will be posted for public comment in the near future.

11 So in short, please know that peer review is the
12 cornerstone of our work. Your work ensures that we use sound science for
13 decision making while honoring innovation and fostering meaningful
14 stakeholder feedback. You are essential to EPA's promotion of chemical safety
15 in the United States and beyond.

16 I also want to take a moment this morning to introduce to
17 you Yvette Collazo-Reyes, who is the new Director of EPA's Office of Pollution
18 Prevention and Toxics, or OPPT. Yvette comes to us from the Small Business
19 Administration where she served as the district director of the Puerto Rico and
20 Virgin Islands office since 2013. Before joining the small business
21 administration, Ms. Collazo was a senior advisor and director for the Office of
22 Technology, Innovation, and Development at the U.S. Department of Energy's
23 Office of Environmental Management.

1 She has decades of experience in risk evaluation and in
2 working with very complex environmental scenarios. We are grateful to have
3 her on board and welcome her to our team. And for those of you who might be
4 trying to connect the organizational chart dots, Ms. Collazo has replaced Dr. Jeff
5 Morris, who retired earlier this year.

6 Once again, all members of the SACC thank you for your
7 efforts in helping us. Thank you for being flexible during the COVID pandemic
8 for us to meet in this virtual fashion. We appreciate your dedication and your
9 sacrifice and your critically important role to helping EPA implement TSCA and
10 fulfilling our mission. With that, I will turn the podium virtually back to Dr.
11 Portier. Thank you so much.

12 **DR. KENNETH PORTIER:** Thank you, Administrator
13 Dunn. And now we're going to begin the main work of the Committee with a
14 technical presentation by the OPPT lead, Dr. Mari Lee. Dr. Lee, I'd like you to
15 introduce yourself to the Committee and public commenters and also introduce
16 the additional EPA staff who are there to provide support to you during this
17 meeting. Dr. Lee.

18 **DR. MARI LEE:** Okay. Sure. My name is Mari Lee.
19 I'm a chemist by training, and I've done a lot of work in environmental sciences,
20 both aerosol science and now in risk evaluation. I specialize in exposure and fate
21 of chemicals in the environment within the risk assessment division. And you
22 can see my team posted -- or you will see my team posted once we start the
23 presentation. So should I go ahead and start, or do you want me to introduce
24 individual members?

1 **DR. KENNETH PORTIER:** So we have a slide here
2 with all these workgroup team leaders -- members, most of which we've met.
3 But I think it would be nice if we kind of knew the expertise that's sitting at the
4 table, so to speak, so that the Committee knows who's there.

5 **DR. MARI LEE:** So Greg Macek is our engineer. He
6 handles occupational exposure. Keith Jacobs and Fran Branch will be handling
7 the health aspects of the Perchloroethylene risk evaluation. Fran is an
8 epidemiologist, and Keith is a toxicologist. Marcy Card will be handling fate in
9 the environment. Jim or James Bressette is our eco toxicologist.

10 Clifton Townsend handled the surface water assessment,
11 so surface water exposure. Tyler Lloyd is from the Chemical Control Division
12 and him, along with Hannah, Niva, Amy, and Kelly, all worked on the risk
13 determination section. Albert is part of the Economics Division and helped with
14 production volumes and the regulatory history a little bit and with assigning -- so
15 the economics of PERC in the U.S. commerce. And I think that's everyone.
16 And Yvette Selby-Mohamadu is our management lead for the risk evaluation.

17 **DR. KENNETH PORTIER:** And I know Stan Barone is
18 sitting there in the background, so I don't want to leave him out of that list
19 because we always look to him for some insight. Thank you, Dr. Lee. That was
20 perfect. Why don't we now proceed with your technical presentation.

21
22 **OPPT TECHNICAL PRESENTATION - OVERVIEW OF**
23 **PERCHLOROETHYLENE DRAFT RISK EVALUATION**
24

1 **DR. MARI LEE:** Sure. Okay. Good morning to the
2 Scientific Advisory Committee on Chemicals, public commenters, and
3 stakeholders. My name is Mari Lee, and I'm the primary lead for the
4 Perchloroethylene team. Our management lead is Yvette Selby-Mohamadu. We
5 are fortunate to be part of a very dedicated and talented team whose names I just
6 went through, are listed and reflect in this presentation. As I go through the
7 presentation, I will call out slide numbers to help anyone following along in case
8 we have connection issues. Let me make sure this works. Okay.

9 Slide 2 is an overview of the presentation. We will begin
10 with a general background and history on PERC, followed by an overview of its
11 physical-chemical properties and the scope of the evaluation. We will then move
12 into an overview of the technical assessment, beginning with the environmental
13 fate and transport and moving into the environmental risk assessment and finally
14 to the human health risk assessment. The PERC risk evaluation had a deeper
15 focus on the human health assessment. However, the presentation first covers
16 the environmental assessment in accordance with the layout of the document and
17 the charge questions.

18 Following enactment of amended TSCA in June 2016,
19 EPA decided to evaluate the first set of ten existing chemical risk evaluations.
20 The 2020 draft risk evaluation includes application of the TSCA systematic
21 review process, assessment of all identified conditions of use, evaluation of risks
22 to environmental receptors, and evaluation of occupational and consumer risks
23 from both inhalation and dermal exposure. In the 2018 problem formulation,
24 EPA identified potential exposure pathways for the general population.

1 However, these are covered under the jurisdiction of other environmental
2 statutes. Therefore, due to this regulatory nexus, EPA did not evaluate hazards
3 or exposure to the general population for risk evaluation.

4 Slide 4 summarizes the physical-chemical properties of
5 PERC. The general structure of the chemical's presented on the left, and a few
6 very -- a few basic physical-chemical properties are provided on the right.
7 PERC is a liquid at room temperature with a boiling point of 121.3 degrees
8 centigrade and a vapor pressure of 18.5 millimeters of mercury. The vapor
9 pressure provides an indication of the relative tendency of the substance to
10 volatilize, which in turn indicates a concern for potential inhalation exposure
11 pathways.

12 The diagram here on Slide 5 depicts each stage of the
13 PERC lifecycle and associated conditions of use as reported in the 2016
14 Chemical Data Reporting, or CDR. Approximately 324 million pounds of PERC
15 were manufactured or imported into the U.S. in 2015 with 65 percent used as an
16 intermediate and the rest used as a dry-cleaning solvent, aerosol degreaser,
17 degreasing solvent, as well as other applications. We are now on Slide 6. This
18 slide presents examples of some occupational conditions of use and
19 corresponding occupational exposure scenarios, or OES. EPA grouped similar
20 conditions of use into single OES and assigned releases and exposures based on
21 data for the applicable OES.

22 Slide 7, this slide shows examples of consumer conditions
23 of use. The consumer exposure assessment recategorized COUs compared to the
24 problem formulation to improve clarity. Additionally, several COUs were split

1 into additional subcategories based on different forms of products, for example,
2 aerosol versus liquid. We are on Slide 8. The PERC risk evaluation assessed
3 various different receptors and populations. For ecological receptors, EPA
4 performed a quantitative assessment for aquatic species. For human health, EPA
5 performed distinct assessments for occupational and consumer exposure
6 scenarios.

7 Occupational populations include workers and
8 occupational non-users, or ONUs. And among those receptor categories EPA
9 also provided estimates for potentially exposed and susceptible subpopulations,
10 including females of reproductive age. Workers are employees who directly
11 handle PERC. ONUs do not directly handle PERC but perform work in an area
12 where PERC is present. EPA assessed both inhalation and dermal exposure to
13 workers and inhalation exposure to ONUs. The consumer assessment covered
14 both users and bystanders and included consideration of different life stages,
15 including children.

16 Consumer users are direct users of PERC-containing
17 products while bystanders are incidentally exposed within the same residence
18 where PERC is being used. Inhalation and dermal exposure was assessed for
19 users and only inhalation exposure was assessed for bystanders. All right.

20 Beginning here on Slide 9, we now introduce the
21 environmental fate and transport aspect of the risk evaluation. This information
22 is described in Section 2.1 of the draft risk evaluation and related to Charge
23 Question 1. Slide 10 describes the fate and transport approach for the draft risk
24 evaluation. EPA evaluated and extracted fate and transport data from 76 studies.

1 Some characteristics were estimated with EPI Suite, a set of predictive models
2 for physical-chemical properties and fate and transport characteristics. EPI Suite
3 was reviewed by EPA's Science Advisory Board in 2007, and individual models
4 have been peer reviewed in numerous technical articles.

5 Slide 11 provides a summary of various environmental
6 fate and transport properties of PERC. These properties include an indication of
7 the partitioning of PERC in environmental media. For instance, the Henry's
8 Law Constant, which is the ratio of vapor pressure to water solubility, indicates
9 that PERC likely partitions to air at the air-water interface of an environmental
10 system. Direct photolysis is up to 174 days, so long-range transport is possible.
11 PERC's soil and sediment organic carbon partitioning coefficient, or Koc,
12 indicates that partition to soil and sediment will be moderate. PERC is not
13 bioaccumulative based on its estimated bioconcentration factor and data from
14 bioaccumulation studies.

15 We are now on Slide 12. Based on physical-chemical
16 properties and environmental fate characteristics, overall, PERC has low
17 bioaccumulation potential, has moderate potential to sorb to biosolids,
18 sediments, and soils, and is expected to volatilize from surface water and soil.
19 PERC may undergo aerobic or anaerobic biodegradation in soil, sediment, and
20 water.

21 Now on Slide 13, PERC is expected to accumulate in
22 biosolids and sediments. Although PERC is expected to absorb to sediment
23 organic matter, potentially rapid biodegradation may depress concentrations in
24 sediment. If released to land via biosolids, PERC is expected to volatilize to air

1 or migrate to groundwater based on its organic carbon partitioning coefficient,
2 water solubility, vapor pressure, and Henry's Law constant. Or it may undergo
3 biodegradation.

4 I would now like to describe the environmental risk
5 assessment, starting with the releases and exposures. This information is
6 described in Section 2.2. and Appendix D of the draft risk evaluation and relates
7 to Charge Question 2.1. I am now on Slide 14 moving on to Slide 15.

8 The manufacturing, processing, use, and disposal of PERC
9 can result in releases to the environment. As previously discussed, EPA
10 categorized the conditions of use into occupational exposure scenarios. For each
11 occupational exposure scenario, a daily water release was estimated based on
12 annual releases, release days, and the number of facilities. EPA used the 2016
13 Toxic Release Inventory (TRI) and 2016 Discharge Monitoring Report (DMR)
14 data to provide a basis for estimating releases. Where releases are expected but
15 TRI and DMR data are not available, releases were estimated using data from
16 other sources such as, but not limited to, literature, relevant Emission Scenario
17 Documents, or ESDs; Generic Scenarios, or GSs; and relevant Effluent
18 Limitation Guidelines, or ELGs.

19 Slide 16, there are some uncertainties and limitations
20 with the wastewater discharge assessment. These uncertainties include
21 limitations in TRI and DMR data, assumptions about the conditions of use at
22 release sites reported by TRI and DMR, and the possibility of day-to-day
23 variations of PERC concentrations in wastewater. Despite these uncertainties,

1 EPA has medium or high overall confidence in the wastewater discharge
2 assessment for all scenarios.

3 Slide 17, to characterize environmental exposure to
4 aquatic species, EPA conducted modeling and considered environmental
5 monitoring data. EPA modeled near-facility concentrations of PERC in surface
6 water using EPA's EFAST model, with releases based on the occupational
7 exposure environmental release assessment. A wastewater treatment removal
8 rate of 80 percent was applied in modeling, when appropriate, to release volumes
9 characterized as off-site transfers or indirect releases, while no wastewater
10 removal was applied for direct discharge volumes, which were based on post-
11 treatment release estimates.

12 Direct discharges were modeled assuming 20 days of
13 release, as well as higher frequency release scenarios informed by the
14 occupational exposure scenarios. Indirect discharges were only modeled with
15 the higher number of release days. Site-specific receiving waterbody flows were
16 used to the extent possible. Otherwise, sector specific average stream flows
17 were applied. Site-specific receiving waterbody stream flows were used to
18 ensure that the measured concentrations reflect localized ambient exposures at
19 the monitoring sites, and the modeled concentrations reflect near-site estimates at
20 the point of release to give EPA the best possible -- best estimate possible for
21 PERC exposure in surface water.

22 Modeled surface water concentrations reflecting low-flow
23 conditions were compared with ecological concentrations of concern for the
24 purposes of risk characterization. EPA also examined surface water

1 concentrations from monitoring data obtained through systematic review. These
2 data were sourced through the Water Quality Portal, as well as from literature.

3 Beginning now on Slide 18, I will describe the hazards
4 and risk characterization associated with the environmental assessment of PERC.
5 This is discussed in Section 3.1 of the draft risk evaluation and relates to Charge
6 Question 3. The diagram on Slide 19 presents the environmental exposure
7 pathways and receptors quantitatively assessed in the risk evaluation. Available
8 TRI and DMR release information indicated that aquatic releases are expected
9 for PERC. As a result, EPA carried out a quantitative risk assessment comparing
10 available environmental hazard data for aquatic species and estimated aquatic
11 exposure concentrations.

12 PERC is expected to be moderately retained in sediment
13 due to its water solubility and moderate partitioning to organic matter.
14 Therefore, PERC is expected to be present in both sediment organic matter and
15 in the pore water at similar concentrations to the overlying water. While no
16 ecotoxicity studies were available for sediment-dwelling organisms, the toxicity
17 of PERC to sediment invertebrates is expected to be similar to the toxicity for
18 aquatic invertebrates because of the similarities in PERC concentrations. In the
19 problem formulation, EPA determined that risks would not be evaluated for
20 land-applied biosolid pathway leading to terrestrial exposure because this
21 pathway is currently being addressed in the Clean Water Act, or the CWA,
22 regulatory analytical process.

23 We are now on Slide 20. This slide includes an overview
24 of the environmental hazard data available for Perchloroethylene's risk

1 evaluation assessment -- sorry, environmental risk assessment. During the
2 systematic review process, 30 acceptable environmental hazard studies were
3 identified on fish, aquatic invertebrates, and algae. Algae was assessed
4 separately from other aquatic organism because durations normally considered
5 acute for other species, for example, 96 hours, can encompass several
6 generations of algae.

7 Of the acute and chronic hazard data, aquatic invertebrates
8 were the most sensitive aquatic species. For algae, there were toxicity values
9 from two EC50 studies and one NOEC/LOEC study. Because the EC50 study
10 results varies by greater than an order of magnitude, EPA used the NOEC/LOEC
11 mortality endpoint for the most sensitive algal species to represent algae as a
12 whole.

13 Here on Slide 21 I will outline the approach EPA used to
14 calculate the environmental hazard to aquatic species. EPA calculated hazard
15 thresholds known as Concentrations of Concern, or COCs. After weighing the
16 scientific evidence and selecting the appropriate toxicity values from the
17 integrated data, EPA applied an assessment factor, or an AF, according to EPA
18 methods to calculate acute, chronic, and algal COCs.

19 The application of AFs provides a lower bound effect
20 level and accounts for differences in intraspecies variability. For fish and aquatic
21 invertebrates, the acute endpoint values are divided by an AF of five. For
22 chronic and algal COCs, an AF of 10 is used. EPA calculated acute COCs, a
23 chronic COC, and an algal COC.

1 This section discusses the environmental risk
2 characterization for PERC, discussed in Section 4.1 of the document and related
3 to Charge Question 6. We are on Slide 22 moving on to slide 23.

4 Environmental risks were estimated by calculating a risk quotient, or RQ, which
5 is estimated environmental concentration divided by the effect level threshold for
6 the taxa of interest.

7 An RQ equal to one indicates that the exposures were the
8 same as the concentration that causes effect. If the RQ exceeds one, the
9 exposure is greater than the effect concentration, and there is potential for risk
10 presumed. If the RQ does not exceed one, the exposure is less than the effect
11 concentration, and there is no risk presumed. To estimate risk to aquatic
12 organisms near facilities, EPA calculated RQs by dividing the surface water
13 concentrations estimated using EFAST by the appropriate COCs.

14 Slide 24, for risk estimates near facilities releasing PERC
15 based on available data for aquatic species, seven of 11 COUs had an acute risk
16 factor greater than or equal to one, chronic risk quotient greater than or equal to
17 one, and 20 days or more of COC exceedances or algae risk quotient greater than
18 or equal to one and 20 days or more of COC exceedances. Acute risk to
19 invertebrates were present at one of four facilities at the incorporation into
20 formulation COU. Chronic risk to invertebrates were identified at two of 18
21 facilities from the processing as a reactant COU and one of four facilities from
22 incorporation into formulation COU. For algae, 21 facilities from seven COUs
23 had an algae risk quotient greater than or equal to one and 20 days or more of
24 COC exceedances.

Slide 25, to estimate risk to aquatic organisms in ambient water, EPA also calculated risk quotients by dividing surface water concentrations reported in monitoring data, either from Water Quality Portal or reported in published literature, by the appropriate COC. Acute and chronic risk quotients less than one or risks to aquatic organism like fish and aquatic invertebrates were not identified in ambient water. Therefore, the risks identified at facilities mentioned in the previous slide are likely localized to surface water area -- or surface water near the facility. Algae risk was identified in ambient water with a risk quotient of 1.2 at the maximum concentration and well below one for the mean concentration, likewise indicating that risks identified at facilities mentioned in the previous slide are likely localized to surface water near the facility.

The next slide, Slide 26, outlines several of the uncertainties discussed in the document that relate to the environmental risk conclusion. For hazard data used, the algae data encompassed a wide range of toxicity values not easily characterized by a single toxicity value from a single study. For the exposure data used, the environmental exposure data could be over or underestimating exposure to aquatic organisms.

For example, EFAST results used to estimate surface water concentrations near facilities uses TRI, DMR, and CDR data as inputs. These datasets may not include every industrial release in the country, so some releases to surface water may not have been captured. On the other hand, PERC is a volatile chemical and EFAST does not account for volatilization. The monitored data used to estimate ambient water concentrations is limited

1 temporally and geographically. Additionally, measured samples are
2 predominately not in watersheds of known PERC releasers.

3 We are on Slide 27. To summarize, quantitative
4 assessments of reasonably available environmental data -- sorry, environmental
5 hazard data indicates that EPA found risks to aquatic invertebrates in the
6 environment near three facilities that release PERC to surface water. Acute risk
7 was identified for a single COU near one of the four facilities, and chronic risks
8 were identified for two COUs near three out of 22 facilities. Risk to algae was
9 identified for seven COUs near 21 of 71 facilities releasing PERC.

10 No acute or chronic risks to these aquatic organisms were
11 identified in ambient water. Therefore, the risks identified for the three facilities
12 are likely localized to surface water near the facility. Algae risk was identified in
13 ambient water with a risk quotient of 1.2 at the maximum concentration -- sorry.
14 Let me finish. I'm going to pause just one second. I'm getting a message --
15 likewise indicating that risk identified at facilities mentioned in the previous
16 slides are likely localized to surface water near the facility.

17 Oh, okay. I was being asked to talk slower. Sorry. That
18 is a -- I do talk very quickly. Let me get back to presentation. Here we go. All
19 right.

20 On Slide 28, I will now transition into a discussion of
21 human health, including the exposures, hazards, and risk characterization. I will
22 begin the discussion of human health with occupational exposure. This
23 information can be found in Section 2.4.1 and relates to Charge Questions 4.1
24 through 4.6.

Slide 29, EPA had several objectives in developing the occupational inhalation and dermal exposure assessment. Those objectives included evaluating and grouping similar worker activities and occupational exposures, determining the distinction between workers and occupational non-users, and ultimately providing the inhalation and dermal exposures for workers and occupational non-users where possible. Slide 30 describes the assessment of inhalation exposure. As part of the assessment, EPA provides the central tendency and the high-end exposure values based on available data. For each OES, EPA also calculated the average daily concentration, the ADC, and the lifetime average daily concentration, or the LADC.

Slide 31, to assess inhalation exposure for workers and occupational non-users, EPA used both monitoring data and modeling approaches. Where monitoring data were available, EPA used personal breathing zone data for eight hour and 12-hour time weighted average exposures from directly applicable scenarios. Key sources of monitoring data come from NIOSH, OSHA, open literature, and submitted public comments.

All the data were evaluated through the systematic review process. Differences in exposure durations were accounted for when calculating AC, ADC, and LADC exposure values. Where EPA had information to construct a model, exposure modeling was performed to supplement monitoring data. To estimate inhalation exposures for ONUs, EPA considered ONU specific personal monitoring data and modeled far-field air concentration. In the absence of these estimates for ONUs, EPA provided worker central tendency exposure values as surrogates for ONU exposures.

Slide 32 provides an example of monitoring data used for aerosol degreasing to develop exposure estimates for workers. The personal breathing zone monitoring data were obtained from four sources, all of which scored a high data quality rating as determined through EPA's systematic review process. No monitoring data were identified for ONUs. Therefore, these exposures were estimated using a near-field/far-field model developed for the OES.

We are now on Slide 33. For several OES, EPA used a two-zone, probabilistic modeling approach to assess inhalation exposure. In this modeling approach, EPA emissions occur in the near-field zone. Workers are assumed to spend their time in the near field when handling PERC.

Occupational non-users are assumed to spend their time in the fair-field zone. Air exchange occurs between the near-field and far-field. Model input parameters, such as the far-field size, work activity pattern, PERC use rate, and environmental parameters were defined using reasonably available data from literature. EPA performed a Monte Carlo simulation to capture variability within the modeling scenario.

Slide 34 provides an example of the two-zone near-field/far-field model used for brake cleaning to develop exposure estimates for workers in the near-field zone and for occupational non-users who are exposed to PERC in the far-field zone. Slide 35 provides an example comparison of modeled estimates with monitoring data.

For the few scenarios where modeling and monitoring data were available, there was typically reasonably good agreement between the

1 modeling and monitoring exposure values for workers. In these examples, the
2 estimates using both approaches were roughly within a factor of five. The
3 worker modeled values shown here are from the corresponding near-field/far-
4 field probabilistic model for brake cleaning and dry cleaning. HE represents
5 high-end, and CT is central tendency.

6 This table on Slide 36 provides a summary of each of the
7 occupational exposure scenarios, or OESs, by indicating whether monitoring
8 data was reasonably available and whether the data was used to estimate
9 inhalation exposures for workers and ONUs. The table also indicates whether
10 EPA used modeling to estimate inhalation exposures for workers and ONUs.
11 The green check mark indicates that monitoring or modeling were available, and
12 the red X indicates that monitoring or modeling were not available.

13 Slide 37, there are uncertainties and limitations in the
14 inhalation monitoring data and modeling approaches. These include
15 uncertainties in how well monitoring data represents PERC COUs, assignment of
16 monitoring data as worker or ONU exposure based on worker descriptions,
17 model input parameters, and model assumptions. Despite these uncertainties,
18 EPA has a medium or high confidence in the assessed exposure values for
19 scenarios where EPA had models or monitoring data to assess exposures for
20 workers or ONUs. This is based on the strength of monitoring data -- all of
21 which received medium or high-quality data scores through the systematic
22 review process -- agreement of monitoring data and model results, where both
23 are available, and the availability of models to capture site-to-site variations by
24 varying input parameters.

Slide 38, to assess dermal exposure, EPA used the *Dermal Exposure to Volatile Liquids* model to calculate the dermal retained dose for both non-occluded and occluded scenarios. The equation modifies the *EPA 2-Hand Dermal Exposure to Liquids Model* by incorporating a fraction absorbed parameter to account for the evaporation of volatile chemicals. The steady state fraction absorption for PERC is estimated to be 0.13 in industrial facilities with higher indoor wind flows or 0.19 in commercial facilities with lower indoor wind speeds based on a theoretical framework provided by Kasting and Miller 2006. This means that approximately 13 or 19 percent of the applied dose is absorbed through the skin following exposure from industrial and commercial settings, respectively.

Here on Slide 39 is an example of how the dermal exposures through the occupational exposure scenarios were grouped, or “binned,” based on characteristics that are known to affect dermal exposure. This slide presents example dermal exposure estimates for Bin 1, which covers large-scale industrial uses that typically occur in mostly closed systems. For these uses, dermal exposure is likely limited to chemical loading/unloading activities, for example, connecting hoses.

Slide 40 discusses uncertainties with the occupational dermal exposure assessment. One limitation of the occupational dermal approach is the use of a fixed fractional absorption term to quantify dermal dose. In reality, dermal absorption may depend on skin loading conditions. Additionally, the model also assumes a single exposure event per day and does not address variability in exposure duration and frequency.

1 Further, there is limited information on glove type and
2 glove use for most conditions of use. Therefore, the actual exposure reduction
3 from glove protection is uncertain. Finally, EPA assumed that ONUs do not
4 have routine dermal exposure to PERC. However, depending on the conditions
5 of use, ONUs may have incidental dermal exposures due to surface
6 contamination. Despite these uncertainties, EPA has a medium overall
7 confidence in the assessed dermal exposures as the model is based on existing
8 peer-reviewed dermal model modified to account for evaporation and absorption
9 of volatile chemicals.

10 The following slides cover the consumer exposure
11 approach, methodology, and uncertainties. Consumer exposures are described in
12 Section 2.4.2 of the draft risk evaluation and relate to Charge Questions 4.7 to
13 4.10. We are currently on Slide 41, moving to Slide 42.

14 A total of 16 consumer COUs were evaluated with full
15 modeling estimation in the draft risk evaluation. Three additional uses were
16 reported based on monitoring data available in peer-reviewed literature but were
17 not modeled based on data and modeling limitations. EPA used the Consumer
18 Exposure Model, CEM, version 2.1 to evaluate inhalation and dermal exposure
19 routes for consumer products and to evaluate dermal exposure to consumer
20 articles in the form of recently dry-cleaned clothes. EPA used a multi-chamber
21 concentration and exposure model, MCCEM, to evaluate inhalation exposure to
22 consumer articles in the form of recently dry-cleaned fabrics. The availability of
23 PERC in consumer products was determined primarily through the development

1 of EPA's 2017 Preliminary Information on Manufacturing, Processing,
2 Distribution, Use, and Disposal of Tetrachloroethylene.

3 We are on Slide 43. Inhalation and dermal exposures
4 were evaluated for acute consumer exposure scenarios -- i.e. for those resulting
5 from short-term or daily exposures. In general, typical frequencies of product
6 use were considered to be too low to generate chronic risk concerns for
7 consumers. Based on physical-chemical properties of PERC, oral exposure was
8 not expected. Exposures were assessed for users or consumers as well as for
9 bystanders in the home. Users are the receptors using a product containing
10 PERC within a residence in an identified room of use, while bystanders are
11 receptors within the residence where the produce containing PERC is used that
12 are incidentally exposed to the product.

13 Slide 44, as described on the previous slide, inhalation and
14 dermal exposures to PERC-containing products were estimated through the
15 modeling of acute exposure scenarios. Key parameters for exposure modeling
16 include use duration, amount or mass of product used, weight fraction of PERC
17 in product used, room of use, air exchange rate, and zone volumes. Three of
18 these inputs -- the duration, mass, and weight fraction -- that describe product
19 use and user behavior patterns were varied to capture a range of exposure by
20 combining low-end, central-tendency, and high-end inputs for the key
21 parameters listed on the slide. This resulted in a maximum of 27 modeling
22 combinations for inhalation scenarios and nine modeling combinations for
23 dermal scenarios. Results were presented for a range of modeling combinations
24 reflected by three exposure scenarios: high-, moderate-, or low-intensity user.

Slide 45, inhalation and dermal exposures to PERC from recently dry-cleaned articles were estimated through the modeling of acute exposure scenarios. Inhalation exposure to PERC from dry cleaned articles was modeled using MCCEM. Key emission parameters were taken from published literature, such as residual PERC retained in dry cleaned fabrics, fabric characteristics and emission rates.

Two key studies, Tichenor et al from 1990 and Sherlach et al from 2011, were used to present a range of assumed dry cleaning technologies, i.e. the generation of machine, for model parameterization. Other parameters were kept consistent with CEM defaults, such as whole house air exchange rates and daily activity patterns for users and bystanders. Indoor air concentrations reported at maximum exposure -- approximately four hours -- and 10 hours after items were brought into the house, as well as the 24-hour time weighted average air concentration for users and bystanders.

Dermal exposure to PERC from dry cleaned articles was modeled using CEM's A-DER2 submodel, which calculated dermal exposure via diffusion of a chemical through an article in direct contact with the skin. The dermal model was parameterized based on measured PERC retained in fabrics after single and repeat dry cleaned events, using a range of presumed dry-cleaning technologies. Articles were assumed to be worn by adults only, and exposure estimates were modeled for full and half-body dermal exposure one to three days after a dry-cleaning event.

We are now on Slide 46. Manufacturer-developed consumer product safety data sheets, or SDSs, were obtained -- were used to

1 obtain the key PERC weight fraction input as well as product density
2 information. The Westat survey is a comprehensive national survey of consumer
3 use patterns and was used to parameterize the key modeling inputs, such as
4 duration of use, mass of product used, and room of use. The survey includes
5 responses from thousands of American households on consumer behavior
6 patterns and product characteristics.

7 EPA considered the similarity of product category and
8 formulation type to align PERC consumer conditions of use with the most
9 appropriate Westat product data. As described, results were presented for a
10 range of modeling combinations reflected by three exposure scenarios: high-,
11 moderate-, or low-intensity user, which are characterized with the displayed
12 combination of low-end, central-tendency, and high-end inputs for mass used,
13 weight fraction, and use duration. Full results for all modeling iterations are also
14 shared in the associated supplemental files.

15 Slide 47, inhalation exposures were evaluated for 16
16 consumer conditions of use. Receptors are products users, which include adults
17 and children 11 years of age or older and bystanders, which could include any
18 age group. CEM and MCCEM predict indoor air concentrations by
19 implementing a deterministic, mass-balance calculation. Both models were used
20 as a two-zone representation of a house, with Zone 1 representing the room of
21 use and Zone 2 being the remainder of the house.

22 The arrows depict air flows between each zone and the
23 outdoors and the air flow between the two zones. Modeled air concentrations for
24 users reflect time spent in Zone 1 during product use, while modeled air

1 concentrations for bystanders reflect time spent in Zone 2 during product use.

2 Both receptors move throughout the house following prescribed activity patterns
3 for the rest of the day.

4 Slide 48, the CEM emission models used for PERC
5 products include E1, or the emission from a product applied to a surface indoors
6 incremental source model; E2, or the emission from a product applied to a
7 surface indoors double exponential model; E3, or the emission from a product
8 sprayed model; and E5, or the emission from a product placed in the
9 environment. E1 was used for liquid formulations, and it assumes the constant
10 application rate and emission rate that declines exponentially over time. E2 was
11 used for liquid formulations that dry or cure, such as paints, primers, and
12 sealants. It assumes a higher initial emission rate due to evaporation, followed
13 by a slower diffusion dominated rate as the product dries.

14 E3 was applied for aerosol formulations, and it assumes
15 overspray and subsequent volatilization from the target surface. E5 was applied
16 for liquid formulations used for immersive cleaning, such as immersive parts
17 cleaners, and assumes emission at a constant rate. MCCEM was used to model
18 inhalation exposure from dry cleaned articles stored in the home.

19 This is Slide 49. Dermal exposures were evaluated for 15
20 product COUs for consumer users, which include adults and children age 11 or
21 older. Dermal exposures were also evaluated for one article COU, dry-cleaned
22 articles, for adult users. Exposures to bystanders were not evaluated as,
23 generally, only users were expected to have direct contact with PERC containing
24 products and articles.

1 Based on the physical-chemical properties of PERC and
2 predictions surrounding levels of volatilization and absorption expected, dermal
3 modeling focused on conditions of use more likely to involve dermal contact
4 with impeded evaporation or scenarios where PERC may not readily volatilize
5 from the skin surface due to a factor such as a product-soaked rag held against
6 the skin or long term direct contact with residual PERC in recently dry-cleaned
7 fabrics. CEM sub-model, P_DER2b, or the Dermal Dose from Product Applied
8 to the Skin Permeability Model, was selected as the most appropriate model to
9 estimate consumer dermal exposure to PERC containing products.

10 This sub-model estimates dermal flux based on a
11 permeability coefficient, or Kp, and assumes a constant supply of chemical
12 through the exposure duration. The Kp used, 0.018 centimeters per hour, is a
13 measured value from Nakai et al published in 1999. CEM sub-model, A_DER2,
14 or Dermal Dose from Skin Contact with Article, was selected as the most
15 appropriate model to estimate consumer dermal exposure to PERC from recently
16 dry-cleaned articles. This sub-model estimates dermal exposures based on the
17 diffusion of chemical within an article to the skin surface via direct contact.

18 This is Slide 50. CEM developers conducted a detailed
19 sensitivity analysis, as described in Appendix C of the CEM user guide and
20 summarized in the Supplemental Information on Consumer Exposure. As
21 explained in the approach slides, EPA varied three input parameters -- the weight
22 fraction, duration of use, and mass -- to capture a range of exposure estimates.
23 These parameters are reflective of consumer products and consumer behavior
24 patterns, two of which are highly sensitive in inhalation modeling -- the mass

1 used and weight fraction. Other highly sensitive inputs for CEM inhalation
2 models include zone volumes and air exchange rates, which were held constant
3 at central-tendency values.

4 We are now on Slide 51. The overall modeling approach
5 was deterministic but captured a range of exposure estimates by varying key
6 parameters. Since a probabilistic approach was not employed and all inputs were
7 not varied, there remains uncertainty regarding the full range of possible
8 exposures. Appropriate product-specific monitoring data were not identified for
9 use in validating modeling results for PERC-containing consumer products.
10 EPA made best efforts to crosswalk Westat survey data to PERC consumer
11 product conditions of use. However, certain associations were weaker than
12 others and are discussed in the risk evaluation. In examining Westat for
13 appropriateness, EPA considered reasonableness of the reported durations and
14 masses used and compared primary formulation type such as liquid versus
15 aerosol.

16 There are two main sources of uncertainty for produce
17 dermal exposure modeling: the assumptions surrounding the likelihood of and
18 duration of dermal contact involving impeded evaporation and the use of
19 measured aqueous Kp to estimate dermal flux in the permeability model. This
20 panel recently provided feedback on the TCE draft risk evaluation regarding the
21 use of aqueous versus neat chemical Kp value. EPA will recalculate the dermal
22 results for PERC products conditions of use using a neat Kp before the final
23 publication but did not have time to include those results in the draft of the
24 document presented today.

1 The article dermal exposure modeling for contact with
2 recently dry-cleaned fabrics is diffusion based and thus sensitive to the fabric
3 thickness. There is also uncertainty regarding the model or generation of dry-
4 cleaning machines still in use, and this leads to uncertainties in total PERC
5 loading in dry-cleaned fabrics. To address this uncertainty, EPA addressed a
6 range of fabric PCE loadings based on assumed age of dry-cleaning technology.

7 Measured emissions from PERC-containing products were
8 not identified for use in modeling. Therefore, emission rates were estimated
9 within CEM. As to the strengths of EPA modeling approach, CEM and
10 MCCEM are peer reviewed and publicly available exposure models. CEM
11 employs well-established, central tendency default values for sensitive
12 parameters such as building and room volumes, the interzonal ventilation rate,
13 and air exchange rate. MCCEM was parameterized using chemical and use-
14 specific emission data from the published peer-reviewed literature.

15 The modeling inputs that EPA selected to vary for product
16 inhalation exposure -- mass used, duration of use, and weight fraction -- are
17 based on high quality survey data across a range of values. Given the
18 uncertainties, limitations, and strengths of the approach, there was overall
19 moderate to high confidence in the consumer inhalation exposure estimates and
20 moderate confidence in the dermal exposure estimates.

21 Now on Slide 52 begins the discussion of Human Health
22 Hazard, which is described in Section 3.2 of the risk evaluation and relates to
23 Charge Question 5. Here on Slide 53 is a breakdown of PERC's toxicokinetics,
24 covering absorption, distribution, metabolism, and elimination. PERC is well-

1 absorbed by all routes, although volatility limits dermal absorption unless
2 exposure is occluded. Adjustment for dermal absorption is accounted for in the
3 exposure estimates.

4 PERC is widely distributed but partitions heavily into
5 adipose tissues. PERC undergoes limited metabolism via both oxidative and
6 conjugative pathways. TCA is the major oxidative metabolite formed in liver
7 while several reactive conjugate metabolites form in kidney following transport
8 of the initial GSH conjugate from liver. PERC has a half-life of up to 55 to 65
9 hours in human adipose tissue with shorter half-lives in other tissue.

10 We are now on Slide 54. For this risk evaluation, EPA
11 utilized the physiologically based pharmacokinetic, or PBPK, model published
12 as part of the 2012 IRIS Assessment. This model allows for cross-species and
13 route to route extrapolation of toxicity data but does not include a probabilistic
14 representation of human variability. Four dose metrics were determined using
15 this model: daily AUC of PERC in blood, fraction of PERC undergoing
16 oxidative metabolism, fraction of PERC undergoing GSH conjugation, and
17 equivalent daily production of TCA per body weight. There is the highest
18 confidence in the AUC metric and highest uncertainty in the GSH conjugation
19 metric.

20 Slide 55, based on previous PERC assessments and results
21 of the EPA/OPPT literature search, EPA evaluated acute toxicity, neurotoxicity,
22 kidney toxicity, liver toxicity, reproductive and developmental toxicity, toxicity
23 to the immune system and blood, and cancer. Acceptable studies were available
24 via inhalation and oral but not dermal routes. Based on the weight of scientific

1 evidence and availability of adequate quantitative data, all but immunotoxicity
2 and blood toxicity were carried forward to dose-response analysis.

3 Slide 56, EPA only selected studies of acceptable data
4 quality with adequate quantitative information available for consideration in
5 dose-response analysis. For acute exposure scenarios, a single study was
6 selected for dose-response analysis: Altmann et al from 1990, which observed
7 visual impairment based on visual neural signaling. This study exposed male
8 volunteers to PERC for four hours per day for four days with incremental
9 latencies and visual-evoked potential observed after each day of exposure.

10 Slide 57, for chronic effects, EPA identified many relevant
11 studies for each hazard domain, often covering multiple endpoints within each
12 domain. Therefore, studies were selected that best represent each endpoint based
13 on data quality score, cumulative UF, endpoint adversity, and relevance. Risk
14 estimates for only those representative studies were presented in the risk
15 evaluation. However, risk estimates for all endpoints can be found in the
16 supplemental files.

17 For neurotoxicity, EPA identified one endpoint for color
18 confusion and another for visual and cognitive deficits, both from occupational
19 studies. The midpoint of the two points of departure, or PODs, was selected for
20 use in risk evaluation because the two PODs represent related endpoints. And
21 those effects were observed in a broad range of studies. Both studies also scored
22 the same for data quality. This precluded selection of only one study for use as
23 the POD. This endpoint was the key chronic endpoint for purposes of risk
24 summary and determination.

1 For kidney, nuclear enlargement and proximal tubules
2 from mouse data was selected for use in risk estimates. Increased angiectasis
3 represented the liver domain. Reduced sperm quality was the only reproductive
4 endpoint identified, while data for decreased pup weight-gain and developmental
5 neurotoxicity was selected to represent the developmental toxicity domain.

6 We are on Slide 58. For dose-response analysis,
7 administered doses or air concentration as reported in the animal toxicity studies
8 were run through the PBPK model to obtain human equivalent concentrations or
9 human equivalent doses, HECs or HEDs. Chronic HECs were adjusted to
10 continuous exposure 24-hour values for consistency across endpoints and with
11 the 2012 IRIS Assessment. Human data was not PBPK modeled and was
12 adjusted based on Haber's rule that concentration times time is constant to either
13 an accurate occupation -- sorry, is constant to either an acute occupational
14 duration or 24-hour continuous exposure basis. Uncertainty factors considered
15 for determining the benchmark MOEs were a UF for interspecies, which is three
16 if the PBPK modeled or otherwise scaled; an interspecies UF for human
17 variability that was ten for all endpoints; a LOAEL to NOAEL UF, which was
18 ten if the POD was based on a LOAEL and one otherwise; and a subchronic to
19 chronic UF, which was ten for chronic risk estimates if a study duration covered
20 less than 10 percent of lifetime.

21 Now on Slide 59, in addition to the POD as described in
22 the last slide, EPA also derived an occupational HEC for the key chronic
23 endpoint of neurotoxicity. Based on assumed average occupational breathing
24 rate of 1.25 cubic meters per hour, representing light activity, and a resting

1 breathing rate of 20 cubic meters over 24 hours, derivation of the eight- or 12-
2 hour occupational HEC results in an elevated internal dose compared to resting
3 breathing rates.

4 EPA derived the occupational HEC using the midpoint of
5 the original unadjusted neurotoxicity study NOAELs, since they both examined a
6 chronically exposed human -- occupational human population and scored the
7 same on data quality evaluation as previously mentioned. For risk estimation,
8 the occupational HEC was compared directly to an eight hour or 12-hour time
9 weighted average depending on the OES. And for most OES the resulting
10 margin of exposure, or MOEs, were 36 percent lower compared to the 24-hour
11 HEC.

12 The PERC PBPK model does not contain a dermal
13 compartment. Therefore, derivation of dermal PODs used route-to-route
14 extrapolation from both inhalation HECs and oral HEDs. When oral HEDs were
15 available, the oral value was used directly as a dermal HED, with dermal
16 absorption considerations accounted for in the occupational consumer exposure
17 assessments. Inhalation HECs were converted to dermal HEDs based on
18 assumed exposure factors for inhalation rate and body weight.

19 An example is shown on the slide. When both derivations
20 were available for a particular endpoint, the most robust and sensitive value was
21 used for risk estimation. Of note, for all endpoints with available derivations via
22 both methods, the resulting dermal HEDs differed by no more than
23 approximately twofold.

1 Now moving on to cancer on Slide 61. For liver, there is
2 evidence for contributions to the cancer MOA from multiple mechanisms,
3 including genotoxicity of metabolites, epigenetics, cytotoxicity, inflammation,
4 and PPAR alpha activation, among others. While there is varying support for
5 each of these, there is no strong causal link between any individual mechanism
6 and the observed in vivo tumorigenesis.

7 For kidney, the strongest evidence suggests a genotoxic
8 MOA based on conjugative metabolites with limited relevance for other
9 mechanisms. Insufficient data is available to support any particular MOA for
10 blood cancers, including mononuclear cell leukemia. Overall, the weight of
11 evidence supports a complex MOA with multiple contributing mechanism.
12 Based on EPA's guidelines for carcinogen risk assessment, the default low-dose
13 linear extrapolation approach is supported because there is some evidence of
14 genotoxicity without enough support for any potential alternative threshold
15 approach.

16 Slide 62, PERC is characterized as likely to be
17 carcinogenic in humans by all routes of exposure based on conclusive evidence
18 in multiple animal studies with limited evidence in humans. Data from the JISA
19 1993 study was selected for cancer dose-response analysis of three cancer types.
20 An NRC peer review panel for the 2012 IRIS Assessment recommended that the
21 hepatocellular cancer data be used for deriving cancer risk. Therefore, EPA used
22 the inhalation unit risk, or IUR, and slope factor, SF, from the hepatocellular
23 tumor data for risk estimation. EPA also presented the dose-response data for
24 mononuclear cell leukemia for comparison.

1 We are on Slide 63. Uncertainties and limitations in the
2 human health hazard assessment include the exclusion of immune and blood
3 effects from dose-response analysis based on ambiguous weight of evidence and
4 insufficient quantitative data, uncertainty in the WOE for liver effects, reduced
5 precision due to an absence of BMD modeling, uncertainty in PBPK dose metric
6 selection, uncertainty in dermal POD extrapolation, and potential over- or under-
7 estimation of cancer POD. Confidence determinations considered the above
8 points along with the range of PODs and the relative influence of various other
9 assumptions.

10 Overall confidence in acute endpoints is medium-high.
11 Overall confidence in chronic non-cancer endpoints is medium-high. And
12 confidence in cancer endpoints is medium, reduced based on the aforementioned
13 uncertainties. There is high confidence in the robust representative PODs
14 selected for use in risk estimation.

15 And finally, here I will overview the human health risk
16 characterization, which can be found in Section 4.2 of the draft risk evaluation
17 and relates to Charge Questions 6.1 to 6.5. This is Slide 64.

18 Here we are on Slide 65. The diagram on the left shows a
19 breakdown of the receptors and exposure routes evaluated in the risk evaluation,
20 as was shown earlier. Both acute and chronic risks were evaluated for
21 occupational scenarios, while acute risks were estimated for consumers. Non-
22 cancer risks were calculated by comparing the MOE, the ratio of the POD to the
23 exposure to the benchmark MOE.

1 For cancer, extra risk was calculated by the lifetime
2 exposure multiplied by the IUR or OSF. All risk estimates were presented both
3 with and without PPE for occupational scenarios, and EPA indicated for which
4 scenarios receptor use was not expected. Risks were not aggregated across
5 routes due to large uncertainties without a dermal compartment in the PBPK
6 model.

7 Here on Slide 66 is an example of occupational risk
8 characterization tables for a single OES, import and repackaging. As you can
9 see, risk estimates were presented for the acute endpoint, each representative
10 chronic endpoint, and cancer. Risks are shown for workers assuming both no
11 PPE and PPE with an APF up to 50 and glove protection factor up to 20, as well
12 as for occupational non-users who are not expected to use PPE. For this
13 particular example, monitoring or modeling data was not reasonably available
14 for ONUs, so EPA assumed that ONU exposure may be comparable to worker
15 central tendency values.

16 And here on Slide 67 is an example of the risk
17 characterization table for a consumer condition of use, aerosol brake cleaners.
18 Risks are identified, in bolded font, to users and bystanders for multiple
19 endpoints at various user intensities via both inhalation and dermal exposure.

20 This is Slide 68. Uncertainties in the human health risk
21 calculations for workers include the assumption that ONU exposure estimates in
22 the absence of ONU monitoring data are comparable to worker central tendency
23 values, resulting in low confidence for these risk estimates. EPA also applied
24 PPE use to worker risk estimates, which assumes proper training, fitting, and use

1 during the work activity. Absorption model parameters and assumptions for
2 worker exposure calculations may over or underestimate risk for any individual
3 based on use patterns, glove use, and other considerations.

4 For consumer exposure, EPA did not quantify chronic risk
5 to consumer users of PERC-containing products. However, chronic hazards are
6 not applicable for the vast majority of consumers based on typical frequency of
7 use. There is uncertainty which consumer COUs are likely to result in exposure
8 with impeded evaporation.

9 This is Slide 69. EPA identified potentially exposed or
10 susceptible subpopulations based on the definition from TSCA. Groups having
11 greater exposure than the general population include workers and occupational
12 non-users, including women of childbearing age and adolescents, along with
13 consumer users and bystanders, including children. Groups with greater
14 biological susceptibility include those with certain genetic polymorphisms,
15 developmental life stages, pre-existing health conditions and other environmental
16 factors.

17 Another major susceptibility factor is higher body fat
18 composition including fatty liver disease. And subpopulations with poor vision
19 or neurocognitive deficiencies may be especially susceptible to PERC effects.
20 The risk evaluation accounted for PESS by providing distinct risk estimates for
21 women of childbearing age and different consumer life stages and inclusion of
22 liver endpoint that may have reduced relevancy to the broader general population
23 without underlying susceptibility. EPA acknowledges being unable to quantify -
24 - quantitatively account for all PESS considerations or the full range of

1 responses. However, the ten times UF for human variability and other
2 considerations previously mentioned are expected to cover the vast majority of
3 the population.

4 Slide 70 covers an overall summary of the human health
5 risk characterization. Risks were indicated when noncancer MOEs were below
6 the benchmark MOE or extra cancer risks were above the benchmark. EPA
7 evaluated occupational risks based on both OES- and sector-specific
8 determinations of assumed PPE use. Risk estimates were shown for all plausible
9 PPE options as a what-if scenario, but these considerations were applied to risk
10 determination. Risks were identified for acute non-cancer, chronic non-cancer,
11 and cancer endpoints for several OES with chronic non-cancer risk estimates
12 being the most sensitive. Acute non-cancer risks were also identified for several
13 consumer conditions of use.

14 On this last slide, Slide 71, I would like to close the
15 presentation by bringing forward the risk characterization considerations per the
16 *Procedures for Chemical Risk Evaluation Under the Amended Toxics Substances*
17 *Control Act*. The same considerations go into the Administrator's
18 determinations about unreasonable risk. These include: integrating the hazard
19 and exposure assessments into quantitative and/or qualitative estimates of risk
20 for the identified populations, including potentially exposed or susceptible
21 subpopulations; describing whether aggregate or sentinel exposures under the
22 conditions of use were considered and the basis for their consideration; not
23 considering costs or other non-risk factors; taking into account where relevant
24 the likely duration, intensity, frequency, and number of exposures under the

1 conditions of use for PERC; and describing the weight of the scientific evidence
2 for the identified hazards and exposures. With that, I would like to conclude this
3 presentation and thank you for your attention.

4 **DR. KENNETH PORTIER:** Thank you, Dr. Lee, for
5 that presentation. At this point in the agenda -- or the next task of the Committee
6 in the agenda is to discuss and entertain questions to the OPPT technical staff on
7 the presentation and aspects of the DRE. I think what we're going to do is take a
8 15-minute break. I have 11:35 at this point.

9 We'll take a 15-minute break to 11:50, giving the panel
10 and the EPA staff a chance to catch their breath after that presentation. I will
11 point out to the Committee that you have been mailed a copy of the presentation.
12 It should be in your mail right now so that you can go back and review it and
13 formulate any questions you have of the PCE workgroup. So let's go ahead and
14 take that 15-minute break now. We'll reconvene at 11:50. Thank you.

15 (BREAK)
16
17

18 **SACC DISCUSSION ON OPPT PRESENTATION**

19
20 **DR. KENNETH PORTIER:** Let's call the meeting back
21 into order. Does anyone hear me?

22 **MS. TAMUE GIBSON:** Yes, I can hear you.

23 **DR. KENNETH PORTIER:** Thank you. So at this
24 point, we have time set aside for the Committee to ask questions of the PCE

1 workgroup team about any aspects of the presentation here today or the draft risk
2 assessment. At this point, we're not going to begin discussion of the product.
3 These are more clarifying questions.

4 I asked the panel to kind of utilize the hands up option in
5 the Webex to let me know if you want to ask a question. And while you're
6 trying to figure that out, I'm going to go ahead and ask my first question. And
7 Dr. Lee, you can pass it off to anyone on your team to answer.

8 But in thinking about your presentation on the near-field
9 and the far-field model, you talk about high-end exposures. And I wondered
10 how that relates or how you guys see that as it relates to the maximum exposure
11 or to something like the likelihood of a worker or a consumer experiencing this
12 high end. I realize you didn't do a probabilistic risk assessment, so I don't
13 expect you to give me a probability number. But I'm trying to figure out how to
14 interpret that term.

15 **DR. MARI LEE:** This is Mari Lee. I did the consumer
16 assessment, and you're correct that we don't have a probabilistic model. So it's
17 a deterministic model. So we are calling the high-end user -- it is the high end,
18 the 96th percentile input for the consumer models. But we don't have NSA exact
19 percentages of those in terms of the output -- the model.

20 But I do believe based on trying to combine all of the
21 high-end inputs that we are getting a higher exposure. I can't say that it's the
22 maximum. So you're correct that for consumer exposure estimates I cannot say
23 that the (inaudible) value I've given is the absolute maximum that a consumer
24 would be exposed to. Greg, would you like to input here?

1 **DR. KENNETH PORTIER:** You guys are breaking up
2 a little bit. Who was that that was speaking so we can get that on the record?

3 **DR. MARI LEE:** Mari Lee.

4 **MS. TAMUE GIBSON:** That's Mari Lee.

5 **DR. KENNETH PORTIER:** Oh, okay. Yeah. Got it.

6 It's just a little bit -- your microphone breaks up a little bit.

7 **DR. MARI LEE:** Sorry about that.

8 **MS. TAMUE GIBSON:** That's better, Mari. Thank you.

9 **DR. KENNETH PORTIER:** Now, Dr. Lee, you pointed
10 to someone else to chime in?

11 **DR. MARI LEE:** Yes, I'm trying to get Greg Macek on,
12 which perhaps he hasn't come back yet from the break. He is our occupational
13 exposure assessor.

14 **DR. KENNETH PORTIER:** Okie-doke. Does anyone
15 else on the Committee -- let's see. Dr. Doucette? Oh, okay. Go ahead. Make
16 your comment.

17 **DR. WILLIAM DOUCETTE:** Ken, you want me to
18 wait then? This is Bill Doucette -- or can I ask my question?

19 **DR. KENNETH PORTIER:** Yeah. I think didn't the
20 EPA guy come back?

21 **DR. WILLIAM DOUCETTE:** I thought I heard him --

22 **DR. KENNETH PORTIER:** Ah, go ahead and ask the
23 question.

1 **DR. WILLIAM DOUCETTE:** Go ahead and ask the
2 question? Okay. So I think I asked at one point --

3 **DR. KENNETH PORTIER:** Yeah. Go ahead and ask
4 your question.

5 **DR. WILLIAM DOUCETTE:** -- on TCE. Okay. I
6 think I asked this previously in the TCE panel review thinking about discharges
7 into the environment. I'm wondering if contaminated groundwater, regardless of
8 the source because PCE is a widespread groundwater contaminate -- how about
9 the issue of groundwater percolating into surface water sources? Is that under
10 our -- under review here, or is that something that should be considered? And
11 I've got a follow up question to that, too, once I get that answer.

12 **MS. YVETTE SELBY-MOHAMADU:** Hi, this is
13 Yvette Selby-Mohamadu. So regarding the question about groundwater
14 percolating to surface water, for this evaluation, we did not evaluate it because of
15 the pathway going to the general population. So we didn't look at that particular
16 pathway. We considered it covered under the regulatory nexus as well as
17 RCRA, which would deal with the potential (inaudible) issues because it is on
18 their hazardous waste list.

19 **DR. WILLIAM DOUCETTE:** But wouldn't that impact
20 the -- potentially in certain areas impact the surface water concentrations and the
21 risk assessment associated with those aquatic organisms exposed to that,
22 regardless of where the source comes from? It's a combined source, then.
23 Maybe that's fine. If you're going to justify that based on the other regulatory --
24 or the regulatory nexus, that's fine.

1 Can you answer another question for me? How about --
2 we talk a lot about wastewater, but one thing that we haven't talked about is
3 septic system discharge, which I think the last statistics are there are like 21
4 million households still within the U.S. that treat their waste for septic tanks.
5 And given the prevalence of PCE in consumer products, it's also likely that they
6 would be disposed that way. Who deals with the septic tank effluence and
7 pathways associated with that?

8 **MS. YVETTE SELBY-MOHAMADU:** Hi, this is
9 Yvette Selby-Mohamadu again. I will have to look into that a little bit further
10 for that specific issue. Typically, sewer or wastewater disposal, you know, is
11 under the POTW. So I will look into the septic tank issue.

12 **DR. WILLIAM DOUCETTE:** Okay. Thank you.

13 **DR. KENNETH PORTIER:** Thank you, Dr. Doucette.
14 I have five more people with their hands up. I'm going to continue with
15 environmental with Dr. Johnson, followed by Vorhees, Kissel, Pennell, and
16 Hossain. Dr. Johnson.

17 **DR. MARK JOHNSON:** Sorry, Dr. Portier. My
18 questions are not for environmental, so I'll put my hand down. Sorry.

19 **DR. KENNETH PORTIER:** Well, no. We can keep
20 with it because the rest of them are not environmental, so just go ahead and ask
21 your questions.

22 **DR. MARK JOHNSON:** Okay. Thank you. I noticed
23 on Slide 58 it was mentioned that DCA was considered the primary metabolite in

1 the liver. What is the primary metabolite for PCE in the lung since we're talking
2 about inhalation exposures?

3 **DR. KEITH JACOBS:** This is Keith Jacobs, human
4 health assessor. We actually -- I'll need to look into that to make sure I get you
5 the most accurate answer. I can look into it during break today and get back to
6 you.

7 **DR. MARK JOHNSON:** Okay. That's fine. Thank
8 you. Let me ask a follow up question. I saw that -- I guess this was on Slide 68 -
9 - that you just looked at acute exposures to consumers, but you looked at chronic
10 exposures to workers. But then I saw also on Slide 68 that there was a
11 continuous 24 hour -- it was adjusted for a continuous 24-hour exposure. So it
12 left me confused. Is there any circumstance -- and I didn't see any results on
13 hazard estimate of exposure to the general population for 24-hour exposures; am
14 I correct? What was the reason for, I guess, adjusting it for a continuous 24-hour
15 exposure is my question?

16 **DR. MARI LEE:** I think that's a misunderstanding for
17 consumers. This is Mari Lee. For consumer exposure, we're not adjusting it for
18 a 24-hour continuous use, but we are assuming a dissipation within the house of
19 use. So someone uses a product for a duration designed by our scenario, and
20 then that person is a stay-at-home -- in this case scenario, a stay-at-home parent.

21 So we're assuming that they are exposed during the peak
22 exposure during their actual use of the product, but then there is a dissipation of
23 that product as the air moves around the house, as there's air exchange from the
24 inside to the outside. So they have an exposure that dissipates throughout the

1 course of the day. So we used a 24-hour time weighted average for that value.

2 It's not a continuous 24 hours of use exposure. Did that help clarify?

3 **DR. MARK JOHNSON:** Yeah, I guess.

4 **DR. MARI LEE:** It's an acute use scenario.

5 **DR. MARK JOHNSON:** It's an acute use. So just
6 looking at repetitious intermittent spikes in exposure, or did you time weight
7 average -- did you smooth those spikes over a 24-hour chronic period?

8 **DR. MARI LEE:** It's a single use. It's a single use event
9 for a specified duration. So it's an acute exposure, single event exposure over
10 that specified duration of use. And then we're allowing that -- it's not multiple
11 uses throughout the day. It's not spikes throughout the day. It's one spike, one
12 use, and then the air concentration throughout the rest of the day as it dissipates.

13 **DR. MARK JOHNSON:** Okay. So you didn't calculate
14 a chronic accumulative concentration for a 24-hour continuous exposure?

15 **DR. MARI LEE:** No, not for consumer.

16 **DR. MARK JOHNSON:** Or not for worker, either,
17 right?

18 **DR. MARI LEE:** Greg, can you answer the question on
19 how you averaged what the occupational exposure scenarios look like in terms of
20 the 24-hour exposure? If Greg doesn't get on, he might be having some issues
21 with --

22 **DR. KEITH JACOBS:** I can chime in on that. I'll let
23 Greg correct me, but I'm pretty sure I know the answer to that. So we'll talk
24 about this later because we did also calculate for some of the COUs based on

1 eight-hour TWAs. But for those in which we did not, there was a -- that was a
2 24-hour average, where if we have an eight-hour TWA data it was averaged over
3 a 24-hour period to match.

4 And that's because the PODs -- to be consistent so we
5 didn't have to have confusion by different PODs for consumer and occupational,
6 the PODs were on a 24-hour basis. So then the occupational exposure was just
7 averaged over a 24-hour basis as well to be equal comparison. The math works
8 out the same either way, but it was just to make a consistent POD for both.

9 **DR. MARK JOHNSON:** Okay. The slide I was
10 referencing was Slide 58. I'm sorry. I'm looking at Slide 68 right now. Yeah.
11 That one. The first bullet is what I was looking at. So you took the IRIS number
12 -- you took the IRIS value that was for a continuous general population 24 hours,
13 and you adjusted for an eight-hour time weighted average?

14 **DR. KEITH JACOBS:** No, it was a 20 -- as it says, this
15 is for chronic. That's why, as Mari said, the acute for consumer's different.

16 **DR. MARK JOHNSON:** Right, right.

17 **DR. KEITH JACOBS:** If there was an eight-hour TWA,
18 let's say, of nine PPM, the 24-hour TWA was three PPM. So it's essentially just
19 dividing by the non-exposed time to get your average over 24 hours. And that's
20 to match the way that the HECs were derived, which was over 24 hours and that
21 would have been for consistency.

22 So we're consistent with the previous assessment, and
23 we're consistent in general throughout, like -- because some PODs were -- I
24 guess in this case acute was not actually used for chronic. But it's mostly to be

1 consistent with the previous assessment so that there was no confusion and
2 people thought that we were maybe changing numbers where we weren't
3 changing numbers. We did go in later, and you'll see that in the charge question.
4 We did in one instance do an occupational specific derivation for comparison.
5 But for most cases, to be consistent with past assessment, everything was on a
6 24-hour basis.

7 **DR. MARK JOHNSON:** Gotcha.

8 **DR. KEITH JACOBS:** Even though we used
9 derivations, it's all matched up.

10 **DR. MARK JOHNSON:** Okay. Yeah. Thank you very
11 much.

12 **MS. TAMUE GIBSON:** EPA, could you identify
13 yourself, please, for the record?

14 **DR. KEITH JACOBS:** Sorry. This was Keith Jacobs.

15 **MS. TAMUE GIBSON:** Thank you, Keith.

16 **DR. KENNETH PORTIER:** Okay. We've had
17 additional people, but the next person with their hand up is Dr. Vorhees.

18 **DR. CHARLES VORHEES:** Yeah. I just have a
19 clarifying question about -- with regard to what's on Slide 69 about potentially
20 susceptible -- exposed or susceptible subpopulations. Help me understand. I
21 thought the purpose of this provision was to provide an additional uncertainty
22 factor when PESS are identified. And you list here a number of potentially
23 susceptible subpopulations.

1 But in this risk assessment, as in some previous ones, you
2 don't actually invoke that 10x extra uncertainty factor but instead subsume it
3 under the UFH. So if that's the case, if you subsume it under the UFH, then
4 what is the purpose of having the PESS additional safety or uncertainty factor,
5 you know, if you don't invoke it?

6 **DR. KEITH JACOBS:** This is Keith Jacobs clarifying.

7 **DR. STANLEY BARONE:** Dr. Portier, this is Stan
8 Barone.

9 **DR. KEITH JACOBS:** Sorry. Can you clarify the
10 specific manufacturing --

11 **DR. KENNETH PORTIER:** Who was that?

12 **DR. KEITH JACOBS:** This is Keith Jacobs, EPA. Can
13 you clarify when you're referring --

14 **DR. STANLEY BARONE:** Keith, this is Stan Barone.
15 I'll respond to this. So Dr. Vorhees, this is Stan Barone. You are correct. We
16 do identify potential exposed and susceptible subpopulations per the TSCA
17 statute. That does fall within the 10X for human variability unless we have data
18 to indicate otherwise. There's not an additional safety factor of ten for
19 susceptibility. That's a misunderstanding, and I think you might be thinking in
20 the context of FQPA, where there's the FQPA factor for food use pesticides
21 where there's an additional safety factor of ten. We do not have that in TSCA. I
22 hope that helps.

23 **DR. CHARLES VORHEES:** I see. Okay. Thank you,
24 Stan. I appreciate that clarification.

1 **DR. KENNETH PORTIER:** Thank you --

2 **UNIDENTIFIED MALE:** You're breaking up.

3 **MS. TAMUE GIBSON:** Dr. Portier, I think he's --

4 **DR. KENNETH PORTIER:** Yeah. Dr. Kissel, you're
5 still muted. You should be able to speak now.

6 **DR. JOHN KISSEL:** Yeah. This is John Kissel. I have
7 questions on three slides. First one is slide number five. So there are -- on Slide
8 5, there are some numbers, not nearly as many as I would like to see, but for
9 instance, under cleaning and furniture care products, there's a number greater
10 than 348,770 pounds. That number is presented to five significant figures, even
11 though it is completely mysterious.

12 In the text in multiple places, there's an indication that
13 roughly 15 percent of total production is used in dry cleaning. Total production
14 is over 300 million pounds, so 15 percent of that is in the range of 50 million
15 pounds. And yet we have a number reported to five significant figures that's
16 only 348,000 pounds.

17 And this strikes me -- if you were looking at a football
18 game program and an offensive lineman's weight was reported as greater than
19 0.333333 pounds, it would be hard to dispute that fact, but that's not useful or
20 informative information. So what is that 348 -- my question is what is that
21 348,770 number, and why did you bother to write it down?

22 **MR. GREG MACEK:** This is Greg Macek from EPA,
23 risk assessment division. Can everybody hear me? Hello?

24 **MS. TAMUE GIBSON:** Yes, we can hear you. Yes.

1 **MR. GREG MACEK:** Yeah. Hi, I worked on -- I'm an
2 engineer assessor in the risk assessment division, so I worked on the wastewater
3 discharge and also occupational exposures. So this lifestyle diagram -- lifecycle
4 diagram, I agree with Dr. Kissel's comments that this really came from the
5 scoping document, which we just represented here. So the PV information in
6 there under the different uses, I agree, is incomplete. It's what we could glean
7 from non-CBI, CDR data. And I think that a comment that's been coming up in
8 the recent SACC meetings has been on constructing a mass balance for these
9 chemicals, which is something we're undertaking as an area we want to develop
10 our methodology.

11 But in the meantime, I do plan to get back to this diagram
12 and revise it for the final. And we'll try to put in the best production volume
13 information that we have, as well as any information on releases. A challenge
14 will be in closing the mass balance due to limitations from CBI and maybe some
15 of the databases we look at. But I agree. Right now, the PV information, other
16 than the starting production volume of 324 million is pretty incomplete on the
17 uses. And we're going to try to address that the best we can in finalizing the risk
18 evaluation.

19 **DR. JOHN KISSEL:** Okay. My second question has to
20 do with Slide 51. And so the third bullet says that there's uncertainties
21 associated with dermal exposure parameters and assumptions, and this went by
22 kind of fast. But what I heard you say was that you didn't have time to fix the
23 assumptions about neat versus aqueous solution exposures. And so basically the
24 numbers that are in the document don't count, and you intend to fix them later,

1 which puts us in kind of a pickle as far as providing an actual review if we don't
2 know what the numbers are ultimately going to be. Am I correct in that was
3 what I heard?

4 **DR. MARI LEE:** Yes, this is Mari Lee, and you are
5 correct. The TCE staff meeting happened not too long ago based on when we
6 have to get all of these documents published and through clearance. You have to
7 about calculate how much time that takes. So there was a limited amount of time
8 to incorporate the comments from the TCE SACC meeting into PERC.

9 But I wanted to note that we are redoing those
10 calculations. I can tell you that -- and we will discuss this, I think, when we get
11 to the -- perhaps when we get to the charge questions for consumer. But as noted
12 from TCE, we had used an aqueous Kp, and there was some questions about
13 whether the production -- sorry, not production, the weight fraction within
14 consumer products has very high percentages of PERC, perhaps above the
15 saturation limit in water. So that would affect the dermal exposures.

16 We -- I have found the neat Kp values, and we have the
17 preliminary recalculated results. And I'm in the process of incorporating them
18 into a final document. I can tell you that what was interesting to me is that the
19 neat Kp value is lower -- orders of magnitude lower than the aqueous Kp value.
20 So we need to do some more looking into really how to interpret that. But we
21 are taking into account the comments the SACC panel has made.

22 Unfortunately, just given the timeframe of when these
23 need to be published, the draft risk evaluation, it was not possible to include the
24 results. But there's still a lot of information in terms of the inputs and the way

1 we modeled exposures, the scenarios for which we modeled dermal exposures
2 that will be very helpful to have feedback on.

3 **DR. JOHN KISSEL:** Okay. Just a quick comment.
4 There's nothing surprising about the neat Kp being much lower because the
5 concentration in the neat solution is a million parts per million, and the
6 maximum saturation is around 200 parts per million. And they should get you to
7 the same place, more or less, barring skin damage. So that's not actually
8 surprising.

9 So my last question has to do with Slide 62. And this is
10 just, at the bottom of the slide in bold, there's an inhalation unit risk of 0.002 per
11 part per million, and then that's defined as a slope factor of 0.002 per milligram
12 per kilogram. But the part per million in the inhalation unit risk is parts per
13 million by volume, not parts per million by mass.

14 So that conversion doesn't actually work. And I don't
15 think that the second number there, the 0.002 per milligram per kilogram, is
16 actually used anywhere in the document. So it doesn't matter other than that it's
17 confusing for a public that's looking at these slides. But can you confirm that
18 that's a typo and not actual EPA science?

19 **DR. KEITH JACOBS:** This is Keith Jacobs, EPA. I did
20 myself double check those numbers because I took a step back when I realized
21 they were the same. I'm looking in our documents now. So the value is -- the
22 equivalent value is two to the negative third times ten to the negative third PPM,
23 or three times ten to the negative fourth in mgs per meter cubed.

1 And that does convert to 0.002 per mgs per kg. And that
2 value is used for the dermal occupational cancer risk estimates. So we do use
3 that number, and it's converted from the three times ten to the negative fourth
4 per mgs per meter cubed value. So probably should have included the mgs per
5 meter cubed value in here.

6 **DR. JOHN KISSEL:** Okay. I will check that.

7 **DR. KEITH JACOBS:** And yes, if that math is
8 incorrect, we certainly -- please let us know. And I can see -- it's on -- I can tell
9 you it's Table -- what table is it -- 3-10, which also includes the exposure factors
10 of how we did the conversion.

11 **DR. JOHN KISSEL:** I'm done.

12 **DR. KENNETH PORTIER:** John, can we move on?

13 **DR. JOHN KISSEL:** Yes.

14 **DR. KENNETH PORTIER:** Dr. Pennell?

15 **DR. MICHAEL PENNELL:** Hi, I got two questions.
16 One pertains to a particular slide. The other is kind of procedural. I'll start with
17 the one pertaining to a slide. So Slide 58 where you talk about -- you display the
18 uncertainty factors. The uncertainty factor of three for extrapolation from
19 animals to humans, is there a technical guidance recommending that factor when
20 the only thing you're extrapolating is due to uncertainty in the toxicodynamics?
21 If not, how was that number derived?

22 **DR. STANLEY BARONE:** Dr. Portier, this is Stan
23 Barone again. With regard to our uncertainty factors, the derivations are based
24 upon our guidance documents, which are referred to in the slide and in the risk

1 evaluation. So you're correct in your summary. And again, there's expert
2 judgement also involved in that. We are using a PBPK model. We do have
3 uncertainty about the pharmacodynamic component of the estimation. So the
4 PBPK model is reducing at least threefold the uncertainty factor. I hope that
5 addressed your question. Is that Dr. Lash?

6 **DR. MICHAEL PENNELL:** No, it's Dr. Pennell. I just
7 wanted to know if there was a technical guidance that you --

8 **DR. STANLEY BARONE:** Yes, there is.

9 **DR. MICHAEL PENNELL:** -- were referring to. Okay.
10 The second question is kind of procedural. So for the points of departure, I
11 noticed pretty much everything was -- you referred to the previous assessment.
12 Were you bound to use those points of departure, or, if you felt it was necessary
13 given maybe sort of advancements in sort of the science since the last
14 assessment, could you do your own dose response modeling?

15 **DR. STANLEY BARONE:** So this is Stan Barone again.
16 There was additional dose response modeling. We are not bound by previous
17 assessments. We did look at the previous assessments, again, evaluated those
18 studies and those points of departures independently. And in many cases, we
19 actually did use the same points of departure for the non-cancer endpoints.

20 **DR. MICHAEL PENNELL:** Okay. Thank you.

21 **DR. KENNETH PORTIER:** Dr. Hossain. And then
22 following Dr. Hossain is Willhite, Anderson, Gilbert, Lin, and Schlenk. Dr.
23 Hossain.

1 **DR. MUHAMMAD HOSSAIN:** Yes. I have one
2 clarifying question on environmental exposure and on Slide 20, for LC50 for
3 fish. So there is several kinds of fish that are there. So all or not, I can see the
4 similar sensitivity to the Perchloroethylene. So could you clarify what kind of
5 fish this is you used to determine the sensitivity for fish?

6 **DR. MARI LEE:** This is Mari Lee from EPA. Can you
7 repeat the question, please, and the slide number?

8 **DR. MUHAMMAD HOSSAIN:** Slide number 20.
9 Twenty, two zero.

10 **DR. KENNETH PORTIER:** It think that was 20.

11 **DR. MUHAMMAD HOSSAIN:** Yeah. I have a
12 question about the LC50 for fish to -- LC50 equal 12mg per liter. So there is
13 several kinds of fishes. So did you -- and all fishes are not similar -- have similar
14 sensitivity to Perchloroethylene. So what kind of fishes did you use to determine
15 the LC50 for fish in general? Did you get the question? Hello?

16 **DR. MARI LEE:** James? Sorry, Jim is working on an
17 answer. I believe he's going to get on in just a moment.

18 **DR. MUHAMMAD HOSSAIN:** Okay.

19 **DR. KENNETH PORTIER:** It looks like page 250 in
20 the risk assessment. It discusses rainbow trout and inland Silverside.

21 **MR. JAMES BRESSETTE:** Yes, this Jim Bressette
22 from the EPA. Am I coming through?

23 **MS. TAMUE GIBSON:** Yes. Yes, we can hear you.

1 **MR. JAMES BRESSETTE:** Yes. So that's correct for -
2 - the acute was inland silverside and also rainbow trout. And so what species we
3 used is dependent on what studies were done with PCE. And then we choose the
4 most sensitive of relevant tests, relevant studies. So we're not in complete
5 control of which fish species we're going to use. Did you also want to know the
6 chronic fish? Even though we didn't base the COC on it, it was the -- a fathead
7 minnow, and it was not as sensitive as invertebrates. But it was comparable.

8 **DR. MUHAMMAD HOSSAIN:** Okay. Thank you for
9 clarification.

10 **DR. KENNETH PORTIER:** Dr. Hossain?

11 **DR. MUHAMMAD HOSSAIN:** Yeah. I got it. Thank
12 you for the clarification.

13 **DR. KENNETH PORTIER:** Was that -- okay. Dr.
14 Willhite.

15 **DR. CALVIN WILLHITE:** Yes. Can you hear me, Dr.
16 Portier?

17 **DR. KENNETH PORTIER:** Just fine. Proceed.

18 **DR. CALVIN WILLHITE:** My question has to do with
19 your comment about groundwater and environmental. You asked about PCE
20 contamination in groundwater. If we go to the public comment letter from Safer
21 Chemicals Healthy Families, there's a description in there of that organization
22 along with some others sued EPA. The case was heard in the Ninth Circuit
23 Court, and the Ninth Circuit Court took the EPA to task on that very problem.
24 And it regards soil vapor intrusion into residences and buildings and whatnot

1 associated with PCE in groundwater. I'd like to get an answer from the EPA
2 where in this document is that covered and did they follow the admonitions of
3 the Ninth Circuit court in that respect. Thank you. I'll take my answer on mute.

4 **DR. KENNETH PORTIER:** Probably Dr. Barone.

5 **DR. STANLEY BARONE:** Dr. Portier, this is Stan
6 Barone. With regard to the question about groundwater and vapor intrusion, that
7 is an issue of regulatory nexus with our sister office of the Office of Land and
8 Emergency Response. So it is covered under other statutes and is being
9 regulated under other statutes, not part of this risk evaluation.

10 **DR. KENNETH PORTIER:** Thank you. Dr. Anderson?

11 **DR. HENRY ANDERSON:** Yeah. Just quickly
12 following up on that, as far as a regulatory approach, I can understand that. But
13 as far as an exposure assessment, clearly the documentation that's been provided
14 -- and there's a lot of data on groundwater contamination -- the statement in the
15 assessment basically assumes that this is all being controlled effectively. And
16 clearly I would suggest that, well, the statutes may there. They're not
17 particularly eliminating the transfer of contamination from groundwater or
18 drinking water into homes. So I think there's perhaps a little difference between
19 exposure assessment and then incorporating that into whether the workers or the
20 consumers may exposed to. So that's mostly just a statement.

21 My question really is to follow up on the past discussion
22 where basically all of these documents we've reviewed so far -- it seems the task
23 has always been covered by that 10x use in the risk assessment. And my
24 question to EPA is, at least going back in my early years, what is your definition

1 of what is covered by that? Typically the tried and true factor of 10 was to
2 account for genetic variability and gender sort of issues. I don't believe it was
3 ever intended to cover the occurrence of chronic diseases and the sort of things
4 that are identified here as being especially vulnerable populations.

5 And similarly, the standard ten didn't cover the fetus and
6 children, and that was the whole intent of the childhood up to a factor of ten for
7 that. And apparently -- how are you incorporating fetal risk because both
8 workers, female workers as well as community, are going to be exposed to that?
9 While you have the age of the individuals covered, you don't really address the
10 proportion of the working population that's actually present -- immediately
11 exposed or in homes where a woman is pregnant or has -- I think you --
12 somewhere, I think, you say that you're only covering ages 13 and above. But
13 just wondering why you don't take into account newborns and younger children
14 or the fetus.

15 **DR. STANLEY BARONE:** Dr. Anderson, this is Dr.
16 Barone in response. So the 10x, according to our Agency guidance, does cover
17 life stages. We will apply a larger uncertainty factor if it's a data derived
18 uncertainty factor. But in general, preexisting conditions and genetic variability
19 in life stage, all the biological aspects cover -- are covered by the 10X human
20 variability factor. They do not cover -- those uncertainty factors do not cover
21 exposure.

22 And on the exposure side of the equation, as we indicated,
23 we're generally using for the risk determination the high end, the 95th or 90th
24 percentile, in some cases the 99th percentile, to evaluate and determine risk for

1 susceptibility as it relates to the exposure. So I hope that answers your question.

2 It may not satisfy you, but I hope that answers your question.

3 **DR. KEITH JACOBS:** This is Keith Jacobs from EPA.

4 I just have a little more I can add. I agree with Dr. Barone. I will say in
5 response to comments from the TCE SACC panel we did add some further
6 discussion to the risk PESS section explaining the uncertainty around what that
7 10X does cover and what it may not cover. And I'm checking now.

8 There is a PESS section that does discuss exposure
9 considerations. And I don't know if it covers the specific percentage of pregnant
10 women, but it does cover -- it has the percentage of reproductive age of
11 employed persons, Table 2-94. It shows 22 percent, for example, of females of
12 reproductive age are in the manufacturing industry. So that does serve as a
13 surrogate for that.

14 **DR. HENRY ANDERSON:** Yeah. I guess what I'm

15 really looking for is the basis -- the science to suggest that actually those factors
16 are covered in the human population. I know -- I say going back over when 10X
17 started to be used, I'm not clear that there was any documentation for any -- that
18 those other groups are covered. So at some point, it would be worth just taking a
19 look at that. And we assume a lot of things, and then it just gradually grows.

20 And the assumption is that it includes all of those groups. But there can be some
21 specific groups that would be quite different.

22 **DR. STANLEY BARONE:** Again, this is Stan Barone,

23 Dr. Anderson. We can refer back to our previous RFC and RFD guidance
24 documents that the Agency's used and we've reviewed. We've had subsequent

1 reviews of the literature to look at human variability. There have been other
2 published articles on human variability as it relates to pharmacokinetics and
3 pharmacodynamics. We can do a better job citing those original publications.

4 **DR. HENRY ANDERSON:** I think that would be very
5 helpful because we really haven't looked at that kind of a thing for quite some
6 time. So at some point, to make references and go back to those documents
7 would be helpful because many of those are kind of lost in the fog of time for
8 me, anyway. Thank you.

9 **DR. KENNETH PORTIER:** Thank you, Dr. Anderson.
10 This is Ken Portier. I was thinking the same thing, Dr. Barone, that if you
11 actually do a risk assessment on a pregnant woman, if you've got the right
12 models, and it falls within that 10x, that's just further support that the 10x UFH
13 of ten actually covers those PESS individuals. Dr. Gilbert.

14 **DR. KATHLEEN GILBERT:** Hey, yeah. This is Kate
15 Gilbert. My question doesn't have anything to do with the presentation, but it
16 does have to do with the DRE. So when I'm going to be talking about human
17 health hazards in a couple of days, I'm going to be talking about what I saw as
18 some important study omissions. So that got me thinking again to the literature
19 flow diagrams, which I only sort of understand.

20 So I looked through the supplemental data files, and they
21 describe the search criteria and the inclusion and exclusion criteria. And I still
22 have a hard time understanding -- like I'm looking at Figure 1-6 on page 56.
23 And you start off with over 7,000 references and winnow that down to 70. So
24 we're ending up with less than 1 percent of the documents that we started with.

1 And I would just like somebody to explain, if they can, where some of those
2 documents go.

3 So in the initial exclusion, we exclude over 7,000 of the
4 documents. And I was just wondering if they could give us examples of what
5 would constitute a reason to exclude them and how -- what are the other search
6 criteria or criteria for determining the unacceptable valuation. Could you give us
7 some examples for that so that I can have a better understanding of how we can
8 start with so many and we end up with so few? And it looks like sometimes
9 we're omitting some important documents.

10 **DR. STANLEY BARONE:** This is Dr. Barone again,
11 Dr. Gilbert. Thank you. So for the search criteria, I don't have them in front of
12 me from the reference, but we'll find that and send that along where we actually
13 describe that. But just off the cuff, there are a number of factors that actually
14 lead to exclusion and inclusion. Primarily some of those factors include that the
15 chemical or the chemical synonym is included in the article, but it's not actually
16 a study of that particular chemical.

17 And the other topic -- one of the other exclusion criteria --
18 and we've discussed this before -- if the chemical is used and it's a single dose
19 study, oftentimes that leads to exclusion and use in the analysis. If the study is in
20 a foreign language journal and not translated, that can lead to exclusion from
21 further consideration. So those are just three of the exclusion criteria that leads
22 to a lot of the setting aside those references. We can trace those references back.

23 And again, we hope to do this in a more transparent way
24 in our future scopes. If you'll look to our scopes that are out for public

1 comment, we have interactive hop tree versus what's shown in the risk
2 evaluation. So we're instituting some technology and some improvements to try
3 to make this easier to follow and easier to understand.

4 **DR. KATHLEEN GILBERT:** Okay. Thank you. I just
5 have one other question. Referring again to that 1-6, you have a box that's
6 totally isolated that says, "Key Supporting Data Sources," that goes into lower --
7 into the -- after the initial data extraction. And it sort of looks like those studies
8 were not identified in the initial search. Or where did they come from?

9 **DR. STANLEY BARONE:** Again, this is Stan Barone.
10 Those studies that are in that box with the arrow that sidelines the search were
11 actually obtained from previous assessments. So we did backwards searching or
12 identified key studies that were identified in previous risk assessments -- peer
13 reviewed risk assessments or hazard assessments. We did not go through the
14 whole search strategy for those.

15 Those were -- bypassed the initial screening and went
16 straight to data evaluation to determine if they were on topic or off topic for the
17 current risk evaluation. And some of them actually were screened out after data
18 evaluation. But most of them actually were in as indicated by the flow diagram.
19 That will not be the case in the future. So we've modified things.

20 **DR. KATHLEEN GILBERT:** Okay. Thank you.

21 **DR. KENNETH PORTIER:** And this is Ken Portier.
22 Dr. Gilbert, it has always struck me that the process has low sensitivity or a high
23 false positive rate, and that's why you see so many of these documents thrown

1 out. They have a broad search. They capture everything, but very little of it
2 really produces information to the next stage. Dr. Lin.

3 **DR. ZHOUMENG LIN:** Hi, I have a question on Slide
4 58. The (inaudible), it is mentioned that human equivalent concentration of dose
5 were calculated through PBPK modelling. Could you clarify how the PBPK
6 model in animals and humans were run, based on what exposure scenarios in
7 order to attain the human equivalent concentration of dose? For example, how
8 long was the exposure duration used in animal model and in the human model?

9 **DR. KEITH JACOBS:** This is Keith Jacobs again, EPA.
10 As was discussed before, for animal studies, the output into an HEC was based
11 on a 24-hour continuous exposure duration for chronic endpoints. That would
12 incorporate the original exposure -- the internal dose derived by the model would
13 be based on the initial exposure duration of the study. But then once that was
14 BMD modeled based on the internal dose, that would be then output into an
15 equivalent human concentration or dose based on 24-hour continuous exposure.
16 So it's two separate steps. We get the internal dose of the animal, and then we
17 say what is that same internal dose in a person translated to the external dose
18 over the specified duration.

19 **DR. ZHOUMENG LIN:** I understand you. All right.
20 And from your explanation, in animal model, the exposure scenario was
21 selectively based on the study design. But what about the human model? If we
22 run the model with different exposure durations, the equivalent dose would be
23 different. So can you clarify if it is a 24-hour exposure, then exposure for how
24 long? For the lifetime exposure, is it 50 years or 70 years or for how long?

1 **DR. KEITH JACOBS:** Correct me if I'm not
2 understanding the question. So this was only used for animal studies. It did not
3 have a module to do human variability, which is why we retained the 10X for
4 intraspecies variability. So it was only based -- it was only used for translating
5 animal into human studies. So there was no -- if there were human studies, we
6 just used the data from the human study without the PBPK model.

7 **DR. ZHOUMENG LIN:** Thank you.

8 **DR. KEITH JACOBS:** And referring to the duration, as
9 I said before, there was some situations where we did also, for comparison,
10 provide a POD based on an occupational exposure. And that's a supplemental
11 analysis that was provided in the DRE. But most cases it was just this 24-hour,
12 seven day a week exposure. I don't think that -- only for cancer, I believe, did
13 the lifetime years of exposure really come into play.

14 **DR. ZHOUMENG LIN:** Thank you. I understand you.
15 It's 24-hour exposure, seven day per week. But my point is in order to attain a
16 human equivalent dose via PBPK modeling, this is kind of animal to human
17 model extrapolation. It has to run animal model first to get animal dosimetric.
18 And then it has to run the human model to get a human equivalent dosimetric.
19 And the animal model simulation can be based on the animal study, but the
20 human model has to be based on the exposure scenario, which include the
21 duration. So I understand it's a seven day per week, 24-hour per day. But my
22 point is for how long this duration?

23 **DR. STANLEY BARONE:** So this is Stan Barone. It
24 depends upon which condition of use we're talking about. And you're

1 absolutely correct. We use the animal model for PBPK model to get the proper
2 dosimetric in the conversion that Keith talked about and use the human model to
3 get to the dose metric depending upon which scenario -- whether we're talking
4 about five days a week, eight hours a day of an exposure. Or, in some cases, we
5 have conditions of use that are 10-hour shifts or 12-hour shifts. So depending,
6 we can develop with the PBPK model other kinds of outputs by running the
7 model backwards what that expected dose would be. But generally, as Keith
8 indicated, it's 24-hours of exposure is the general output that we're using.

9 **DR. ZHOUMENG LIN:** Okay. Thank you.

10 **DR. KENNETH PORTIER:** Thank you. This is Ken
11 Portier. That was my understanding, too, when I looked at the model. It
12 depends on the condition of use that sets the exposure time, and then you back
13 calculate what concentration over that exposure time would produce the internal
14 metric. Next is Dr. Schlenk.

15 **DR. DANIEL SCHLENK:** Yeah. I have -- I have a real
16 quick one. It has to follow up actually on Dr. Gilbert's sort of exclusion criteria
17 for the eco-hazard data. Just a very specific question about the Spencer et al
18 2002 study. This was a developmental tox study using Japanese medaka where
19 everything was ranked high, but then it was excluded. And it didn't provide -- at
20 least in the QAQC evaluation, it did not provide a rationale for why it was
21 excluded.

22 So I know you probably don't have that at hand right now,
23 but if you could look that up and get information back, that would be very, very
24 useful. My guess is it's maybe the concentrations were nominal and not

1 measured. But that's not listed at least in the evaluation document that I could
2 find. So that one I'm pretty sure Mark has a question about amphibians, too.
3 But the one I was really specific -- was really interested in was the Japanese
4 medaka developmental study that was done by Spencer et al 2002. So real
5 quick.

6 **MR. JAMES BRESSETTE:** Jim Bressette, EPA. I'll
7 look into that and then answer back to figure out why it didn't make the final list.

8 **DR. DANIEL SCHLENK:** Thank you very much.

9 **DR. KENNETH PORTIER:** Yeah. Dan, include that in
10 the discussion when we get to it. I have Dr. Doucette, Dr. Johnson, Dr. Cobb.
11 Dr. Doucette? Bill, I see you still muted on Webex. I'm going to go to Dr.
12 Johnson.

13 **DR. MARK JOHNSON:** Okay. Briefly, I saw that
14 Altman et al was referenced for the acute effects to the general population, and I
15 wasn't able to get the paper. So this question is just as much for my colleagues
16 as it is for the EPA. I noticed they measured pattern reversal visual load
17 potentials in the brain or on the surface of the scalp. And I guess these are
18 measured in terms of voltages and delays thereof. And they did note there's a
19 physical difference.

20 I was able to look at this -- at the abstract at 50 but not 10
21 ppm. And I was just wondering about the biological significance of that. It
22 sounds like it's something that's often measured, and it's very descriptive. I just
23 didn't know if it was just statistically different or if it was biologically significant

1 if that makes sense. And I was wondering if you could address the issue of
2 biological significance.

3 **DR. KEITH JACOBS:** This is Keith Jacobs, EPA. I
4 believe there was a discussion of the significance of EPs. I will have to find that
5 within the document. I do know that we did have an internal discussion about
6 that and found that they do represent a sensitive output of visual neural
7 processing. But, as I said, I'll try to find that now, and I can get that to you later.
8 And if we left that out of the document, that is something that we would
9 appreciate a comment on so that we can include it for the final.

10 **DR. MARK JOHNSON:** Yeah. That'd be great. Thank
11 you. It's an 800-page document. I could have missed it. I looked for it. But
12 yeah. If you could find out what the clinical significance is of those EPs, that
13 would be great. Thank you.

14 **DR. KEITH JACOBS:** And please let us know if -- the
15 papers should all be available for download. So, please, anyone else let us know
16 if, for whatever reason, you are having trouble. We might be able to just send
17 them to you if you need it.

18 **DR. STANLEY BARONE:** Just for -- this is Stan
19 Barone, in reference to that question from Dr. Schlenk. Visual evoked potentials
20 are measured in humans and in rodent models. There is internal validity for
21 those measures. And in the human data, there is quite a robust set of data
22 showing visual evoked potentials being altered by numerous chemicals and
23 drugs, both acutely and chronically following chronic exposure as well. So it is

1 an indication of an adverse effect and alterations in neural processing and neural
2 function.

3 **DR. MARK JOHNSON:** Thank you, Dr. Barone. This
4 is Mark Johnson. Yeah. I don't disagree there. I guess my question was -- and I
5 just want to be more specific -- is that if the EPA could be more specific or
6 explicit on how much is too much, that would be great. Over.

7 **DR. STANLEY BARONE:** Thank you for that
8 clarification.

9 **DR. KENNETH PORTIER:** Why ask for the moon
10 when you can get the solar system? Dr. Doucette.

11 **DR. WILLIAM DOUCETTE:** Sorry, Ken. I took my
12 hand down. It was left up from a previous comment.

13 **DR. KENNETH PORTIER:** Okay. Good.

14 **DR. GEORGE COBB:** Did we lose Ken?

15 **DR. KENNETH PORTIER:** George, your phone may
16 be on mute. Are you back?

17 **DR. GEORGE COBB:** Yeah. I'm here. I didn't hear
18 you call on me, Ken. Am I coming through?

19 **DR. KENNETH PORTIER:** Yeah. George? Yeah.
20 Yup. You're coming through. Go ahead and ask your question.

21 **DR. GEORGE COBB:** Okay. So this is probably for
22 Stan and follow up to several of the questions that have come through. I'd like
23 to know if there's any information on the progress of the evaluations for
24 biosolids and air by the Agency and how those -- the progress on those risks is

1 going to be incorporated into a comprehensive Agency-wide risk determination
2 for PCE in response to the TSCA requirements. That's the question.

3 **DR. STANLEY BARONE:** This is Stan Barone.

4 There's work underway on multiple chemicals, and I don't have a short answer
5 for you. These are part of ongoing efforts across the Agency, so there's not a
6 quick answer to that.

7 **DR. KENNETH PORTIER:** Dr. Davies.

8 **DR. HOLLY DAVIES:** Hi, I have a few questions after
9 looking at EPA's 2014 *Framework for Human Health Risk Assessment to Inform*
10 *Decision Making*. First question is about audience. The document mentions that
11 risk assessment should be presented to be readily understandable and useful for
12 the intended audience. And I'm still not sure who the audience is for these draft
13 risk assessments. And I think it would clear up some of our comments if we
14 knew exactly who it's intended for.

15 The second question is on environmental justice. Section
16 2.1 has a good description of environmental justice, and I'm wondering if the
17 Agency's environmental justice staff is involved in the consideration of the
18 potentially exposed and susceptible subpopulations in these risk evaluations.
19 And the third question goes back to the systematic review and how this
20 integrates with the systematic review.

21 Some of the ten risk evaluations that are out, the draft ones
22 that are out, only mention one use for this document. But most of them mention
23 it twice, both for using Section 2.2. in developing the problem formulation and
24 then the use of this to evaluate, extract, and integrate the human health hazard

1 and dose response information, which seems really similar to what the
2 systematic review is supposed to do. So I'm wondering how this works together.

3 **DR. STANLEY BARONE:** Dr. Davies, could you repeat
4 the last part of that question? This is Dr. Barone.

5 **DR. HOLLY DAVIES:** So the last part -- the third
6 question was about how this risk assessment to inform decision making
7 document works with the systematic review because the draft risk assessments
8 mention both of them for evaluating, extracting, and integrating the data for
9 human health hazard and dose response. And in some of the draft risk
10 evaluations, table -- figure 3 -- what's used as Figure 3.1 in the beginning of the
11 human hazard, sometimes it says that that process is from the systematic review.
12 And sometimes they say the process is from this 2014 document, and sometimes
13 they say it's from both of them.

14 **DR. STANLEY BARONE:** Thank you. This is Stan
15 Barone. So I'll actually answer the last question first with regard to systematic
16 review and we could be more clear. So the applications document that Dr.
17 Davies referred to in 2014 is the rudimentary protocol for the TSCA risk
18 evaluations. So it does contain the description of how we implement systematic
19 review in our problem formulations and our actual risk evaluations.

20 And we have received many comments about that, as well
21 as comments from you -- you, particularly, Dr. Davies, and others on the
22 Committee -- and are working to take your comments into account. There isn't
23 another systematic review protocol or generic protocol. That is what is existing

1 right now and the description that we have in the risk evaluations themselves, the
2 specificity of each systematic review elements in the risk evaluation.

3 With regard to the intended audience, we've had
4 discussion previously at these meetings about the intended audience, and the
5 intended audience is broad. It serves our risk managers. These risk evaluations
6 will serve risk managers, decision makers within the Agency. Of course, we
7 view you, the Scientific Advisory Committee on Chemicals, as a key audience,
8 key customer because you represent the scientific credibility and evaluation for
9 the community outside of EPA. We also look to try to incorporate plain
10 language for the public as much as possible.

11 It is a science document, and we cannot obviate or skirt
12 the scientific responsibilities of the analysis that's required. So it's multiple
13 audiences that these documents are trying to inform, but we hope that we have
14 included enough information in the body of the document and the appendices to
15 underpin future science-based, risk-based assessments. And your comments, of
16 course, help us in improving the readability, clarity, and the technical analysis of
17 the documents.

18 With regard to PESS, our sister offices do review and
19 comment on our description of PESS. We have been actively engaged with our
20 Office of Environmental Justice and Office of Children's Health Protection who
21 have commented in the past. The Environmental Justice Office deals more with
22 us in the context of risk management, generally, and implementation. Whereas
23 our Office of Children's Health Protection works more from soup to nuts in the

1 problem formulation scoping all the way to the risk management. So that's just
2 how we work internally, but hopefully that clarifies how we're interacting.

3 **DR. HOLLY DAVIES:** Yes, thank you.

4 **DR. KENNETH PORTIER:** Ruthann Rudel.

5 **MS. RUTHANN RUDEL:** Thank you. Sorry for the
6 delay unmuting. I have three questions, so I'm going to try and make them fast
7 because I think we're in lunchtime. Two are about exposure concentrations.
8 One is about the study choice for neurological endpoints.

9 So I noticed -- and I think this is related to what Mark
10 Johnson was asking about earlier. I was surprised to see that the acute exposure
11 concentrations that you calculated for workers and ONUs are lower than the
12 eight-hour TWAs, time weighted average measured or modeled exposures. I
13 guess they're mostly measured. I think that I understand this is because you
14 average them over 24 hours. But acute effects -- what's the rationale for
15 averaging eight-hour exposures over 24 hours for acute effects, I guess? That's
16 question number one.

17 And second is what is your rationale for not considering
18 chronic health effects from consumer exposures, for example, from dry
19 cleaning? And my third question is about the choice of studies for the neural
20 effects. I'm curious why you didn't use the Getz 2012 or the Roberts 2013, both
21 of which were included in the discussion of this endpoint and seem to be high
22 quality studies, to supplement the two older studies that you chose as the basis
23 for this point of departure.

1 **DR. STANLEY BARONE:** I'm going to ask Dr. Branch
2 and Dr. Jacobs to address your two questions. This is Stan Barone.

3 **DR. KEITH JACOBS:** Sorry. I was on mute. Thank
4 you, Stan. I started speaking but to nobody. The acute endpoints actually were
5 compared directly to the applicable TWA kind of as was alluded to before in
6 response to a previous question. They were not adjusted to a 24-hour basis. So
7 I'm looking at Table 3-5, for example, acute PODs. If the occupational exposure
8 -- sorry, I misspoke. It's a bit different if you're talking about consumer or
9 occupational. For consumer because it's based on, as Mari Lee went into, a 24-
10 hour --

11 **MS. RUTHANN RUDEL:** I was definitely talking about
12 occupational -- occupational because -- I'll try to find the table. Yeah.

13 **DR. KEITH JACOBS:** Yeah. For occupational, it was
14 used directly with an eight hour or 12-hour TWA, depending on the condition of
15 use. So there's a table where we basically have the POD for difference
16 equivalent durations. It's a four hour, eight, 12, and 24. So either the eight- or
17 12-hour value was used.

18 I'd have to sit down and compare that closer to the chronic
19 numbers to see how they come out because you're not comparing exactly apples
20 to apples. You're comparing eight-hour value to eight-hour value versus 24-
21 hour value to 24-hour value. So it's a bit harder to make that jump.

22 And there is a discussion, as you said, about Getz and the
23 other studies. This was the studies chosen for chronic -- if you're talking about
24 chronic now, or are you talking about the acute for the study selection?

1 **MS. RUTHANN RUDEL:** For the Getz and Roberts, my
2 question was related to chronic.

3 **DR. KEITH JACOBS:** So the selection of those studies
4 was consistent with previous assessment. And I'd have to look -- delve deeper
5 into to see why specifically those were chosen over Getz. I do know we
6 discussed Getz. I can't off the top of my head pull up why those specific
7 selections were chosen.

8 **MS. RUTHANN RUDEL:** Okay.

9 **DR. KEITH JACOBS:** It might be study duration. It
10 might be -- since it's -- I know general considerations that broadly we use are if
11 there was a longer exposure duration or if the doses used covered a broader or
12 more sensitive range, the population that was exempt. Because they were
13 occupational studies, the ones that were chosen.

14 **MS. RUTHANN RUDEL:** They were not. Those two
15 are both general population studies.

16 **DR. KEITH JACOBS:** Sorry. I mean human. Sorry.
17 Yeah. They're human studies.

18 **MS. RUTHANN RUDEL:** They're human studies of the
19 general population. One is from the Cape Code park leaching from the drinking
20 water pipes, and one is from the Nurses' Health study. I thought that they
21 provided an opportunity to look at maybe lower exposures than were in the other
22 two studies. But I'm not sure about that. But no, that's okay. You don't need to
23 speculate.

1 So going back to my question about the acute averaging
2 time, so can you explain at like Table 2-59 there's eight and 12-hour TWA
3 exposures. And then the acute concentration is in the next column. And it's
4 always lower. And it seems like it's lower because it's eight divided by 24. But
5 maybe you can help me understand, or maybe this is --

6 **DR. KEITH JACOBS:** So that's -- I'd have to find that
7 table, but that seems to be what I was discussing before where that's if the 20 --
8 if a 24-hour chronic value is used, yes, the 24-hour average is less than the eight.
9 But for the acute -- that would probably be used for the chronic, tied to the
10 chronic studies. For the acute, they were compared directly to eight hour or 12-
11 hour TWAs.

12 And I think the easiest way sometimes to look at the -- get
13 at this is in the risk -- the supplemental risk calculator file where it contains the
14 PODs and the exposure values and then MOEs, and you can directly see in the
15 formulas how they're compared for each COU and each endpoint. Because it is
16 complex when you're talking about acute versus chronic versus dermal versus
17 inhalation and occupational difference they used.

18 **MS. RUTHANN RUDEL:** All right. Well, I just -- what
19 I see in the 2-59 is that the eight or 12-hour TWAs are all high end, and then the
20 acute concentration -- this is just inhalation, but maybe there's something
21 different that happens later in the process.

22 **DR. KEITH JACOBS:** The eight-hour exposure -- this
23 is exposures you're talking about, so that's not PODs. That's the exposure
24 section.

1 **MS. RUTHANN RUDEL:** Yes.

2 **DR. KEITH JACOBS:** Yeah. So the average -- the
3 eight-hour value is the actual exposure weighted average. That average over 24
4 hours is less because you're only exposed for the duration of your workday,
5 whether eight hours or 12 hours. And then that is averaged over the full 24-hour
6 workday. And as previously discussed, that's to be consistent on the POD side.

7 But then it does make -- so essentially the POD -- the
8 MOE math ends up the same. Your adjusting the PODs to be more sensitive
9 over a 24-hour period, but then you're also equivalently reducing the average
10 exposure over that period. So it depends how you're using it, but the numbers
11 come to the same.

12 **MS. RUTHANN RUDEL:** Okay. I see what you're
13 saying. And then did you answer the question about why the consumer dry
14 cleaning exposure is not used in context of chronic health effects.

15 **DR. MARI LEE:** Hi, this is Mari Lee on the phone. I
16 can talk about that. So over the -- across the board, we made a decision to be
17 consistent across chemicals and to assess them. We did assess actually all
18 conditions of use for both acute and chronic but only present acute risks. I agree
19 that there is a potential for chronic exposure for someone that uses dry cleaning
20 on a regular basis. And that's a very good point, and that's something that we
21 will consider for the final risk evaluation.

22 **MS. RUTHANN RUDEL:** Thank you.

23 **DR. KENNETH PORTIER:** This is Ken Portier. I
24 realize we're into the lunch break, and I'll extend it a little bit because I have one

1 question on Slide 62. On Slide 62, you -- can we move it to 62? There we go.
2 The first bullet, you say PCE is characterized as “likely to be carcinogenic in
3 humans by all routes of exposure.” And I’m assuming that this follows the
4 assessment -- the 2012 IRIS assessment as well.

5 And I’ve been thinking about weight of evidence and how
6 that kind of fits into this statement. And I was looking at what the pesticide
7 program uses when they move from likely to be carcinogenic to actually
8 carcinogenic, the higher evidence level, if you like. And in describing
9 carcinogenic to human, the first bullet point -- it basically says there’s kind of
10 two conditions under which it can be carcinogenic. One is you have convincing
11 epidemiology evidence -- epidemiologic evidence of a causal association. And
12 I’m assuming that’s kind of strict Bradford Hill criteria. You go through the
13 whole thing and there it is.

14 But the second bullet point says “exceptionally,” and it
15 lists four conditions under which you might consider a chemical being
16 carcinogenic instead of likely carcinogenic. And as I look at this chemical and
17 the evidence that you’ve laid out in this DRE, I see kind of strong evidence for
18 all four of these secondary conditions. So my question to you is whether
19 TSCA’s using a slightly different set of criteria than the pesticide program, or
20 basically have you just not considered this exceptional case?

21 **DR. STANLEY BARONE:** So this is Stan Barone, Dr.
22 Portier. We all use the 2005 cancer guidelines for hazard classification for
23 carcinogenicity. And as you pointed out, the data for PERC is -- there’s not that

1 strong epidemiological evidence of a causal association. There is
2 epidemiological evidence, but it's really the animal evidence which is strong.

3 And again, what is a high likely versus a human
4 carcinogen, how much -- how far do you go to reach that tipping point is
5 something we discuss and cogitate over. But it is strong evidence that this is
6 carcinogenic to humans, and it falls in the likely -- into that likely bin. We
7 haven't changed that from the previous IRIS assessment.

8 **DR. KENNETH PORTIER:** Okay. Just wondering, and
9 I suspect this is going to come up again in our discussion in the committee. Dr.
10 Johnson, I see your hand still up. Oh, gosh. Ruthann, your hand's up. Others.

11 **DR. MARK JOHNSON:** Yeah. Ken, this is Mark
12 Johnson.

13 **DR. KENNETH PORTIER:** Yes, Dr. Johnson.

14 **DR. MARK JOHNSON:** Hopefully, this will be a quick
15 question. You looked at acute exposures to the general population. You looked
16 at chronic exposure to workers. Why -- this is an obvious -- why did you not use
17 the AEGLs for acute to the general population, and why would you not consult
18 the other existing industrial hygiene values that are out there for the occupational
19 worker? Over.

20 **DR. KEITH JACOBS:** This is Keith Jacobs. If you're
21 referring to why we did not, I believe we include a discussion of the AEGLs. If
22 we did not, that was an oversight. I thought it was perhaps in the occupational
23 section. The AEGLs typically are less sensitive than PODs for specific

1 endpoints. The AEGLs are more overt clinical signs and tend to be much less
2 representative of molecular changes.

3 **DR. STANLEY BARONE:** This is Stan Barone to add
4 to Dr. Jacob's comments about the AEGLs. The acute exposure guidelines were
5 developed level 1, level 2, level 3 for emergency responders. And again, while
6 we use them in the peer review and POD development of the AEGLs, oftentimes
7 -- and particularly when we're talking about risks to the consumer and general
8 population, we're not talking about emergency responders.

9 So we look at studies -- high quality studies that are
10 appropriate for the condition of use. And in many cases, we have even better
11 studies than what were considered for the AEGL program for those conditions of
12 use. And they may be chronic. They may be acute. So that's in addition to what
13 Keith offered.

14 **DR. KENNETH PORTIER:** Thank you. I think the last
15 comments will come from Dr. Willhite, and then we'll break for lunch. Calvin.

16 **DR. CALVIN WILLHITE:** Yes, sir. I'd like to correct
17 Dr. Barone on the AEGLs. They are not simply for the fire department or law
18 enforcement. These are used in land use planning. They're used in planning for
19 and avoiding such incidents. That's number one. But the question that I have --
20 and it went to nice lady who explained a little bit about dry cleaning. The
21 comment was concerning acute and chronic exposures.

22 Acute I can see where you've tried to model somebody
23 bringing home their newly cleaned blouse or trousers. However, we have a
24 whole series of studies from the state of New York. I'll read one.

1 “Tetrachloroethylene levels in residential dry-cleaning buildings in diverse
2 communities in New York.” Second one, “Apartment Residence and Daycare
3 Workers, exposures to Tetrachloroethylene and Deficits in Visual Contrast
4 Sensitivity.” How was it that you handled these chronic exposures that are well-
5 documented by the state of New York? Thank you. I’ll take my answer on
6 mute.

7 **DR. MARI LEE:** Hi, this is Mari Lee. So we certainly
8 saw those articles. We reviewed those articles. However, there is legislation
9 that will exclude the use of Perchloroethylene in residential co-located buildings
10 I believe this year. I believe it’s 2020. So that was not included in the risk
11 evaluation because it is already being regulated. And dry cleaners that use
12 PERC will no longer be allowed to do so in residentially co-located buildings.

13 **DR. KENNETH PORTIER:** Thank you. Dr. Kissel,
14 you had a final comment.

15 **DR. JOHN KISSEL:** Yeah. I just wanted to follow up
16 on my previous question about Slide 62. So the inhalation unit risk converts to a
17 -- directly to a dermal slope factor of 0.01, not 0.002. The 0.02 is listed, and
18 there’s no explanation of this in the text. It’s listed as an oral to dermal slope
19 factor, and I don’t understand how you get an oral to dermal slope factor from an
20 inhalation study. So if you could explain the conversion from the inhalation to
21 dermal to oral to dermal, I would appreciate it.

22 **DR. KENNETH PORTIER:** I think I’ll ask EPA to kind
23 of put that in a memo and send it to the DFO who can send it to us later today
24 because I think it’s really time we break for lunch. We planned on a 45-minute

1 lunch break reconvening at -- I've got to look at my agenda here -- 1:45. I think
2 right now we need to reconvene a little bit after 2:00. So let's shoot for
3 reconvening at 2:00. And we'll probably really start at 2:05. Thank you.

4 **MS. TAMUE GIBSON:** Okay. Thank you.

5 **DR. KENNETH PORTIER:** Tamue, would you let the
6 public commenters know we're going to start 15 to 20 minutes late?

7 **MS. TAMUE GIBSON:** Yes. I'm crafting my email
8 now. Yes.

9 **DR. KENNETH PORTIER:** Okay.

10 **MS. TAMUE GIBSON:** Thank you.

11 **DR. KENNETH PORTIER:** We'll see you guys all
12 back at five after the hour.

13 **MS. TAMUE GIBSON:** Thank you.

14 (LUNCH BREAK)

15 **DR. KENNETH PORTIER:** Okay. I have 2:00. Let me
16 go ahead and -- it looks like we're ready. We're up. Panelists, if you're on, if
17 you would just raise your hand in Webex, I'll know you're back, and we can
18 actually do a quick roll call here. So Tamue, it looks like most of the Committee
19 -- almost all of the Committee is back again. I'm going to proceed with a quick
20 roll call.

21 **MS. TAMUE GIBSON:** Panelists, if you'll unmute your
22 line, we can go through this pretty quickly. I'll just call your name and say here.
23 We'll start with Dr. Anderson.

24 **DR. HENRY ANDERSON:** Present.

1 **DR. KENNETH PORTIER:** Dr. Barton? Dr. Bennett?
2 Dr. Blystone?
3 **DR. SHERI BLYSTONE:** Here.
4 **DR. KENNETH PORTIER:** Dr. Bruckner?
5 **DR. JAMES BRUCKNER:** Here.
6 **DR. KENNETH PORTIER:** Dr. Cory-Slechta? Dr.
7 Davies?
8 **DR. HOLLY DAVIES:** Here.
9 **DR. KENNETH PORTIER:** Dr. Doucette? Dr. Gilbert?
10 **DR. KATHLEEN GILBERT:** I'm here.
11 **DR. KENNETH PORTIER:** Dr. Johnson?
12 **DR. MARK JOHNSON:** Here.
13 **DR. KENNETH PORTIER:** Dr. Kaufman? Dr. Kissel?
14 **DR. JOHN KISSEL:** Here.
15 **DR. KENNETH PORTIER:** Dr. Rowlands?
16 **DR. CRAIG ROWLANDS:** Here.
17 **DR. KENNETH PORTIER:** Ruthann Rudel?
18 **MS. RUTHANN RUDEL:** I'm here.
19 **DR. KENNETH PORTIER:** Dan Schlenk?
20 **DR. DANIEL SCHLENK:** Here.
21 **DR. KENNETH PORTIER:** Dr. Apte?
22 **DR. UDAYAN APTE:** Yeah. I'm here.
23 **DR. KENNETH PORTIER:** Dr. Cobb?
24 **DR. GEORGE COBB:** Here.

1 **DR. KENNETH PORTIER:** Dr. Daniels?

2 **DR. MICHAEL DANIELS:** Here.

3 **DR. KENNETH PORTIER:** Dr. Grant? Dr. Hossain?

4 **DR. MUHAMMED HOSSAIN:** I'm here. I am here.

5 **DR. KENNETH PORTIER:** Thank you. Dr. Lash? Dr.

6 Lin?

7 **DR. ZHOUMENG LIN:** Here.

8 **DR. KENNETH PORTIER:** Dr. Meliker?

9 **MS. TAMUE GIBSON:** He's out for this afternoon.

10 **DR. KENNETH PORTIER:** Oh, that's right. He's out

11 this afternoon. Dr. Roby?

12 **DR. KATHERINE ROBY:** Here.

13 **DR. KENNETH PORTIER:** Dr. Vorhees?

14 **DR. CHARLES VORHEES:** Here.

15 **DR. KENNETH PORTIER:** Dr. Willhite? Calvin, you

16 here? He may be on mute. I see your hand up.

17 **DR. CALVIN WILLHITE:** Am I back?

18 **DR. KENNETH PORTIER:** Dr. Pennell? Yup.

19 There's Calvin. Thank you. Dr. Pennell?

20 **DR. MICHAEL PENNELL:** Here.

21 **DR. KENNETH PORTIER:** Dr. Barton? Dr. Cory-

22 Slechta? Dr. Kaufman?

23 **MR. ALAN KAUFMAN:** I am here.

1 **DR. KENNETH PORTIER:** There we go. Dr. Grant?

2 Dr. Lash?

3 **DR. LAWRENCE LASH:** I'm here. Can you hear me?

4 **DR. KENNETH PORTIER:** Yup. Gotcha.

5 **DR. LAWRENCE LASH:** Okay. Good.

6 **DR. KENNETH PORTIER:** Okay. We're missing Dr.

7 Grant and Dr. Cory-Slechta and Dr. Barton. Let's proceed, Tamue, with the

8 public comments.

9

10 **PUBLIC COMMENTS**

11

12 **MS. TAMUE GIBSON:** Okay. All right. Public

13 commenters, you have five minutes. First on the list -- and I apologize for the

14 mispronunciation of your name. Abdel Jalil Mekkaoui, you're first on the list to

15 present your public comments to the Committee. Are you here? Are you

16 available? Battelle, is that individual on the line? Can you see that?

17 **MR. MARTIN ALVARADO CORTES:** Tamue, that

18 person is not on the line.

19 **MR. VINCENT BROWN:** Yeah. We can't see his

20 name, so he may be dialing in but needs to reconnect to the Webex against first

21 and last name, he or she.

22 **MS. TAMUE GIBSON:** All right. We'll come back.

23 The next individual is registered as Tanyatap Meliam. Tanyatap Meliam?

1 **MR. MARTIN ALVARADO CORTEX:** Tamue, that
2 person is also not on.

3 **MS. TAMUE GIBSON:** Okay. Great. Thank you. The
4 next individual is Gary Timm. If you can unmute your line, Gary Timm.

5 **MR. GARY TIMM:** Yes, do you want me to go ahead
6 and make my presentation now?

7 **MS. TAMUE GIBSON:** Yes, would you please. Yes.
8 Thank you.

9 **MR. GARY TIMM:** I would be happy to do so. Good
10 afternoon. My name is Gary Timm. Today I am representing the Environmental
11 Protection Network, an organization comprised over 500 EPA alumni
12 volunteering their time to protect the integrity of EPA, human health, and the
13 environment.

14 First, I want to express empathy for the EPA staff who are
15 shouldering a heavy workload and working under tight deadlines to conduct the
16 risk evaluations under TSCA. We have all been there. However, EPA needs to
17 ensure that its risk evaluations address all important components and provide
18 adequate time for public input before peer review.

19 The court decision in *Safer Chemicals Healthy Families*
20 *vs. EPA* in the Ninth Circuit now obligates the Agency to consider legacy uses
21 and disposal when conducting risk evaluations. Thus, EPA must provide
22 documentation of the absence of any legacy uses or identify and assess these
23 uses for both environmental and human health consequences. In the real world,
24 people may be exposed to chemicals of concern in a work setting and as a user,

1 consumer, or bystander of a product, as well as through the ambient
2 environment.

3 The Agency states in the risk evaluation rule that they
4 must describe whether or not they have considered aggregate exposures in their
5 assessments. EPA has not, however, conducted such an assessment. The
6 Agency has neither accounted for multiple routes of exposure known to occur
7 simultaneously during a specific condition of use -- in this case inhalation and
8 dermal -- nor with consideration of exposures from non-TSCA related scenarios.

9 There is another dimension to the human health and
10 environmental assessments that should be acknowledged and incorporated into
11 the PERC risk evaluation. That is cumulative risk assessment. We identified
12 several criteria that should be applied when determining when a cumulative risk
13 assessment would be appropriate: one, concomitant exposure to a category or
14 subcategory of conditions of use; two, close structural similarities -- that is
15 members of the same chemical class; three, shared metabolic pathways and
16 byproducts of metabolism; four, similar toxicity profiles; and five, similar modes
17 or mechanisms of action of shared toxicity endpoints.

18 The sextet of chlorinated VOCs listed in Table 3-4 meet
19 most, if not all, of these criteria. The lack of aggregate and cumulative
20 assessment clearly leads to an underestimation of exposure and risk and
21 potentially a declaration of no unreasonable risk when one actually exists. PERC
22 has been detected in rain from industrial cities in the UK and the U.S.A. and in
23 snow in Australia, Italy, and (inaudible). It is found in human blood, urine, and
24 breastmilk. It's widespread presence in outdoor/indoor air is well-documented.

1 Yet EPA does not address risks to the general population
2 and actually concludes that chronic health effects are not relevant to consumers,
3 despite the evidence of ongoing chronic exposure. The risk evaluation should be
4 integrating these findings and examining their implications not only under TSCA
5 but under other laws like the Clean Air Act where there is reason to believe that
6 emissions are not being adequately controlled and risks are excessive.

7 With regard to environmental risks, confidence in acute
8 and chronic concentrations of concern for fish and invertebrates is high.
9 However, confidence in the algal COC is medium given it is based on a single
10 study and all three algal species tested may not represent the most sensitive
11 species. Therefore, one recommendation that would help improve EPA's aquatic
12 risk evaluation would be to conduct further algal testing using additional species.

13 With respect to the risks to human health, the hazard
14 database available on PERC reveals substantial numbers of studies in both
15 humans and animals that would appear to adequately address the needs for a
16 robust assessment without having to account for any key data deficiencies.
17 However, there are two exceptions to this. There are indications in both human
18 and animal studies that PERC has the potential to produce adverse effects on the
19 immune system and various hematological components. However, as EPA
20 notes, the data on these endpoints were not adequate to determine dose response
21 and are not accounted for in this risk evaluation.

22 The consequences of this insufficiency is that a conclusion
23 of no unreasonable risk could be made with regard to a condition of use when
24 one actually exists. Therefore, we recommend the following: one, incorporate an

1 additional uncertainty factor of at least three for data deficiencies in each chronic
2 benchmark MOE for all the noncancer endpoints used in the risk evaluation;
3 revise chronic inhalation and dermal risk estimations and determinations for
4 conditions of use; three, use enhanced testing authority to require additional
5 observations in the human cohorts and/or nonhuman studies to answer the
6 outstanding questions using standardized or tailored study designs and
7 incorporate these results in a final evaluation; and four, if the results of the new
8 study show the PODs for other endpoints are sufficiently protective any potential
9 immune or hematological effects, reduce the benchmark MOEs accordingly.

10 Thank you for this opportunity to present a summary of
11 EPN's comments. We invite your attention to our full written comments.

12 **MS. TAMUE GIBSON:** Oh, great. Thank you so much
13 for your comment. And if you could email that to me, I would greatly appreciate
14 that. Next commenter is Anthony Tweedale. Are you on the line? Anthony
15 Tweedale? Battelle, is Anthony Tweedale on the line?

16 **MR. VINCENT BROWN:** He's overseas, and he was
17 trying to connect by phone only. So we still have not found him. We're going to
18 keep looking for him. We'll let you know if we find him on the attendee list.

19 **MR. MARTIN ALVARADO CORTES:** I don't see
20 him at this time, Tamue.

21 **MS. TAMUE GIBSON:** I'm sorry. Repeat?

22 **MR. MARTIN ALVARADO CORTES:** I don't see
23 him on the attendee list at this time right now.

1 **MS. TAMUE GIBSON:** Okay. We'll come back to him.

2 He did provide his comments. Next individual is Nicholas Chartres, and I
3 apologize for the mispronunciation. Are you on the line, Nicholas Chartres?

4 **DR. NICHOLAS CHARTRES:** Can you hear me?

5 **MS. TAMUE GIBSON:** Yes.

6 **DR. NICHOLAS CHARTRES:** Thank you.

7 **MS. TAMUE GIBSON:** You're welcome. Go right
8 ahead.

9 **DR. NICHOLAS CHARTRES:** Good morning. My
10 name is Nicholas Chartres, and I'm the Associate Director of the Science and
11 Policy at the Program on Reproductive Health and the Environment at the
12 University of California San Francisco. And my comments today will focus on
13 our concerns with the application of systematic review in the Perchloroethylene
14 draft risk evaluation. Next slide, please. I have no conflicts to disclose. Next
15 slide, please.

16 EPA's required by TSCA statute to use the best available
17 science and the weight of the scientific evidence to make decisions about
18 chemical risks. EPA defined the weight of the scientific evidence in its 2017 risk
19 evaluation rule as the systematic review method that uses a pre-established
20 protocol to comprehensively, objectively, transparently, and consistently identify
21 and evaluate each stream of evidence, including strengths and limitations and
22 relevance of each study and to integrate evidence as necessary and appropriate.
23 However, EPA states in the draft risk evaluation for PERC that although EPA
24 will make an effort to adopt as many best practices as practical from the

1 systematic review community, EPA expects modifications to the process to
2 ensure timely regulatory decision making under the aggressive timeline for the
3 statute.

4 Authority bodies, U.S. agencies, and academic scientists
5 have developed and implemented validated environmental health and systematic
6 review methods, including NTP's Office of Health Assessment and Translation
7 and UCSF's navigation guide. If EPA uses one of these aforementioned
8 methods, the Agency will not have to make an effort to adopt as many best
9 practices as practical. Next slide, please.

10 Today, we'll highlight that, one, EPA's TSCA method
11 utilizes a quantitative scoring method that is incompatible with the best available
12 science in fundamental ways and, two, EPA has failed to account for all
13 references identified in a literature search for human health hazards. Next slide,
14 please. EPA utilizes a quantitative scoring method in the PERC draft risk
15 evaluation that is incompatible with the best available science in fundamental
16 ways.

17 Firstly, quantitative scores for assessing the quality of an
18 individual study are arbitrary and not evidence based. Implicit assumption in a
19 quantitative scoring method is that we know empirically how much each risk
20 device may contribute to study quality. Secondly, EPA's scoring method only
21 conflates how well the study's reported with how well the underlying research is
22 conducted. And thirdly, EPA's scoring method excludes research based on one
23 single reporting or methodological limitation. Next slide, please.

1 As shown here, 14 of the 22 metrics can be scored as
2 unacceptable due to a serious flaw. We have several issues with this. Firstly,
3 EPA considers all these flaws to be of equal importance, and such weightings are
4 arbitrary and not science based. Secondly, EPA's list of serious flaws are not all
5 related to real flaws in the underlying research. For example, as shown here,
6 four of the 14 serious flaws -- metrics three, four, six, and seven -- are based on
7 reporting guidelines.

8 Finally, statistical power, metric 13, which is not an
9 appropriate measure of bias -- for example, small studies may be imprecise, but
10 that should not be confused with whether they are biased or not. Third, the small
11 underpowered studies can be combined in a measured analysis that increase the
12 statistical power of the body of evidence to reflect the relationship between
13 exposure and health outcome. Next slide, please.

14 EPA should not have a single evaluation exclude a study
15 from consideration. However, in the draft risk evaluation for PERC, EPA's
16 excluded ten studies, with five due to an unacceptable rating in metric four and
17 three due to an unacceptable rating in metric 13. EPA has therefore excluded
18 valuable evidence from the PERC draft risk evaluation. Next slide, please.

19 We highlight here the comments -- previous comments
20 and recommendations made by the SACC to EPA on issues identified in
21 previous draft risk evaluations. And these include that several Committee
22 members discuss in depth that it's not appropriate to determine unacceptable
23 rating during data quality evaluation based solely on one criterion. Next slide,
24 please.

1 As you can see in Figure 1-9, the literature flow diagram
2 for human health hazards, EPA states that there are 79 studies to go through data
3 evaluation. However, as noted in the bottom righthand corner and as shown in a
4 previous slide, there's 93 epidemiological studies alone that go through data
5 quality evaluation. Then at the data extraction step below, EPA states that only
6 66 studies have gone through data extraction. Yet, as shown on the previous
7 slide, 83 epidemiological studies alone should be included for data extraction.
8 Therefore, there are 17 epidemiological studies that have been removed from the
9 PERC draft risk evaluation without any explanation from EPA. Next slide,
10 please.

11 Again, we highlight the previous comments made by the
12 SACC to EPA, including that the evaluation flowcharts suggest a full systematic
13 review was performed and the text describes a more limited review. Next slide,
14 please. In sum, multiple SACC Committees have made extensive comments and
15 recommendations to the U.S. EPA on how to improve the TSCA systematic
16 review method, yet the draft risk evaluation for Perchloroethylene still fails to
17 incorporate the majority of key steps identified. Thank you very much for your
18 time.

19 **MS. TAMUE GIBSON:** Thank you very much. Thank
20 you. Right at five minutes. Thank you. The next individual is Jolene Keplin.
21 Jolene Keplin, you're the next commenter.

22 **MR. VINCENT BROWN:** Tamue, this is Vince. Her
23 phone is not connected to her profile, so she needs to reconnect and try again.
24 She needs to connect her audio to her main in the attendee list.

1 **MS. TAMUE GIBSON:** She is on the line. However,
2 she needs to reconnect?

3 **MR. VINCENT BROWN:** Reconnect her audio.

4 **MS. TAMUE GIBSON:** Jolene Keplin, please reconnect
5 your audio by calling in the toll-free number. We'll come back to you. Next
6 commenter is Robert Sussman. Robert, are you on the line? Dr. Sussman, are
7 you there?

8 **DR. ROBERT SUSSMAN:** Can you hear me?

9 **MS. TAMUE GIBSON:** Yes. Go right ahead.

10 **DR. ROBERT SUSSMAN:** You do?

11 **MS. TAMUE GIBSON:** Yes.

12 **DR. ROBERT SUSSMAN:** Okay. Fabulous. I'm
13 pleased to be here today to share the perspective of Safer Chemicals Healthy
14 Families on EPA's draft risk evaluation for PCE. Today, I'd like to focus on one
15 issue which is a significant concern for PCE and for other chemicals like PCE.
16 The draft evaluation only estimates risk to consumers from acute exposure to
17 PCE.

18 EPA's position is that consumers have limited and
19 intermittent exposure to PCE, and so therefore there is no risk of chronic health
20 effects like cancer and developmental toxicity. We believe that EPA is wrong
21 and that multiple lines of evidence demonstrate that consumers have long-term
22 PCE exposure. SACC should highlight this flaw in EPA's approach because it
23 has significant implications for the health of millions of consumers.

1 As we show in our comments, there is extensive data
2 demonstrating the presence of PCE in indoor air. The draft evaluation identifies
3 19 valid studies with a median detection frequency of 95 percent. The PCE
4 concentrations vary, but some are quite high. According to the 2012 IRIS
5 assessment, at the higher levels measured in indoor air the lifetime cancer risk
6 would be greater than one in 100,000.

7 Another line of evidence is the presence of PCE in human
8 blood, urine, and breath samples in multiple studies described in the draft
9 evaluation. These samples show a high frequency of PCE detection. And as the
10 draft evaluation notes, there is a consistency in the blood levels across studies
11 and over time.

12 In addition, although the amount of data is smaller, PCE
13 has also been found in human breastmilk. The consistent detection of PCE in
14 human blood, urine, breath, and breastmilk provides strong evidence of
15 continuous exposure to PCE by consumers. Reinforcing this conclusion is
16 relatively short elimination half-life of PCE.

17 There are probably multiple sources that account for the
18 long term PCE body burden in the human population. One is contaminated
19 drinking water. Another is PCE air emissions. A third is exposure pathways
20 related to dry cleaners, which take a number of forms, including air emissions,
21 co-location of dry cleaners with businesses and apartment buildings, and the
22 wearing of clothing dry cleaned with PCE. A fourth source is vapor intrusion of
23 PCE in buildings near contaminated waste sites.

1 However, EPA's exclusive focus in the draft evaluation is
2 on a single source of exposure: consumer product use. This is surely an
3 important contributor to overall exposure. But it should not be assessed in
4 isolation from other known pathways of human -- of consumer exposure and
5 without considering evidence of the long-term body burden of PCE in
6 consumers.

7 Even looking just in consumer products, we disagree with
8 EPA that it is unlikely that the expected use patterns would cumulatively result
9 in repeated exposure. There are clearly significant subpopulations that engage
10 in repeated use of PCE containing consumer products. Moreover, while EPA's
11 draft assumes use of a single product type during the day, many consumers likely
12 use different PCE containing products on the same day or over time.

13 We are troubled by EPA's statement that it cannot account
14 for these chronic risks because of, quote, the uncertainty regarding the
15 extrapolation from continuous studies in animals to the case of repeated
16 intermittent human exposures. This is a strange position. Risk assessors
17 typically use repeated dose toxicity studies to estimate the long-term health risk
18 of similar exposure scenarios, including in the workplace. We believe that EPA
19 can and should do that here.

20 In sum, failure to address the risk of chronic exposure
21 would be a serious gap in public health protection because a major exposure and
22 risk scenario would be excluded from the PCE evaluation. Thank you.

23 **MS. TAMUE GIBSON:** Thank you. The next
24 commenter is --

1 **MR. VINCENT BROWN:** Tamue, I'm sorry. This is
2 Vince Brown. We have Jolene Keplin on the line. She was the previous on the
3 schedule.

4 **MS. TAMUE GIBSON:** Okay. Jolene, are you ready for
5 your comment? Jolene?

6 **MR. VINCENT BROWN:** Maybe her phone is muted.
7 She's not muted in Webex.

8 **MS. TAMUE GIBSON:** Jolene, we'll come back to you.
9 We'll finish up and then we'll come back to those who may have had some audio
10 difficulties. The next individual is Jennifer Sass. Jennifer, are you ready to
11 provide your comment?

12 **DR. JENNIFER SASS:** I am. Yup. Can you hear me?

13 **MS. TAMUE GIBSON:** Yes. Go right ahead.

14 **DR. JENNIFER SASS:** Great. Thanks for your help
15 with this by the way. You guys have been really great in helping to help
16 navigate people through the technology. So thank you and thank you for making
17 it so available to public speakers. I really appreciate that.

18 **MS. TAMUE GIBSON:** Thank you.

19 **DR. JENNIFER SASS:** Thank you to the SACC
20 committee for undertaking again another chemical. I realize this is a tremendous
21 amount of work for you and especially during a time when people are being
22 pulled in all directions. Academics are having to move all their classes online,
23 and public health people are being pulled into COVID direct responses. So
24 thank you so much for doing this.

1 I'm going to keep my comments to two points. The first
2 is the Q0 question. I'm calling it Q0. It's the systematic review where EPA said
3 in the charge questions that they're not given a specific charge question on
4 systematic review but that they're inviting -- EPA will except comments on the
5 systematic review approach used in this evaluation. So on that point, I would
6 like to suggest that the SACC committee could advise EPA to cease using the
7 TSCA systematic review and to instead apply one of the recognized peer
8 reviewed systematic review methodologies, such as from the EPA IRIS program.
9 And in this, we support the previous commenter, Nick Chartres, and UCSF
10 comments.

11 I also want to point out that the SACC strongly
12 recommended that EPA move forward with the National Academy's review of
13 its TSCA systematic review method, a commitment on which EPA is only now
14 just beginning. Both the IRIS and NIEHS systematic review methods have been
15 extensively peer reviewed and praised by the National Academies. So we
16 encourage the EPA to use those.

17 My next comments are going to focus on your Question 4
18 of the charge questions on occupational uses. I have two concerns there that I'd
19 like to bring up -- well, a couple, but I'm going to focus only on two. The first
20 one is to direct your attention to Table 5-1 in the PCE draft risk evaluation. In
21 my written comments, I've extracted the data from that table which find that
22 there is no unreasonable risk.

23 We're very concerned about the no unreasonable risk
24 finding for a number of reasons. First of all because we don't think that the data

1 supports many of those findings, a lot of them because they're ONUs, the
2 occupational nonusers, which EPA has made assumptions about the exposure
3 that the SACC has criticized numerous times. For example, the SACC
4 committee recognized in its methylene chloride report that the Agency should
5 consider exploring different categories of ONUs, including workers who don't
6 handle the solvent directly but who's job requires them to be in the same areas,
7 also including cleaning staff that could be exposed after hours to residues in the
8 work area and office or managerial workers that could be incidentally exposed
9 when visiting a worker area but are not at risk from exposure routinely because
10 their potential risk likely varies. That's from the SACC methylene chloride
11 report, page 31.

12 In the same report from SACC, page 44, the Committee
13 said that ONUs are likely a heterogeneous population of workers and could be
14 exposed more than just occasionally to high concentrations. This possibility
15 should be included explicitly as a source of uncertainty. As recommended
16 earlier, EPA should consider the different categories of ONUs potentially at risk.
17 So based on those previous recommendations of the SACC report and EPA's
18 continuing disregarding of this ONU as potential nearfield exposures and also
19 high exposures is a great concern to us and should prevent EPA from designating
20 no unreasonable risk determinations for these workers.

21 The comments by TURI, the Toxic Use Reduction
22 Inventory -- Institute, sorry, in Massachusetts have also said previously in
23 methylene chloride and other comments to the SACC that some of these
24 occupational nonusers can actually have much higher exposures than designated

1 users because they're doing things like cleaning up spills or working next to the
2 area but aren't provided with the PPE or protective equipment. They gave an
3 example that they've observed of breakrooms in close proximity to workstations
4 or laboratory students and graduate students working next to other students that
5 are in fume hoods.

6 So our recommendation to the SACC to consider is to
7 recommend to EPA that it use appropriate designations for near and far field
8 workers with appropriate assigned exposures. And the SACC could also
9 recommend to EPA that the near field workers should be presumed to have
10 exposure to PCE as appropriate. The current presumptions that they're far field
11 workers is unsupported and wrong. SACC could also recommend to EPA that
12 EPA do a broader outreach to get all the information that's reasonable available
13 as required by TSCA. This would include union health and safety staff,
14 industrial hygienists, government experts at the local, regional, and state level as
15 appropriate, and TURI staff as well.

16 We also want to ask the SACC if it would consider in
17 Table 5-1 where EPA has designated the ONUs as finding no unreasonable risk -
18 - if SACC members could help provide any insight into what these ONU tasks
19 are. Who does them? How a job station may be laid out and what workers may
20 be in the near or far field? Because I have surveyed experts that I could find
21 around the country, and nobody understands what these jobs are. They're not
22 categorized in the way that we understand workplaces.

23 As someone said to me, it's not like you have an ONU
24 whose job it is to use adhesive and sealant products. That's not how it works.

1 They could be using adhesive and sealant products for an hour and then go to
2 paint and coating products and then do something else and then clean up a spill.
3 So we need to understand these better and SACC could help us.

4 I want to make a quick repeated point about EPA's
5 continuing presumption that personal protective equipment is available,
6 provided, fitted properly, used consistently, and would be adequately protective.
7 There's not only no evidence for that, but there's evidence to the contrary. And
8 the SACC has repeatedly underscored that an expectation of universal PPE use is
9 contrary to the realities of workplace practices and sound principles of worker
10 protection. Thank you for the opportunity to provide comments and thank you
11 for your work.

12 **MS. TAMUE GIBSON:** Absolutely and thank you.

13 Next commenter is Liz Hitchcock. Are you on the line, Liz Hitchcock? Okay.
14 Next, Andrew --

15 **MR. VINCENT BROWN:** Tamue, she is on the line.

16 **MS. TAMUE GIBSON:** She is on the line. Liz, can you
17 unmute your line -- your audio? Can you unmute your audio?

18 **MR. VINCENT BROWN:** Actually, she -- I'm getting a
19 note that she requested to be moved to last place.

20 **MS. TAMUE GIBSON:** Alrighty, which is -- okay.
21 Next individual is Andrew Maier. Andrew Maier?

22 **DR. ANDREW MAIER:** Yes, I'm here.

23 **MS. TAMUE GIBSON:** Go ahead with your comment,
24 please.

1 **DR. ANDREW MAIER:** Okay. Excellent. Well, thank
2 you so much. Good afternoon, everyone. My name's Andrew Maier, and I'm a
3 certified industrial hygienist and toxicologist. Most of my 25-year career has
4 been as a non-profit scientist or university professor. I served as a toxicology
5 fellow at NIOSH, contracted with EPA, and risk assessor and trainer for many
6 federal scientists. I'm currently a principle science advisor at Cardno ChemRisk,
7 and my comments today are supported in part by a Halogenated Solvents
8 Industry Alliance.

9 I really appreciate the opportunity to comment on the
10 Perchloroethylene risk evaluation. I have also submitted written comments to
11 the EPA docket. My comments today focus on the exposure assessment related
12 issues.

13 My first comment address issues in industrial hygiene data
14 for inhalation risk assessments. For chemical manufacturing uses, combining all
15 IH sampling data into a single dataset is not appropriate. This overestimates the
16 central tendency and high-end estimates. High end values include exposures
17 from non-routine tasks that occur infrequently and are not representative of daily
18 conditions. In contrast, the EPA's data lumping approach -- a think a similar
19 comment from a prior speaker -- similar exposure groups that are more refined
20 and those sorts of methods are commonly used in industry and are preferred.

21 EPA's exposure assumptions do not reflect current control
22 practices. Tasks that involve significant chemical handling are covered under
23 specific job hazard analyses and standard operating procedures. Scenarios that
24 generate higher exposure are tightly managed in those circumstances.

1 High end exposures should not be compared with
2 exposures with limited or no PPE for risk evaluation. High end exposures are
3 not routine and should not be compared to long term data average benchmarks.
4 Assumptions regarding exposure to occupational nonusers are also not realistic
5 because process unit of access is tightly controlled. Fixed monitoring systems
6 provide direct empirical data for general unit exposures and validate that non-
7 task exposures are minimal in most cases.

8 Many assumptions included in the exposure estimations
9 and data use are not aligned with chemical industry reality. The dermal
10 modeling assumptions are an example. Significant liquid contact with neat
11 PERC is limited. For example, taking samples and contacting transfer lines
12 occurs over the course of minutes, not hours.

13 Sampling is typically done a few times over a shift, not
14 continuously. Specific equipment designed to limit the release of liquid
15 products, such as quick hose disconnects and close looped sample quarts. For
16 scenarios without gloves, EPA assumes that a worker comes into contact with
17 undiluted PERC one time per work shift after which the material stays on the
18 hand until it evaporates, or it's absorbed. The impact of absorption rate and
19 PERC skin saturation kinetics was not adequately included in the assessment.

20 For scenarios with gloves, EPA assumes that a worker
21 wears the same pair of gloves for the entire work shift with no breaks. While a
22 glove protection factor of 20 assumes that chemically resistant glove and worker
23 training, which are appropriate use conditions. But that still assumes 5 percent
24 of the PERC will still permeate the glove.

1 In reality, there's little if any penetration of PERC through
2 the glove. Tasks with liquid contact are short in duration. Glove selection and
3 use protocols are designed to limit contact, and glove selection ensures that
4 breakthrough protection exceeds the task durations that are assigned.

5 For occluded scenarios, EPA assumes PERC splashes into
6 the glove, uniformly coats the entire hands or hand, does not evaporate back out
7 of the glove and 100 percent is absorbed. Again, this is not realistic. In short, all
8 the assumptions of dermal scenarios do not reflect chemical manufacturing
9 industry practices. In discussion with other experienced CIHs, none of the them
10 could recall an event with sustained full glove emersion in any common routine
11 use scenario.

12 So to strengthen EPA's assessment, surveys of PERC
13 facility chemical manufacturing experts should be conducted. That will help
14 improve the task assumptions, and that includes assumptions related to durations,
15 contact volumes, exposure controls, and PPE practices. Thank you. I really
16 appreciate the opportunity to provide comments.

17 **MS. TAMUE GIBSON:** Thank you. Next up is
18 Jonathan Kalmuss-Katz. Are you on the line?

19 **MR. JONATHAN KALMUSS-KATZ:** Hello. I am on
20 the line. Can you hear me?

21 **MS. TAMUE GIBSON:** Yes, I can. Go right ahead.

22 **MR. JONATHAN KALMUSS-KATZ:** Thank you.

23 Good afternoon and thank you for the opportunity to speak. I'm John Kalmuss-
24 Katz from EarthJustice. Several of the deficiencies the SACC has identified in

1 prior risk evaluations recur in the current draft. Rather than rehashing those
2 points, I would like to focus on three issues that have received less attention in
3 prior SACC reports.

4 First, EPA ignores the risks associated with the
5 acknowledged degradation of PCE into other hazardous chemicals, including
6 trichloroethylene, or TCE. While this is not the first time that EPA has
7 overlooked chemical degradation, what is particularly striking here is that EPA
8 just evaluated TCE and it did not consider TCE exposures from PCE degradation
9 in that evaluation either. EPA knows that the use and disposal of PCE will result
10 in exposures not only to PCE but also to its degradation products, a phenomenon
11 that is observed in contaminated groundwater claims across the nation. Yet EPA
12 failed to consider those exposures in either of the risk evaluations where it could
13 have done so. And this significantly understates PCE's risks.

14 Second, EPA does not evaluate the risks to the most
15 susceptible subpopulations as required by TSCA. Instead, as it has in many prior
16 risk evaluations, EPA lists a variety of genetic, life stage and behavioral risk
17 factors that can leave people more susceptible to PCE and then assumes that all
18 of them, individually and in combination, will be addressed by the use of the
19 tenfold intraspecies variability uncertainty factor. EPA admits that it is unknown
20 whether this tenfold factor will cover the full breadth of human responses to
21 PCE. Yet it makes no effort to answer that critical question.

22 Given that a single genetic risk factor to PCE, CYP
23 metabolic capacity, can vary by 20 to 50 times among the population, EPA's
24 default tenfold factor to account for all sources of human variability is almost

1 certainly under protective. The SACC should call on EPA to quantify variability
2 among known risk factors and to separately calculate risks for potentially
3 exposed and susceptible subpopulations or, at a minimum, to apply a chemical
4 specific uncertainty factor that is known to protect the most susceptible among
5 us.

6 EPA also fails to consider the presence of PCE in sewage
7 sludge. EPA falsely claims that these exposures are currently being address
8 under the Clean Water Act. It is important for the Committee to understand what
9 EPA means by that. EPA does not mean that the Clean Water Act regulates the
10 presence of PCE in biosolids. It does not. Instead, EPA relies on a passing
11 mention of PCE in a biennial review of chemicals that could potentially be added
12 to EPA's biosolids rule. Now, what EPA fails to disclose is that PCE first
13 appeared in this biennial review in 2005, that EPA has not taken any action to
14 regulate PCE in biosolids since then, or that in 20 years EPA has never added
15 any chemical from a biennial review to its biosolids rule. And if the SACC is
16 interested in more information, last year the EPA inspector general put out a
17 report on this.

18 It's not merely a problem for biosolids. For air, drinking
19 water, and soil pathways as well EPA excludes general population exposures
20 based on the conclusory and improper assumption that any unreasonable risks
21 will be eliminated by other environmental laws. They won't be, and the SACC
22 should not permit EPA to continue to ignore these known pathways of exposure
23 and risk.

1 Finally, EPA acknowledges evidence of PCE's
2 immunotoxicity and hematological effects but asserts that there's an absence of
3 adequate quantitative information available to carry those endpoints forward to
4 dose response analysis. Now, once again, EPA ignores its authority and
5 obligation under TSCA to generate the information that it needs for a risk
6 evaluation. The SACC should call on EPA to use that data gathering authority
7 or, at a minimum, to increase its uncertainty factors to account for these known
8 data gaps. Unless there are any questions, I thank you for your time,
9 consideration, and service.

10 **MS. TAMUE GIBSON:** Thank you. Okay. We're
11 going to circle back to those who may have not had an opportunity to unmute
12 their lines. So I'm going to call your name. We're going to go back to Abdel
13 Jalil Mekkaoui. Are you on the line? And I've got confirmation that he's not on
14 the line. I will also go back to Tanyatap Meliam. And noted that she's not on
15 the line as well. Anthony Tweedale, are you available? Okay. Moving on to
16 Jolene Keplin. Are you ready, Jolene Keplin, to provide your comment?

17 **MR. VINCENT BROWN:** We can see her, and her
18 phone is unmuted. But maybe her local phone is muted or local computer is on
19 mute or something. We see her name. We just can't hear her.

20 **MS. TAMUE GIBSON:** Okay. Jolene?

21 **MR. VINCENT BROWN:** Oh, she's muted again.

22 **MS. TAMUE GIBSON:** Okay. All right. We'll move
23 on. Jolene, are you ready to provide your comment? Okay. We'll move on to
24 Liz Hitchcock.

1 **MS. LIZ HITCHCOCK:** Hi, can you hear me?

2 **MS. TAMUE GIBSON:** Yes, go right ahead. Yes.

3 Thank you.

4 **MS. LIZ HITCHCOCK:** Terrific. I'd like to thank you
5 all for your patience and tech support. Good afternoon. My name is Liz
6 Hitchcock, and I direct Safer Chemicals Healthy Families. We are a national
7 campaign to protect Americans from hazardous chemicals used in our homes,
8 our workplaces, and in the many products that our families and children are
9 exposed to each day.

10 I'd like to thank the Committee for the opportunity to
11 testify about EPA's draft risk evaluation for Perchloroethylene, or PCE, under
12 the Toxic Substances Control Act. I'd also like to thank the Committee for your
13 contributions to these very important evaluations under tight timelines and
14 challenging meeting circumstances. The final risk evaluations that EPA
15 produces for these first ten chemicals will set the tone for the TSCA program as
16 we move forward, and our families and our communities are counting on the
17 Science Advisory Committee on Chemicals for rigorous review of the draft risk
18 evaluations.

19 Working with our colleague organizations at NRDC,
20 EarthJustice, and the Environmental Health Strategy Center, we submitted
21 detailed comments on the draft PCE evaluation that I hope that the committee
22 has had an opportunity to review. In summary, on one issue we are troubled by
23 EPA's exclusive focus in the draft evaluation on consumer product use. While
24 this is undoubtedly an important contributor to overall exposure, it should not be

1 considered in isolation from other known pathways of consumer exposure and
2 without considering evidence of the long-term body burden of PCE in
3 consumers. TSCA mandates that EPA determine whether a chemical substance -
4 - not particular uses of a chemical substance -- presents an unreasonable risk in a
5 single comprehensive determination. To pick and choose conditions of use of
6 PCE violates TSCA's plain language.

7 Likewise, we're concerned that the draft evaluation
8 estimates risks to consumers only from acute exposures to PCE, thereby
9 assuming that since consumers may have limited and intermittent exposure to
10 PCE they bear no risk of chronic health effects like cancer and developmental
11 toxicity. There's substantial evidence to demonstrate that consumers have long-
12 term PCE exposure, and we urge the SACC to highlight this flaw in EPA's
13 approach because of the consequences for the health of millions of Americans.
14 PCE is present in human blood, in urine, and breath samples in multiple studies
15 that are described in the draft risk evaluation. PCE has also been found in
16 human breastmilk.

17 A consistent detection of PCE in human blood, in urine, in
18 breath, and breastmilk is incompatible with an assumption that consumer
19 exposure is short-term and episodic. Rather, it's very strong evidence of
20 continuous exposure to PCE by consumers. There are probably multiple sources
21 that account for the long-term PCE body burden in the population, including
22 contaminated drinking water in many different areas of the U.S., PCE air
23 emissions particularly in areas near vapor degreasing and other unenclosed
24 industrial operations, vapor intrusion of PCE in buildings near contaminated

1 waste sites or legacy industrial facilities like large dry cleaning operations, and
2 exposure pathways related to dry cleaners, including air emissions, dry cleaners
3 that are in the same buildings along with businesses and residential apartments,
4 and wearing clothing that has been dry cleaned with the chemical.

5 The draft evaluation for PCE underscores just how
6 arbitrary it is to pick and choose which exposure scenarios to review when it is
7 the combination of all sources that likely results in long term exposure to PCE by
8 consumers and the risk of chronic health effects. There are clearly significant
9 groups whose repeated use of consumer products containing PCE exposes them
10 on a chronic basis. And many consumers are likely to use different products
11 containing PCE on the same day or over time. In fact, intensive users of PCE
12 containing consumer products are plainly exposed to PCE on a chronic basis, and
13 these users should be a potentially exposed or susceptible subpopulation under
14 TSCA. And EPA must directly address whether they are at risk of chronic health
15 effects.

16 Before I close, I would like to echo Dr. Sass' critique of
17 the evaluation's expectation of universal personal protective equipment, or PPE
18 use. It is contrary to the realities of the workplace and to sound principles of
19 worker protection. None of EPA's draft evaluations have provided any evidence
20 of widespread use of PPE and effective controls of exposure in workplaces
21 where the chemicals are manufactured, processed or used.

22 For this reason, a no PPE scenario is the only defensible
23 basis for determining whether PCE presents an unreasonable risk to exposed
24 workers. Again, Safer Chemicals Healthy Families thanks the Committee for the

1 opportunity to provide these comments and for its important work on these draft
2 risk evaluations. Thank you.

3 **MS. TAMUE GIBSON:** Many thanks. Thank you.

4 Okay. This concludes our list of public commenters. At this time --

5 **MR. VINCENT BROWN:** Do you want to try Jolene
6 one more time? I'm sorry.

7 **MS. TAMUE GIBSON:** Okay. Is she on the line?
8 Jolene? Is she on the line?

9 **MR. VINCENT BROWN:** We can see her.

10 **MS. TAMUE GIBSON:** Jolene Keplin, are you will or
11 are you available to make your comment to the Committee? Okay. We're going
12 to move on. Dr. Portier, this concludes our public commenters session. I hand
13 the rest of the meeting to you.

14 **DR. KENNETH PORTIER:** Thank you, Tamue. And I
15 want to thank all of the ten public commenters for taking the time out of, I know,
16 their busy lives to raise these issues with the Committee. I counted at least 18 to
17 20 issues -- excuse me, many of which the Committee has addressed in previous
18 draft risk evaluations and will likely address in this risk evaluation.

19 At this point, I have five minutes to 3:00. We need to take
20 about a ten-minute break as we transition over into the part of the meeting where
21 the Committee begins to discuss the questions that EPA has posed to us. So let's
22 reconvene at five minutes after 3:00.

23 Oh, and before I forget, any of the commenters who were
24 unable to connect with us, there's still the opportunity to send written comments

1 to Tamue Gibson so that they can be included in the docket and transmitted to
2 the Committee. Ten-minute break.

3 **MS. TAMUE GIBSON:** Thank you.

4 (BREAK)

5 **DR. KENNETH PORTIER:** Okay. Let's reconvene,
6 please. At this point, the Committee is ready to begin its discussion of the
7 questions that EPA has proposed to the panel. As one of the public commenters
8 mentioned, our Question 0 is always on the issue of the adequacy of the
9 systematic review. And that topic is fair game in any of these questions. So just
10 remind the Panel that if we have systematic review issues that they can come up
11 at any time during our discussion.

12 So if we could bring up the charge questions, and I'm
13 assuming, Dr. Lee, you're going to read them in or someone on your group is
14 going to read them in. That's not good. I think we have problem. I think we
15 have a problem with Dr. Lee's connection.

16 **MR. MARTIN ALVARADO CORTES:** Dr. Lee, this is
17 Martin with Battelle. Can you try reconnecting your audio?

18 **DR. KENNETH PORTIER:** Try again with the
19 comment.

20 **MR. MARTIN ALVARADO CORTES:** It appears that
21 Dr. Lee is experiencing audio connection problems right now.

22 **DR. KENNETH PORTIER:** That's fine. Is there
23 anyone else from the EPA workgroup coming in from a different source that
24 could read the questions?

1 **MR. VINCENT BROWN:** Yvette Selby was the
2 alternate presenter.

3 **MS. YVETTE SELBY-MOHAMADU:** I am. So I was
4 just speaking. I hope everybody can hear me. This is Yvette Selby-Mohamadu,
5 and I can read the first charge question.

6 **DR. KENNETH PORTIER:** Thank you.

7

8 **CHARGE QUESTION 1: ENVIRONMENTAL FATE AND TRANSPORT**

9

10 **MS. YVETTE SELBY-MOHAMADU:** So Question 1,
11 Environmental Fate and Exposure, EPA assessed the fate and transport of PCE in
12 sediment pathways based on its physical-chemical and fate properties. Exposure
13 to aquatic organisms in surface water was assessed for the environmental
14 releases based on the conditions of use. Question 1.1, please comment on EPA's
15 assessment of pathways based on physical-chemical and fate properties. And
16 this is found primarily in Section 2.1.2 and Section 4.1.3. And Question 1.2,
17 please comment on the data approaches and/or methods used to characterize
18 exposure to aquatic receptors in surface water and found in Section 2.3.

19 **DR. KENNETH PORTIER:** Thank you. And we're
20 going to take these questions in order. Dr. Doucette is the lead for the first
21 question, and he has four associates. Dr. Doucette?

22

23 **CHARGE QUESTION 1 (1.1)**

24

1 **DR. WILLIAM DOUCETTE:** Yeah. Just to let
2 everybody know, we felt that -- we recognized that the magnitude and
3 complexity of the task that's been given to the Agency. And we're really
4 commending those of you that are working on this and providing us with these
5 reviews. Unfortunately, the accelerated timeline minimizes or sometimes
6 prevents the opportunity for EPA to incorporate comments made in the previous
7 SACC reviews to the current review.

8 And I think this is especially important when dealing with
9 chemicals of similar environmental behavior and health risks like PCE and TCE
10 and carbon tet. And their accelerated timeline I think also kind of limits the
11 discourse between SACC members at times. And I just wanted to kind of
12 preface my comments with that statement.

13 Many of these issues that I'm going to raise have been
14 raised in previous risk assessments, so I'm not -- I'm going to just try to hit on
15 the highlights and then allow my other discussants to -- they sent me comments,
16 and I'll try to address those. But they'll probably chime in after I get done.

17 So the first thing I'm going to talk about is physical-
18 chemical properties. And it's still not completely clear how the physical-
19 chemical property values are selected in terms of quality from low to medium to
20 high. And that deals with the overall systematic review process.

21 Experimental versus estimated values, this is just for a
22 single example. A single Koc, which is an organic normalized sorption
23 coefficient, was used instead of the range of experimental values that are
24 provided in the literature. And it was not clear why that was.

1 I think it in part is due to an overreliance on the EPA Suite
2 -- the database contained within the EPA Suite software of physical-chemical
3 properties. And it's just a single value was pulled out instead of a range. And a
4 question that I have for the EPA, I was involved on the first -- I think it was back
5 in 2007 -- the panel that reviewed the EPA Suite. And I'm not sure anymore
6 how often the database of physical-chemical properties that is incorporated in
7 EPI Suite -- when the last time it was updated.

8 If you look at most of those references provided in the
9 physical-chemical property table -- I believe that's 2.1 -- the references are fairly
10 old. That's not surprising given PCE's been around that long. But I'm not clear
11 as to when the database has actually been modified at all.

12 And I think this next part is related to the need to address
13 the variability of the physical-chemical properties and how that variability would
14 impact models. For example, if sorption coefficient ranges a half an order of a
15 magnitude, how is that going to impact the environmental fate and exposure
16 model assessments that is done by EPA. Another example might be if the
17 octenal water partition coefficient varies, how would that impact PBPK models.
18 So there's no discussion or no assumption of variability within the phys-chem
19 properties.

20 The fourth comment is -- a lot of it is terminology, but it
21 continues to be frustrating that equilibrium properties such as Henry's Law
22 constant and vapor pressure and sorption coefficients are used to directly infer
23 rates like volatilization. And they are equilibrium properties, and they cannot

1 directly be used to estimate volatilization rates. And it just keeps coming up in
2 the last four or five different reviews.

3 The next point I want to bring up is the conceptual figure.
4 It was helpful to some, misleading and inaccurate the others. The arrows -- and
5 again, it's adapted over time. The arrows indicated -- the size of the arrows
6 indicated the direction which the transport tended to go.

7 But it's important that all this was based on partition
8 coefficients, and partition coefficients by definition have arrows in both
9 directions. And it would help if there were some arrows indicating in that
10 particular figure the main introductions into the environment. That's really
11 important in understanding the direction of flow.

12 For example, if there were no emissions to any
13 environmental phase other than the atmosphere, the arrow that you have going
14 from water to air would not exist. It would go the other way. It would go from
15 air to water. And I think Dr. Cobb has a table discussing or at least illustrating
16 that within the fugacity model. So I think that's important.

17 Related to that -- the fugacity -- related to the fugacity
18 model within EPI Suite and the sewage treatment plant model within EPI Suite, I
19 would suggest not using the default model inputs. The default model inputs
20 introduce the chemical into various phases. And that may or may not be
21 appropriate depending on the chemical. So I think by doing that it can result in
22 misleading output, and I think that's important and needs to be addressed.

23 In addition, the fugacity model within EPI Suite -- it's a
24 subset of the complete model developed by Don Mackay and others at Trent

1 University. You can actually use it to predict concentrations. So percentages
2 within the environment can be misleading if the compartment is very large, for
3 example, air. The air compartment is ten times or 100 times greater than any of
4 the other compartments. So the percent in that compartment can be very large,
5 but the concentration can be relatively low. So I think it's both -- it's important
6 to look both at percentages and concentrations.

7 There also -- and this was brought up by the public --
8 some of the public comments. There was a limited discussion on metabolic
9 pathways, the environmental behavior of the breakdown products, and co-
10 contaminants, which are often found when using PCE as a degreaser. There
11 were a couple of comments on the lifecycle diagram 1.1. I think Ruthann
12 commented -- and she can expand on this -- that most of the PCE that was not
13 used as feedstock will ultimately be introduced into the environment and how
14 that might impact overall background exposures. And I think that came up in
15 several of the public comments, too, the impact of background concentrations of
16 PCE in both indoor and outdoor air on the total exposures.

17 A question I brought up earlier -- and I'm not sure if we
18 received the answer yet. We talk about wastewater indirect, so those released
19 after its been through treatment, or liquid water direct charges released into the
20 environment. I'm still not clear if septic tank discharges are considered, and I
21 think that might be something, too, the EPA should look at, considering that at
22 least the figures that I look at -- over 20 million septic tank users in the U.S.

23 And the only other thing I'm -- it's a continuing question -
24 - is this impact of mixtures since, especially for degreasing situations, solvents

1 are relatively -- it's rare that solvents are relatively 100 percent pure. So there's
2 typically other chlorinated solvents within that and how would be deal with those
3 combined exposures. So Ken, that's all I have right now. I know I received
4 comments from Ruthann and George and Sheri. And if they would like to add to
5 this, that would be great. Thank you.

6 **DR. KENNETH PORTIER:** Thank you, Bill. So I'll
7 just call and see if any of the associates want to add anything. Dr. Blystone?

8 **DR. SHERI BLYSTONE:** Yeah. Very little. As usual,
9 Bill did a great job. I would echo his comments about some level of sensitivity
10 analysis, like we do with the human health models to do that also with the
11 environmental models, so variations in the inputs -- how sensitive is the output
12 as a result of that, whether it's physical-chemical data or other? And I think the
13 only other thing that I'll just mention so that we can get it in there somehow is
14 when I looked in Table 2.1 I thought there was an error or some missing data.

15 I was also one of the ones in Figure 2.1 that thought it was
16 better than -- and the accompanying text that went with it -- that thought it was
17 better than previous risk evaluations. Probably still more work to go, as Bill
18 discussed already. And I think that's it.

19 **DR. KENNETH PORTIER:** Thank you. Dr. Cobb?

20 **DR. GEORGE COBB:** Can you hear me?

21 **DR. KENNETH PORTIER:** Yeah. We're still on
22 Question 1.1. Yes, we can hear you.

1 **DR. GEORGE COBB:** I had the figure that was possibly
2 going to be presented. If not I'll just work through it. So yeah. I'll just start
3 with this.

4 **DR. KENNETH PORTIER:** It's up.

5 **DR. GEORGE COBB:** Okay. I'll just start with this
6 figure then. As we discussed in the TCE evaluation, and Dr. Doucette just
7 relayed, putting equal amounts of any chemical into the environment in water,
8 air, and soil is probably unrealistic. And that's what the Agency did is what's in
9 the top row -- put 1,000 kilograms an hour of PCE into the three different
10 compartments.

11 And you can see going into the next -- the purple box,
12 that's the percentage distribution in the various compartments at equilibrium.
13 And then the percentage of the mass from input is over there on the right-hand
14 column. I used that scale default, which is basically the sum of all the
15 information that was in the problem formulation from all the compartments and
16 just say, "Okay. Let's throw them in there equally. Let's just divide -- sum it
17 up, divide by three so that you've got equal concentrations." And that's just to
18 demonstrate that no matter what the actual number is in the air, water, and soil
19 box, if the ratios are the same, you still get the same relative outputs. So that's
20 just to demonstrate that.

21 And then if you go to the problem formulation line, you
22 see that's actually the numbers from the problem formulation if you take the total
23 kilograms per year and divide it by 24 hours a day, 365 days a year. So you can
24 see approximately 81 percent -- that's probably more like 85 percent -- goes into

1 air, one and a half percent or so into water, and about 10 percent into soil. And
2 when that partitions in the purple-blue box, you see you still end up with 92
3 percent in air and it looks like a small percentage in water, 3 percent.

4 However, that 3 percent, if you go over to the right-hand
5 column, it's 260 percent of what the input was. So that's indicating that the
6 estimates in water are probably low by a factor of two to three if you're going to
7 stick to these equilibrium models as your predictors. And I went on a little bit
8 further, and I just took the soils out because that's not being considered in this
9 particular assessment. And you still get about 267 percent estimated increase in
10 what's in the water.

11 So long story short, just from this alone, if you're going
12 not to have any data and you're going to use modeling estimates, you're going to
13 have to multiply all the concentrations in water by about 2.6 or 2.7 to get to a
14 defensible concentration in water. So that's the first point. And then I have
15 several other things to go through unless there's any questions or discussion
16 about that table.

17 So if there's none, I'll go on to say the Agency actually
18 acknowledges what I'm talking about in Section 2.1. Very briefly they state,
19 "Environmental transport is the movement of chemicals within and between
20 environmental media," and then goes right on to discount any information about
21 PCE being input into the air and that possibly influencing what's in the water.
22 The only consideration is that when PCE is released to water it may volatilize to
23 air if there's no PCE already in air. So this is already actually acknowledged and
24 then completely discarded by the Agency.

1 The other thing that's related to the information in this
2 table goes back to comments that Dr. Doucette has made in the past about using
3 unitless Henry's Law constants. If the Henry's Law constant in that table was
4 unitless, you'd be able to see that if the concentrations in air and water are
5 relatively the same, you can kind of quickly get to partitioning from the air into
6 the water. But the way those units are expressed it's difficult for a layperson to
7 see that or even someone that's even rudimentary educated in environmental
8 chemistry. So again, just to reiterate, failure to consider air and groundwater and
9 soil releases is leaving a serious data gap in this assessment.

10 Also, the toxicity profile for vinyl chloride, which is
11 mentioned on page 62 -- there's no information given about the toxicity of vinyl
12 chloride, how much vinyl chloride may be produced and how that might
13 influence risk. And that's another major consideration. In the atmosphere,
14 degradation (inaudible) mentioned that PCE will degrade in the environment, but
15 there's no information about what those transformation products will be, what
16 their concentrations might be, or how that might influence a risk assessment.
17 And then there's one more that the assumption of no discharge to water due to
18 the fact that the compound is so volatile, as mentioned on lines 1816 through
19 1821, are erroneous because of the fugacity discussion we just had. And with
20 that, I am done.

21 **DR. KENNETH PORTIER:** What was the page number
22 for those lines?

23 **DR. GEORGE COBB:** Ken, I'm sorry. I don't have that
24 page number right at my -- the page number would be --

1 **DR. KENNETH PORTIER:** Okay. I got page 62 where
2 you had vinyl chloride.

3 **DR. GEORGE COBB:** It's around 33 or 34. No. The
4 last comment was 1816, so that's going to be page 65.

5 **DR. KENNETH PORTIER:** 65. Okay. You know,
6 sometimes the line numbers change by section, so we kind of need to know page
7 numbers as well. Dr. Kissel, did you want to add anything?

8 **DR. JOHN KISSEL:** Yes. I did. So this is John Kissel.
9 I wanted to endorse what Bill said to open up and George also. And I also agree
10 with Sheri that the description of Figure 2.1 is a little better than it has been in
11 the past. We got rid of the language that said the compound just will all be in
12 water and we don't care about solids. So that's good. But I still find substantial
13 fault with both Figure 1.1 and Figure 2.1.

14 So I am an aggressive proponent of mass balances, and I
15 think we have two large stumbling blocks to presenting mass balances in these
16 documents. One is the CBI question, which EPA seems to be hung up on. I
17 think if CBI prevents you from doing a mass balance, just ignore the CBI. I
18 don't avoid the rules. I mean just don't use that data or attempt to use that data.

19 If the National Toxicology Program can estimate that 65
20 percent of the compound is used in synthesis and 15 percent is used in dry
21 cleaning and 10 percent is used in degreasing, then EPA can also estimate those
22 amounts. So we could start with the 300 million pounds plus and have 200
23 million pounds go to synthesis and 50 to dry cleaning and 30 to degreasing and
24 start to have an idea of what's going on with this compound in the environment.

1 And wrangling over what you do or do not or can or cannot reveal from CBI is a
2 useless diversion.

3 Secondly, with respect to -- that was Figure 1.1. Figure
4 2.1 has got arrows, and to a lay reader, what that says is the only way that PCE
5 ever gets to groundwater is through land application of biosolids. And that's just
6 not even a useful fairytale. There is a large -- it's mostly grey literature. It's
7 mostly not peer reviewed.

8 But there's a very large commercial real estate literature
9 which has to do with site cleanup and site evaluation and liability and other sorts
10 of stuff. And the general assessment -- that kind of gross oversimplification -- is
11 that any property that either is currently a dry cleaner or historically has been a
12 dry cleaner has a very large probability of being contaminated. And that
13 happens because, over time, tanks leak, spills -- lots of things happen.

14 One of the issues we have here -- the other issue besides
15 the CBI problem -- we have this attempt to bifurcate by regulatory parent. So
16 RCRA -- if RCRA covers groundwater, then we're not supposed to do
17 groundwater. But that's -- if you want to make that aside, if you want to say,
18 "Well, we're not dealing with the groundwater contamination because that's a
19 RCRA problem, then put that on the diagram with an arrow which says "Large
20 amounts of stuff wind up in groundwater, but that's covered under RCRA. And
21 we're not going to discuss it further here."

22 But at least acknowledge that it happens. Historically,
23 very large amounts of PCE have found their way to groundwater and caused very
24 large social cost. And to present a figure which shows only what the trivial

1 amounts of PCE that are in biosolids getting to groundwater just really is
2 extraordinarily misleading for people that are already not knowledgeable.

3 The other things I wanted to say had to do with physical-
4 chemical properties. Bill sort of alluded to this but didn't say it explicitly. So I
5 will add it. For carbon tet and for TCE, we made lists, recommended tables of
6 physical-chemical properties having to do with dermal exposure, and that would
7 certainly apply here, also. So that same list should be added.

8 The other thing is in the description of the compound
9 somehow the language about how PCE is -- or PERC is distributed in the
10 environment is missing some, I think, more evocative language. If you were
11 going to design a groundwater contaminant, starting with PCE would be a really
12 good place. It is extremely fit for purpose as a groundwater contaminant and has
13 a specific gravity greater than one, which means it sinks into depressions in
14 aquicludes which makes it very hard to get out and makes it kind of a permanent
15 contaminant. It has solubility which is high enough to present toxic
16 concentrations but low enough that it's not so soluble that you can pump it out.

17 So it defeats pump and treat. It's also not very degradable.
18 And while it is somewhat volatile, it's not so rapidly volatile that it would strip
19 out of groundwater and go away. So it is an exceptionally good groundwater
20 pollutant. And it seems to me if you're writing an overall assessment of a
21 chemical in commerce and you want to have some concept of what kind of
22 problems it presents as well as what its utilities are, a compound like this you
23 have to mention what an extraordinarily good groundwater pollutant it is and not
24 just gloss over that. So that's what I had for this question.

1 **DR. KENNETH PORTIER:** Thank you, Dr. Kissel.

2 Ruthann Rudel, do you wish to comment?

3 **MS. RUTHANN RUDEL:** Hi, this is Ruthann. Thank
4 you. I really -- I want to just endorse or second everything that John just said.
5 And I particularly like his suggestion for the lifecycle diagram in Figure 1.1,
6 which is to do a mass balance and to highlight where it's going. And you can
7 see suggested what regulatory program maybe is intended to address that.

8 So I definitely would like that diagram to provide more
9 information about the reality of how people encounter PCE in the world and to
10 highlight that the majority of PERC that's produced and not used as skewed
11 stock for producing other chemicals ultimately is emitted into the atmosphere.
12 And then a bunch of it is ending up in groundwater, as John said. I think it
13 should be discernible to the reader that the most significant exposures to the
14 general population outside of these conditions of use that are being evaluated,
15 like drinking water, ambient air, indoor air via use -- via soil vapor from
16 contaminated groundwater, because those are relevant to evaluating whether
17 some background exposure in addition to these COUs needs to be considered,
18 which I advocate it is.

19 I wanted to ask the Agency whether all the CBI claims
20 within Figure 1.1 are fully justified, and maybe the Agency could push back on
21 some to try to get better information. And I wanted to offer, as I have in the past,
22 the California Air Resources Board data on emissions from consumer and
23 commercial products. I think it could be useful in a variety of ways.

1 They survey consumer and commercial products that
2 contain PERC and actually use them to make emissions estimates for the state as
3 a part of their smog reduction regulatory program. But their data are available
4 and could be useful for checking the completeness of the consumer and
5 occupational conditions of use. It could be useful estimates of total PERC
6 emissions from these products to ambient air. That could be helpful for doing
7 population level models.

8 There's estimates of PERC emissions from individual
9 product categories associated with specific conditions of use, which could also
10 support exposure modeling and estimates of the size of the exposed population
11 used in conjunction with the Westat data. They have sales data for PERC
12 containing consumer and commercial products. So for example, in California, it
13 looks like about 30 tons a day of PERC containing products are sold and an
14 estimated 0.75 tons per day of PERC is emitted to the atmosphere from those
15 products. So I will provide Tamue with an Excel file with this data and some
16 documentation. Thank you.

17 **DR. KENNETH PORTIER:** Thank you, Ruthann.
18 George, I see your hand is up. George Cobb?

19 **DR. GEORGE COBB:** Yeah. That's correct, Ken. If I
20 may, first of all, I agree with what Ruthann just said about the California data.
21 And there's actually a fair amount of the California literature in the
22 documentation that is part of either this document or the problem formulation. I
23 don't remember which. I've reviewed so many documents related to this DRE.

1 The other thing I'd like to say is back on Figure 1.1 I
2 realized I put this in my response to Question 2 erroneously. And maybe Bill
3 doesn't have to say anything about it now. But on Figure 1.1, I just noticed in
4 this review -- I think it's consistent in all of the other reviews. In the industrial
5 commercial uses, the only arrow out of that box is to disposal. There's no arrow
6 out to anything else that says releases to waste -- releases and waste disposal.

7 And I also noticed there's no arrow that just goes to
8 release. That figure says that all of the PCE is disposed, and it's not. Some of it
9 is simply discarded. And I think there needs to be another arrow that's just
10 release separate from the arrow that says disposal, but maybe I'm in the minority
11 there. But I do think that an arrow out of that industrial commercial uses needs
12 to indicate that it's not necessarily disposed. Some of it is simply discarded.

13 **DR. KENNETH PORTIER:** Thank you. Dr. Willhite
14 and then Dr. Doucette. Dr. Willhite? Your phone may be muted, Calvin.

15 **DR. CALVIN WILLHITE:** You got me now?

16 **DR. KENNETH PORTIER:** Yup. Proceed.

17 **DR. CALVIN WILLHITE:** Yes? Okay. I'm wanting to
18 comment that Dr. Kissel is absolutely correct. One thing that could be done
19 instead of just setting aside this we're going to call it disposal to land where dry
20 cleaner guys take their solvent out in the back behind the building and just dump
21 it in a ditch or what have you, the thing that could be done is to explain the soil
22 vapor migration -- and its contributions to the data are rather widely known and
23 published in the open literature -- about we have ambient air concentrations
24 background. And you can at least at a minimum tell the reader what the increase

1 is the range of increase from what you had as ambient background to indoor air.

2 You can talk about that and tell the reader that rather than just brushing it off.

3 The other thing that's well, well, well described is
4 bacterial degradation of Perchloroethylene to its intermediates 1-2DCE, 1-1DCE,
5 and vinyl chloride, of course. At a minimum, you can tell the reader that we
6 know about that, and for whatever political reason it was made to just set this all
7 aside -- and it's handled by some other department and not this one -- I think it's
8 incumbent upon the current authors to explain that. Thank you.

9 **DR. KENNETH PORTIER:** Dr. Doucette and then I see
10 Dr. Kissel with his hand up and Ruthann Rudel with her hand up. And Dr.
11 Barone, you have last word.

12 **DR. WILLIAM DOUCETTE:** Ken, is it okay if I go
13 now? Oh, sorry.

14 **DR. KENNETH PORTIER:** Yeah. Go ahead.

15 **DR. WILLIAM DOUCETTE:** I want to thank all the
16 associates on this discussion for all their help and their great comments. And as
17 I was doing this review, I tried not to go back in time because, if you look at the
18 comments we made as a group on all the volatile halogenated components, we
19 talked about groundwater contaminants. We talked about vapor intrusion. It
20 seems like it's déjà vu all over again. We're repeating this. And I think the
21 reason I wanted to mention this -- it gets to my first point about the timeline.

22 We're not giving -- or the timeline is so accelerated we're
23 not giving really -- EPA doesn't have the chance to incorporate our comments
24 into the latest iteration. Some of them are, but a majority of them are not. And

1 as a panel member, it's getting really frustrating to see the same issues brought
2 up time and time again and not being addressed. So I guess I'm standing on my
3 soapbox but hoping that after these first ten chemicals are finished that we can
4 come up with some sort of this is what we've learned over this ten and really
5 incorporate that into the next ten chemicals. That's all I really want to say about
6 it. I just hope we can do that soon. Thank you.

7 **DR. KENNETH PORTIER:** Thank you, Bill. John
8 Kissel?

9 **DR. JOHN KISSEL:** Sorry to be slow. Unchecking a
10 couple of boxes is awkward. So I just wanted to respond to George's comment
11 about the Figure 1.1 and point him toward Figure 2.1 in the scoping document,
12 which actually did have air emissions in that ultimate box. So there were four or
13 so things there. Then ultimately in the draft risk evaluation, they were all
14 lumped into just disposal.

15 So I'm not sure whether EPA is considering air emissions
16 as a disposal. I think one could interpret air emissions -- fugitive air emissions
17 as disposal, but it's ambiguous. But the Figure 1.1 in the DRE is a modification
18 of the corresponding figure in the scope, which I think is actually a better figure.
19 So that's that.

20 **DR. GEORGE COBB:** Yeah. John, this is George. I
21 concur with that thought. So thanks for reiterating that.

22 **DR. KENNETH PORTIER:** Ruthann Rudel and then I
23 think we're going to close out this discussion. Ruthann?

1 **MS. RUTHANN RUDEL:** Yup. I'm just going to add
2 having seen email from Tamue that has a response about the septic systems. It
3 says EPA -- this is coming from EPA -- did not include evaluation of individual
4 onsite septic systems, which are regulated by states, tribes and local government.
5 And I guess I just want to say that those entities don't really have any capacity to
6 address PERC disposal into septic systems because of it's used in consumer and
7 commercial products.

8 And I feel like that's an indefensible position on EPA's
9 part, and I encourage the Agency to reconsider that. And then I want to echo
10 public commenter Kalmuss-Katz' clarification about biosolids not being
11 effectively regulated under the Clean Water Act, though EPA is asserting that
12 that is how they'll be dealt with. Thank you.

13 **DR. KENNETH PORTIER:** Thank you. Dr. Barone,
14 I've got 21 issues on this first discussion. Do you wish to comment or any
15 additional clarifying questions?

16 **DR. STANLEY BARONE:** Yeah. Yes, thank you,
17 chair. A number of the comments seem to revolve around the regulatory nexus.
18 And the lifecycle diagrams and the conceptual models that are included in our
19 risk evaluation have focus -- at least in this case have focused on what's in the
20 risk evaluation that are TSCA uses. And I think what I'm hearing, other than a
21 contaminant being a condition of use, which contaminants are not a TSCA
22 condition of use, is a suggestion to include the lifecycle diagram and the
23 conceptual models that were more inclusive of all the pathways in the revised
24 risk evaluation. Is that an adequate summary? Because a lot of the comments

1 seem to revolve around we have it in the scope or we had it in the problem
2 formulation, but we don't have it in the current risk evaluation. And I'm just
3 wanting to make sure I'm understanding this correctly so we can make this
4 actionable.

5 **DR. KENNETH PORTIER:** Yeah. This is Ken Portier.

6 To me, what the most actionable is communicating where all this stuff goes and
7 who's responsible if it's not under TSCA. And I think that statement complete
8 lifecycle and disposition -- so it's people don't want to know just about the fate
9 and exposures under TSCA in this Section 2. They want to kind of know
10 where's all of it going. And I think that gets to our mass balance discussion that
11 we've had before and a lot of the issues that we've talked about in the last 50
12 minutes. I'm going to turn to Dr. Doucette. Is there any final comment?

13 **DR. WILLIAM DOUCETTE:** Oh, go ahead. Go ahead,
14 John.

15 **DR. JOHN KISSEL:** So I want to direct a question to
16 Stan Barone. So the language -- the plain language in Lautenberg says that
17 circumstances -- and I'm chopping things out because the overall language is
18 regulatory and quite long. And there is a clause in there about "as determined by
19 the Administrator" -- but "circumstances under which a chemical substance is
20 reasonably foreseen to be used or disposed of." And given the history with dry
21 cleaners, I would say it is reasonably foreseen that underground storage tanks
22 will leak.

23 In fact, I think you would have to be deliberately obtuse to
24 believe that underground storage tanks don't leak. So I'm not a lawyer, but I'm

1 reading Lautenberg. And I'm not getting the definition that you're sighting to
2 us. And I wonder is there a formal statement by the Administrator which
3 eliminates contaminants because actually I didn't search for contaminants?

4 But I did a word search in Lautenberg for leak and spill,
5 and neither word every appears in the statute anywhere. So I would like
6 clarification -- and it may be that what you're telling us is perfectly correct. But
7 could we see the language or some official statement to that effect as opposed to
8 interpretation because I think the lay interpretation is that leaking tanks
9 constitute normal disposal and should be included.

10 **DR. STAN BARONE:** So leaking tanks are not normal
11 disposal, and leaking tanks are actually regulated by OLAN, our sister office. So
12 again, this gets at the regulatory nexus. Spills and accidents are also not a
13 condition of use and not under TSCA, again, regulated by our Office of
14 Emergency Response. So these are other kinds of actions that are regulated by
15 other offices within EPA.

16 **DR. JOHN KISSEL:** Well, the word "spill" appears
17 nowhere in Lautenberg. So if spills are excluded, that's because somebody has
18 written guidance of some kind, and that's -- what I'm asking for is where is that
19 guidance?

20 **DR. STANLEY BARONE:** Understood.

21 **DR. KENNETH PORTIER:** I'm going to bring this
22 conversation to a close and ask Dr. Doucette for last words before we move on to
23 Question 1.2. Bill, any last words?

1 **DR. WILLIAM DOUCETTE:** I was going to try to get
2 some clarification, and actually maybe we can just do this. Some of the
3 questions that I had regarding the sensitivity analysis in models, physical-
4 chemical properties, how often the EPI Suite database is updated, those sorts of
5 things -- if I could just get someone from EPA to let me know that, then I can
6 incorporate that into the comments. Otherwise, I think I'm done for now, Ken.
7 Thank you.

8 **DR. KENNETH PORTIER:** So Bill, if you'll write
9 those three or four questions down and try to submit them to Tamue --

10 **DR. WILLIAM DOUCETTE:** I will do that.

11 **DR. KENNETH PORTIER:** -- she can send that written
12 to the team, and we can see if we can get a response.

13 **DR. WILLIAM DOUCETTE:** Fantastic. Thank you.

14 **DR. KENNETH PORTIER:** At this point, I'd like to
15 move on -- I'd like to move on to Question 1.2. We're about a half hour, 25
16 minutes behind our schedule. And I'm a little worried that we may not get to
17 Question 3 today, which will push back tomorrow. But anyway, let's go on to
18 Question 1.2 about data approaches and/or methods used to characterize
19 exposure to aquatic receptors and surface waters. And the lead on this is Dr. Dan
20 Schlenk. And Dan, you have minus 15 minutes to discuss this.

21
22 **CHARGE QUESTION 1 (1.2)**
23

1 **DR. DANIEL SCHLENK:** Nice. No pressure, huh?

2 Yeah. Let me just point out at the beginning that a lot of this information is
3 probably better suited for Question 2 as well, but I'll just throw it out there
4 anyway for -- since it seems that wastewater discharge probably is one of the --
5 well, it's actually documented as the primary input into aquatic receptors. So I
6 kind of spent a little bit of time on that, as did some of the other Committee
7 members.

8 So the Agency did use the surface water monitoring as
9 well as monitoring data from other governmental agencies to determine
10 concentrations of PCE across the country in a given year. And they also used
11 this EFAST model based upon the TRI input data, which, again, is Question 2
12 info. But as Bill mentioned in the first part of this question, we've kind of dealt
13 with this in some of the other DREs. But the surface water data doesn't really
14 seem to be consistently take from discharge data, which is readily available from
15 the NPDS or the DMR database. It seems to be present in the problem
16 formulation, but it doesn't seem to be translated into the DRE for whatever
17 reason.

18 It's unclear to some Committee members why surface
19 water data in some cases is 20 miles downstream from any wastewater treatment
20 plant is even targeted in terms of the assessment. On page 41 of the problem
21 formulation document, it was indicated that MPDS PCE monitoring data in
22 surface water -- and this is presumably receiving water -- from top dischargers
23 had an average concentration of 19 parts per billion -- this is micrograms per liter
24 -- from 70 samples and average maximum discharge values of 50 micrograms

1 per liter. Now, what's unclear is why these data were not compared to any of the
2 EFAST estimates to examine the model efficacy.

3 It seems that in Section 2.3.4.2.2, the Agency clearly
4 states that WQP data was filtered. And this was filtered -- 94 percent of that data
5 was filtered out, which is very surprising, and did not include municipal waste as
6 this was considered off topic media. The concern here is that municipal waste is
7 often blended with industrial waste, and it may actually be the actual site of
8 where the waste -- the input actually occurs.

9 So the Committee does not agree with this exclusion, and
10 since municipal waste is monitored under NPDS, it would seem that you could
11 actually take PCE concentrations from those data to compare with the model
12 predictions when you've got a discharge that's transported to a treatment facility.
13 The Agency states in the problem formulations that concentrations measured and
14 discharged in receiving streams do not present actual stream concentrations, in
15 quotes. This really contrasts what NPDS permits actually do is that they do
16 require measurements of priority pollutants in receiving water concentrations
17 downstream of discharge.

18 I actually checked this out with a colleague of mine for
19 LA County sanitation district. They have to report surface water discharge,
20 receiving water discharge data to NPDS for their permitting. Again, although
21 these are values that are near discharge facilities, these are surface water
22 concentrations that are present that can be used for comparison and sensitivity
23 analysis, at least for the modelling data.

1 Again, so given that TRI data is available for specific
2 facilities, it's unclear why the Agency doesn't rank the top discharge sites based
3 on that TRE data and then conduct -- look at the DMR data, i.e. the NPDS data,
4 from wastewater effluence and receiving water. That way the EFAST data could
5 be compared to the monitoring data at the discharge and receiving stream. So for
6 example, the DRE indicated that this one company, the GM Components
7 Holding in Lockport, New York, has a significant user discharge for PCE from
8 the TRI data.

9 It's unclear why the Agency doesn't search out the
10 wastewater treatment plant, or treatment facility if it's a non-POCW, that
11 receives PCE from this user and evaluate that NPDS monitoring data from its
12 discharge facility and then compare to the EFAST predictions. That seems to me
13 a pretty straightforward analysis. And again, I think we submitted this in the
14 earlier DREs for other compounds.

15 So while it's useful to examine overall surface water
16 concentrations of PCE throughout North America, without source identifications,
17 it's unclear how these data can actually be related to industrial or commercial use
18 categories for TSCA. In addition there are no comparisons between any of the
19 EFAST predicted values or any of the global monitoring data with those
20 provided from the literature in the problem formulations. These would be
21 numbers that came from Europe, from the U.S., and from Canada from other
22 documents that were actually presented in the problem formulation. So there
23 seems to be this disconnect between the problem formulation and what's actually
24 in the DRE, at least for the exposure side.

1 Also, at least concerning the aquatic receptors in surface
2 waters, it seems that given the log Kow and the log Koc values -- they're all near
3 three -- it would seem that this compound probably accumulates in organisms
4 that have limited biotransformation. And this is demonstrated by the VCS that
5 have been sort of proposed in algae, marine algae, being 100 to 300. That
6 doesn't seem to me to be a low potential for bioaccumulation. It actually seems
7 quite high.

8 Now, the number is a lot lower in fish, and that's likely
9 because fish metabolized a lot more readily than, say, invertebrates and algae.
10 So consequently, I think disregarding that is somewhat short sighted, and it
11 should probably at least be put in at least to uncertainty analysis in the risk
12 characterization section of the document.

13 The WHO document clearly shows that sediment values
14 are present, at least one to 50 microgram per kilogram in Germany and up to five
15 micrograms per kilogram wet weight in the U.S. There are sediment guidelines,
16 and I've presented those in Question 3 when we get to that stage. So again, to
17 disregard sediment and accumulation at least tropically is somewhat, I think,
18 shortsighted and should be addressed at some point.

19 As had been pointed out in earlier DREs, the Committee
20 does not agree with the exclusion of terrestrial organisms from the risk
21 evaluation. The problem formulation on page 43, Table 2.9, clearly shows that
22 terrestrial organisms -- and these would be associated with aquatic receptors. So
23 these would be aquatic birds, aquatic mammals -- would undergo exposure not
24 only through ingestion of water but also via inhalation. I've submitted at least

1 some references that can address that, at least, I think in Question 3 as well. If
2 the EFAST models are predicting volatilization for discharge, then terrestrial
3 organisms should also be considered receptors.

4 Regarding EFAST model predictions, the 215 TRI data
5 indicates 349 pounds of Perchloroethylene were reported as directly released into
6 surface water. 857 pounds were sent to POTWs, but 9,187 pounds were sent
7 offsite to non-POTW wastewater treatment. So if the majority of PCE is -- or
8 PERC is non-treated, it's unclear if the WTP model for EFAST is actually even
9 needed or used or omitted from these predictive discharge scenarios from these
10 industrial facilities. Hence, that 80 percent loss estimate may be overestimated
11 and again is highly uncertain.

12 Some specific comments that were put forth by some of
13 the associates address Table 2.6, that some footnotes were missing. Figure 2.5
14 would probably work better as pie charts. There seems to be a supplemental file
15 missing on page 98. It would be useful to add some regulatory limits for Figure
16 2.6 for comparison.

17 On page 108, it's a wonder why the Agency only refers to
18 underestimation of risk. There certainly could be overestimation of risk that
19 could be addressed as well. And in the final paragraph on page 109, there seems
20 to be some clarity issues of what the EPA's trying to make in terms of the
21 confidence. Perhaps they should just state that the impact of the availability
22 monitoring data has based -- what that is based on their own aquatic exposure
23 data. It's also a little bit weird to have discussions regarding COC exceedance
24 when the COC hasn't been addressed yet in a later section.

1 Another Committee member noted that elimination of 99
2 percent of PCE related data remains troubling. This is brought out in page 56,
3 Figure 1.6. It's difficult to accept that 99 percent of data are inadequate for
4 assessment given that much of the toxicity data are based on treatments that use
5 nominal PCE concentrations. Several Committee members indicated a BCF --
6 I'd mentioned this earlier -- BCF of 312 should not be considered low. Again,
7 more emphasis on BAFs should be used, which is bioaccumulation factors which
8 considered water and food.

9 It's unclear how the Agency incorporated uncertainty in
10 the degradation rates when estimating persistence removal from wastewater.
11 Simply acknowledging uncertainty is inadequate. There are significant
12 uncertainties -- where there are significant uncertainties to potential unacceptable
13 risks are allowed to pass undetected should be minimized with adjustment
14 factors, uncertainty factors, or estimates from conservative ends of data
15 distributions. For estimated releases by industry type, the number of days are
16 unclear. What are the number of days of discharge for each facility type, or are
17 these simply annual totals divided by 365?

18 It's important considerations given there's multiple
19 assumptions made in the hazard association for this DRE. The maximum daily
20 release date represent only a 50th to 80th percentile facilities for seven of 12
21 COUs and represent the 86th percentile for two others. Thus the average
22 maximum daily values are conservative estimates for only 25 percent of the
23 selective COUs. Some other estimate of a higher percentile than average
24 maximum is needed.

1 Several Committee members wanted each user to be
2 assessed, even if there are no reported TRI data. The Agency is estimating many
3 other environmental parameters which there are limited or no data and is
4 ignoring other parameters for which there are data. There are too many users to
5 allow this gaping hole in release estimates. The Agency should require or collect
6 monitoring data for each major user type, or perhaps each of the known users
7 should be considered to release the maximum predicted for any industry in tables
8 above.

9 On page 89, the treatment of facilities that had no
10 designation of release to wastewater treatment plants or directly to water bodies
11 is handled correctly and points to the proper approach for all non-reported PCE
12 releases. If there are no data to document proper disposal, than discharge
13 without wastewater treatment of at least 25,000 pounds per facility should be
14 assumed until release data are available. Also on page 89, it would seem that the
15 facility location could be easily determined and used to locate stream flow data
16 for USGS gauging data. Failing that, the surrogate NPDS must be chosen to
17 maximize release to maintain conservatism. Having the actual data from the
18 streams in question is much preferred.

19 Page 89, in the absence of monitoring data, the 10th
20 percentile of the 7210 data should be used. On page 90, equations 2.1 and 2.2
21 have the same numerical outcome for calculation of numerator, but the
22 rearrangement of terms give the initial impression that there's something
23 fundamentally different about the numerators of these equations when they are in

1 fact the same. Also on page 9, for surface water concentration in static water
2 bodies, the range of acute to chronic dilution factors is very broad.

3 It was unclear what dilution factor was used for each
4 water body or if that is part of the EFAST site specific data. If these dilution
5 factors are uniform for river or standing water bodies, then the two dilution
6 factors should be noted in the explanation of the SWC equations. If dilution
7 factors are not standard for each water body type, dilution factors should be
8 listed in the tables where the R2s are presented. And that's all I got.

9 **DR. KENNETH PORTIER:** So Dan, that was only 23
10 issues. Dr. Blystone, do you want to add anything?

11 **DR. SHERI BLYSTONE:** Actually, no. I think Dr.
12 Schlenk did a great job of capturing all my comments.

13 **DR. KENNETH PORTIER:** Dr. Cobb?

14 **DR. GEORGE COBB:** Are you hearing me?

15 **DR. KENNETH PORTIER:** Yes.

16 **DR. GEORGE COBB:** So I'd like to thank Dan for
17 going through that so thoroughly. A lot of what he was reading was my stuff, so
18 I'd like to thank him and say that I don't have any further comments.

19 **DR. KENNETH PORTIER:** Thank you. Dr. Doucette.

20 **DR. WILLIAM DOUCETTE:** No additional comments.
21 Although, I do have one -- maybe a clarifying question. There was some
22 confusion to me in the text. My understanding is that the STP model within EPI
23 Suite was used to predict treatment effectiveness of a wastewater treatment plant.
24 Then, that effluent resulting from that treatment efficiency, which I think was

1 roughly 80 percent, goes into the EFAST model. Is that correct? And then that
2 EFAST model is used to predict concentrations through the aquatic receptors.
3 So I guess I'm asking EPA on this one.

4 **DR. KENNETH PORTIER:** Either EPA or someone
5 else on the panel might have understood that better.

6 **DR. WILLIAM DOUCETTE:** So it's two separate
7 models. The treatment model -- the treatment plant model, which is in EPI Suite,
8 and then the EFAST model is once it gets to the stream or the lake. I just want to
9 make sure I've got that correct.

10 **DR. MARI LEE:** This is Mari Lee from EPA. Yes,
11 that's correct. EPI Suite is estimating physical-chemical and fate properties,
12 whereas the EFAST model is measuring exposure concentrations.

13 **DR. WILLIAM DOUCETTE:** Okay. Thank you. And
14 then one other thing I just want to iterate, Dan mentioned the lack of a terrestrial
15 organism assessment. I think that is also important, especially given the
16 properties of this compound, which also reminds me that I think it was several
17 reviews ago that both John Kissel and I recommended, in addition to the dermal
18 properties that John mentioned, that an octanol air partition coefficient should be
19 added to the list of environmental fate and/or physical-chemical properties
20 because that can be used to predict bioconcentration within air breathing
21 organisms. Thank you.

22 **DR. KENNETH PORTIER:** Got it. Somebody needs to
23 mute their line. We're getting some feedback. Let's see. Ruthann Rudel? You
24 had your hand up.

1 **MS. RUTHANN RUDEL:** Sorry. That must be just left
2 over from before. Sorry.

3 **DR. KENNETH PORTIER:** Okey-doke. Dr. Cobb?

4 **DR. GEORGE COBB:** Yeah. Ken, this is just a quick
5 follow up on something that Bill brought up. That 80 percent of removal from
6 wastewater treatment -- a lot of that due to volatility -- actually, if you look at
7 that table back -- that table that I just reviewed for you, that predicts basically
8 that you're going to get two and a half times more water than you would predict
9 by the EFAST because you're going to get partitioning back into the water. So
10 all of those estimates have the potential to be wrong.

11 **DR. KENNETH PORTIER:** Okay. Dr. Schlenk?

12 **DR. DANIEL SCHLENK:** Yeah. Actually, Bill asked a
13 question. I was going to ask this during the presentation phase but forgot. So
14 what I'm still unclear about is are all of the estimates done with EFAST
15 assuming STP treatment? Because based upon what the problem formulation
16 said, very little of it actually gets treated. It looks like 9,000 pounds versus 300
17 pounds actually goes to non-POTW sources. So it looks like most of -- at least
18 that was stated in the problem formulation, most of it is not treated through a
19 standard POTW treatment. So I'm wondering in those particular cases is that
20 STP module of EFAST used?

21 **DR. KENNETH PORTIER:** That's a good question.
22 Doucette and then Dr. Lin.

23 **DR. WILLIAM DOUCETTE:** This is Bill Doucette.
24 My understanding is that they treat both -- they call them indirect and direct

1 releases. So EFAST is used if there's a direct input into a surface water body, in
2 other words that's not treated through a wastewater treatment system. And then
3 the 80 percent removal is only used if it does go through a wastewater treatment
4 plant. I think that's correct, but maybe they can add to that.

5 **DR. MARI LEE:** Excuse me, Mari Lee again. Yes,
6 that's correct. So we are applying a release volume to the EFAST model. And
7 then depending on how we classify the release, it either has the 80 percent
8 removal taken out through the EFAST, so the concentration is reduced. Or if it's
9 an indirect release, then there's no removal.

10 **DR. KENNETH PORTIER:** Thank you. Dr. Lin?

11 **DR. ZHOUMENG LIN:** Hi, I have one comment on
12 equation 2-3 on page 88. The chemical release to wastewater equal to annul
13 loading multiplied days released per year, I believe this multiply symbol should
14 be changed to divide. So it should be annual loading divided by the days
15 released per year. Thank you.

16 **DR. KENNETH PORTIER:** That could be a major
17 change. Okay. I think the Committee's -- I guess I'll open it up to anyone else
18 on the Committee that wants to comment. Otherwise, I'll turn to EPA. Any
19 clarifying questions of the, by my count, 26 issues that we've brought up on this
20 question?

21 **DR. STANLEY BARONE:** This is Dr. Barone. No, not
22 at this time.

1 **DR. KENNETH PORTIER:** It's going to be a fun write
2 up. Okay. Let's move on to Question 2. Dr. Lee's back, so I guess, Dr. Lee,
3 you're going to read?

4 **DR. MARI LEE:** Yes. Can you hear me? Can everyone
5 hear me?

6 **DR. WILLIAM DOUCETTE:** Yes, I can.

7 **DR. KENNETH PORTIER:** Yes, we can.

8
9 **CHARGE QUESTION 2: ENVIRONMENTAL RELEASES AND**
10 **EXPOSURE**
11

12 **DR. MARI LEE:** Okay. Question 2, Environmental
13 Releases and Exposure, EPA estimated releases to the environment using Toxics
14 Release Inventory, TRI, and Discharge Monitoring, DMR, data. These releases
15 data were used as inputs to EFAST 2014 to estimate exposure concentrations in
16 surface water. EPA evaluated monitoring values of PCE in surface water and
17 where possible compared those values to estimated release concentrations.
18 Question 2.1, please comment on the data and approaches used to estimate the
19 amounts of wastewater discharge for the different scenarios from Section 2.2.
20 And Question 2.2, please comment on the approaches, models, and data used in
21 the water release and exposure assessment including comparison to monitored
22 data, Section 2.2 and 2.3.
23

CHARGE QUESTION 2 (2.1)

DR. KENNETH PORTIER: Thank you. Let's start with Question 2.1. The lead is Dr. Doucette.

DR. WILLIAM DOUCETTE: Thank you. I received comments, and I'll let my fellow commenters jump in on this. Just a couple of things. A lot of these are overlap between or at least a little bit of overlap between the things that we discussed in previous reviews and also in Question 1. My question on septic tank effluence was answered and basically based on it being someone else's regulatory problem, which we can agree or disagree, but at least that was answered for me.

In terms of discharge, I mentioned this in previous discussions. EFAST -- and this was also mentioned in the document -- is still not appropriate for volatile compounds. While likely conservative, it sets a poor precedence when you use an inappropriate model to predict environmental exposure concentrations. So again, I think it probably is conservative, but, again, it's poor form, I think.

There was also a point on, I think, it's page 35 of 316. It talks about the definition of major and minor discharges is set by the state and could be based on discharge volume or facility size. And there's limitations associated with this. And basically it says that, due to these limitations, some sites that discharge PCE may not be included in the DMR data set. And I felt that there could have been a better description on how one incorporates these sorts of uncertainties into the overall wastewater discharge estimates.

1 Several of the commenters brought up this idea of co-
2 contaminants and having similar biological impacts on metabolites and how
3 those might influence what is discharged into the -- or by the wastewater. There
4 was a comment from one of the other associates that was curious about the
5 potential for groundwater contaminating surface water or vice versa for surface
6 waters contaminating ground water. I think Ruthann had a comment regarding
7 the ecological assessment used monitoring data for 2016 instead of the most
8 recent or the average of 2013 versus 2017. That wasn't clear, especially when it
9 looks like 2016 has lower levels comported to the -- compared to the other years.

10 And then George had a comment that he just brought up in
11 the previous discussion about release arrows and the industrial use commercial
12 box. I think we've got that settled. So I think that's it other than if any of the
13 other co-discussants wants to add to that.

14 **DR. KENNETH PORTIER:** Dr. Blystone, did you want
15 to jump in?

16 **DR. SHERI BLYSTONE:** Nothing further. Bill does a
17 great job, as always.

18 **DR. KENNETH PORTIER:** Dr. Cobb?

19 **DR. GEORGE COBB:** Yeah. I have one follow up to
20 what Bill just said, and maybe to ask any of the discussants about this. I think
21 that EFAST may be conservative for downstream treatments of concentrations if
22 you get out of the proximity of the release point. But if you consider the concept
23 of pseudo-persistence, coupling fugacity modeling with EFAST right near the
24 facility's probably not too bad. But again, that's going to mean that EFAST

1 alone might not be conservative if you're not considering the partitioning from
2 air into water. But I may considering this overly conservative or overly
3 simplifying that situation for some of those that might be more adept at some of
4 this modeling than I am.

5 **DR. KENNETH PORTIER:** Ruthann Rudel?

6 **MS. RUTHANN RUDEL:** I just have one thing to add to
7 the importance of considering co-contaminants that are similar and maybe in
8 some cases the TCE is a degradation product of PCE. But I wanted to point the
9 Agency to 2006 USGS study of VOCs in groundwater and drinking water supply
10 wells. The most frequently detected mixture or combination of two chemicals in
11 aquifer samples was PCE and TCE at one and a half percent of the samples
12 taken. So those are drinking water. And I just thought that that was an
13 important additional resource for thinking about aggregate risk assessment across
14 the co-occurring compounds and exposures. Thank you.

15 **DR. KENNETH PORTIER:** Thank you. Dan -- oh,
16 Dan put his hand down. Bill Doucette?

17 **DR. WILLIAM DOUCETTE:** Yeah. I just want to
18 follow up on George's comments and maybe clarify mine. I agree that EFAST is
19 conservative in that for a volatile compound it doesn't allow volatilization out of
20 the water. But I agree with George in the fact that, at a nearer facility where the
21 air concentrations are high, it might not be conservative because I agree that you
22 could have transfer from the air into the water, elevating the exposure
23 concentrations. So just a point of clarification there. Thank you, George.

1 **DR. KENNETH PORTIER:** Dan? Your hand's back
2 up.

3 **DR. DANIEL SCHLENK:** Yeah. I took it down and put
4 it back up again because I'll be addressing this in the uncertainty section of the
5 characterization but wanted just to follow up since George brought it up. A
6 worst-case scenario is a wastewater dominated stream, which we have a lot of in
7 the desert southwest. And those basically get no dilution. So consequently,
8 EFAST would completely underestimate the exposure that takes place in those
9 wastewater dominated systems.

10 **DR. KENNETH PORTIER:** Good point. Any
11 additional comments? Anyone on the panel? EPA, any clarifying questions on
12 the comments on Question 2.1? Let's go ahead and move to discussion on
13 Question 2.2 on approaches, models, and data used in the water release and the
14 exposure assessment, including comparison to monitoring data. Dr. Cobb, you
15 have the lead.

16

17 **CHARGE QUESTION 2 (2.2)**

18
19 **DR. GEORGE COBB:** Sorry, Ken. I'm trying to get off
20 of mute. Am I there? Can you hear me?

21 **DR. KENNETH PORTIER:** Yes, you are. Mute, it's
22 kind of being slow today. You know, you click on mute and you have to wait
23 three seconds before it actually beeps so you can hear it. But I can hear you
24 now.

1 **DR. GEORGE COBB:** Well, then I'll be honest. My
2 Webex got buried beneath three different windows. Somebody sent me an
3 email, and it rearranged all my windows. So I had to find it. That was part of
4 the problem. Okay. I think that --

5 **DR. KENNETH PORTIER:** You only have three open?
6 Okay.

7 **DR. GEORGE COBB:** I think I've captured
8 everybody's comments for this. And if I haven't, please chime in here. But I'm
9 just going to go through this kind of as quickly as I can. This is not the entire
10 written comments, but it's enough that I think we can capture it for discussion. I
11 will say that we have eight recommendations out of this, four of which we've
12 gotten pretty good consensus on and four of which we're wrangling with
13 wording. So just as an example for what this one will probably hold for
14 recommendations.

15 So to start off, Table 2.5, related to confidence of release
16 estimates is actually a welcomed addition. That's on page 75. And there are
17 comments about the content of this table and uncertainties later in the charge, but
18 having that table is a valuable addition.

19 Going on, there are no biomonitoring data, page 107, and
20 there are no systematic measurements of PCE for determination of commercial
21 releases to or effects on any environmental media. Several of us noted that the
22 American Chemical Society has publicly available statements regarding the need
23 for more robust monitoring datasets and biomonitoring in robust regulatory risk
24 assessments and risk determination frameworks. And I have a reference for that.

1 And we mentioned this in TCE document as well, back to
2 Bill's point, is this is going so fast the Agency simply doesn't have time to
3 address some of these comments. Also, there are significant improvements in
4 language regarding exposures, environmental exposures. This should still be
5 refined a bit more, and there's some specific wording recommendations that I
6 won't go into. Also as noted in the TCE review, the probabilistic dilution model
7 is a very good tool for estimating these downstream toxicant concentrations.

8 However, I will continue to repeat that probabilistic
9 dilution model, as cited by the Agency, is for non-point source runoff. And the
10 Agency has then also excluded non-point source runoff from this assessment and
11 all of the other assessments that we've done. If the chemical's being used in
12 commerce and it's running off non-point source, then that is a discharge to a
13 water body or can be a discharge to a water body.

14 Also, the ambient concentrations of PCE in water bodies -
15 - I think Dr. Schlenk kind of relayed to this in a previous question. They're
16 really not relevant to this risk assessment unless they're relatively short distances
17 downstream of the facility. An ambient water quality monitoring station that's
18 two mountain ridges away from a release point really doesn't have a whole lot of
19 meaning.

20 There are some considerations about EFAST, considering
21 volatilization but also not considering the fact that chemicals could partition back
22 into water. We've discussed that a little bit. The omission of land applied TCE -
23 - excuse me, not TCE -- land applied PCE leaves a major gap in the exposure
24 data for receptors. In the problem formulation -- actually, the document states

1 that in the problem formulation, EPA determined that risk would not be
2 evaluated for a land applied biosolid because PCE is currently being assessed by
3 the Clean Water Act regulatory analytical process.

4 And again, that's not contributing to this risk assessment
5 or risk determination. It's just admitting there's a big gap in anything that's
6 being presented here. And all of that information needs to be somehow
7 incorporated into an overall determination for this product. And that is it, and
8 I'll turn it over to the other discussants.

9 **DR. KENNETH PORTIER:** Dr. Blystone, anything to
10 add?

11 **DR. SHERI BLYSTONE:** I think that George covered it
12 all. So I think I'm good. Thanks.

13 **DR. KENNETH PORTIER:** Dr. Doucette?

14 **DR. WILLIAM DOUCETTE:** Yeah. I'm also fine with
15 what George put forth. Thank you.

16 **DR. KENNETH PORTIER:** Dr. Lin, your hand is up?

17 **DR. ZHOUMENG LIN:** Yes. Hello, everyone. I have
18 one comment on Table 2-9 on page 99. If we look at this Table 2-9, the data do
19 not seem right. For example, if we look at year 2013 -- let's look at the range --
20 and the concentration in both impulse, and then we compare the average.

21 So the average value is even higher than the upper bound
22 of the range. This doesn't seem right to me, so the average is 2.3 multiplied E to
23 the power of zero, negative 0.001. But the other is the upper range -- the upper
24 power of the range is 9.2 multiplied E to the power of two. It seems strange.

1 And the other comment is regarding the concentration in
2 only samples above the detection limit. If we look at the year 2013, there are
3 366 samples measured and only two samples had a concentration higher than the
4 detection limit. These two samples is not enough to represent an entire 366
5 samples. So I feel to present the range and average of two samples, the data is
6 not representative. This data does not represent an entire 366 sample result.
7 Thank you.

8 **DR. KENNETH PORTIER:** Any additional comments?
9 Dr. Cobb, your hand is up?

10 **DR. GEORGE COBB:** Yeah. Ken, just on that last
11 point, I had that in my Q6. That was actually something I had in my Q6, very
12 similar comments. Who gave that last response so that I can follow up and get
13 their information for this question?

14 **DR. KENNETH PORTIER:** That was Dr. Zhoumeng
15 Lin.

16 **DR. GEORGE COBB:** Okay. Thank you.

17 **DR. KENNETH PORTIER:** L-I-N.

18 **DR. ZHOUMENG LIN:** Thank you.

19 **DR. KENNETH PORTIER:** Any additional comments
20 on Question 2.2? Dr. Lin, we've seen these kind of things before. Thank you
21 for reading with that much attention to detail. I missed that. Usually, I look at
22 those kind of things. Okay. Why don't we move on to Question 2.3?
23

CHARGE QUESTION 2 (2.3)

DR. MARI LEE: All right. This is Mari again.

Question 2.3, please provide any specific suggestions or recommendations for additional data or estimation methods, including modeling approaches, that would be considered by the Agency for conducting or refining the water release and exposure assessments and its relation to monitoring data, Section 2.2 and 2.3.

DR. KENNETH PORTIER: Okay. The lead for Question 2.3, Dr. Blystone.

DR. SHERI BLYSTONE: Yeah. So this should be fairly quick unless people -- some of the other discussants have additional comments. And I think there were some suggestions on data in previous responses, so we might just have to move things around a little bit. I think what we've heard from many people, including the public commenters, is it would be nice to have additional monitoring data that was more specifically relevant. And Dr. Cobb's talked quite a bit about where you would gather that from as being important, as well. But it would be nice if we had more actual data on water concentrations to follow up.

One of the public commenters at least, and I think some others have noted this as well -- is that in the data there were some PCE facilities that didn't appear to have an NPDES permit or it wasn't clear where those releases were going. And it seems reasonable that EPA could follow up with those facilities to figure out exactly what's happening. Ruthann, I know you had

1 several comments on data that you've already said. You might have some more,
2 or maybe some of the other discussants have additional data. But that's what I
3 had so far.

4 **DR. KENNETH PORTIER:** Thank you, Sheri. I'm
5 going to go ahead and ask Dr. Cobb, Dr. Doucette if they've got additional
6 comments. And then we'll add Ruthann Rudel. Dr. Cobb?

7 **DR. GEORGE COBB:** So thank you, Ken. Can you all
8 hear me?

9 **DR. KENNETH PORTIER:** Yes.

10 **DR. GEORGE COBB:** Okay. So I have a few things to
11 follow up on and thanks, Sheri, for getting the majority of our comments. Some
12 very basic things just so that they're on the docket. There's some conflicting
13 statements about the number of studies that were used in Section 2.3.4.2.3, and
14 there'll be more detail about that in the write up.

15 And again, the data filtering and cleansing statements
16 indicate that risk estimates are not allowed -- excuse me, that eval- -- let me start
17 again. Data filtering and cleansing statements on page 93 indicate that estimated
18 values are not allowed. But one thing that everybody needs to realize is that
19 non-detects require that you estimate any mean that you calculate from a dataset
20 that has non-detects in it. There's more about that, but just to get that on the
21 docket, as well.

22 And maybe it's a reemphasis, but the geospatial
23 evaluations of the HUC8 and the HUC12 scale watersheds is actually very useful
24 but perhaps not for assessing where there are risks now. They're most useful in

1 assessing where to place monitoring stations for the future or for when you have
2 facilities for future DREs that the Agency may have to undertake.

3 Also on page 94, the estimated concentration maximum
4 for 20-day releases is three times higher than the max for 200 to 300-day
5 releases. And that needs some explanation because there's a 10X difference in
6 the number of days, but there's only a 3X difference in the maximum. So there
7 has to be something going on with that distribution, most likely in the
8 probabilistic dilution model. And something about how that distribution
9 selection has allowed that not to follow the same multiplier needs to be
10 addressed.

11 I'm scanning through these comments to make sure that
12 there are no other things that we need to go through here. It seems on page 98
13 that surrogate stream flows should be refined by using site specific data rather
14 than some estimate that might be a mean. It might be very far off. And
15 measuring those strength loads is not that difficult, and there are actually
16 databases that are maintained, some of which by the Department of Energy but
17 others that have historical data in them for that type of thing.

18 There's an incorrect title on page 98, but we'll have more
19 about that in the written comments. And on page 100, I've got a question about
20 why was only the 2016 data used and not all the data. You've got higher
21 concentrations in 2013, and you have more detectable concentrations in 2014.
22 So some explanation for why 2016 was chosen over what would seem to be a
23 more robust dataset seems to be in order.

1 Also, this goes to one of the comments we just heard. The
2 central tendency data for the Pacific Ocean in Table 2.2 have some issues that
3 will be covered in the written comments. And the rest is redundant for things
4 that were comments in other sections, so thank you for listening.

5 **DR. KENNETH PORTIER:** Thank you, George. Sheri
6 Blystone mentioned that Ruthann Rudel might have some comments. Ruthann?

7 **MS. RUTHANN RUDEL:** No, I don't have anything.
8 Thank you.

9 **DR. KENNETH PORTIER:** Okay. Just checking.
10 Anyone else on the Committee wish to comment? I'm not seeing any. Okay.
11 I'll turn to EPA. Any clarifying questions on the comments by the Committee?

12 **DR. STANLEY BARONE:** Not at this time. Stan
13 Barone.

14 **DR. KENNETH PORTIER:** Okay. Thanks, Stan. So I
15 have we're just short of a quarter to 5:00. And I know that Dr. Johnson, who's
16 the lead on Question 3, has to leave -- kind of has to leave at 5:00. So I'd like to
17 go ahead and read in the question. And Dr. Johnson, in 15 minutes you can at
18 least start the discussion. We can have maybe a little bit of additional discussion
19 once you leave, and we'll finish the question first thing in the morning. So I'll
20 ask Dr. Lee to read in Question 3.

21
22 **CHARGE QUESTION 3: ENVIRONMENTAL HAZARDS**
23

1 **DR. MARI LEE:** Question 3, environmental hazards,
2 EPA evaluated environmental hazards for aquatic species from acute and chronic
3 exposure scenarios. Please comment on EPA's approach for identifying
4 environmental hazards for each risk scenario, e.g. acute-aquatic or chronic-
5 aquatic. What other information -- what other additional information, including
6 hazards, should be considered? This is based on Section 3.1.

7
8 **CHARGE QUESTION 3 (3.1)**

9
10 **DR. KENNETH PORTIER:** Dr. Johnson, you had
11 written me that you had a lot of things to talk about.

12 **DR. MARK JOHNSON:** Yes, sir. If you can hear me, I
13 have over five -- or close to five pages of questions or comments. The good
14 news is most of them are all consistent, so I think we have consensus with our
15 contributors. So I thank you all for that. I still have some wordsmithing to do.

16 But I'd like to begin by saying that I am incredibly
17 empathetical and sympathetic-al to the EPA regarding the issue with developing
18 toxicity benchmarks, not just for environmental receptors but for human health
19 as well. This is hard stuff. We've tried to do that arterially ourselves, and it's
20 very difficult. And this kind of gets to Question 0 about the systematic review a
21 little bit. So I think it might be worthwhile just to begin here with that.

22 There's basically two things you have to do when you do a
23 systematic review. One, you have to share that you haven't missed anything.
24 You've done your due diligence and found all the documents and level of effort

1 and everything you could find. And anyone else could try to repeat that lit
2 review.

3 But you also then have to use the best practices that are
4 out there and objective valuation of the data that's used. And that's where it gets
5 tricky. How do you use those best practices? How do you judge the quality of
6 studies and the relevance? Two different things. So clearly EPA has done a
7 robust job of looking at the quality of the evidence. The relevance is another
8 issue.

9 So when you look at a dataset like with PCE, you have
10 lots of information. Most of us were very discouraged not to see that
11 information displayed somehow specially. Typically, what we all -- a lot of us
12 recommend is a species sensitivity distribution like we saw for TCE where you
13 have that information up there and you can see where the spread of the data are.
14 But we also realize that there's variation in that data, and the variation is often
15 not always attributed to differences between species.

16 Sometimes there's issues associated with data quality,
17 issues associated with methods. There seems to be at least ten studies out of
18 about 374 results that many of us did a separate sort of lit review going through
19 ecotox database and looking for results. There's lots of information out there.
20 We didn't see that information displayed here in this assessment.

21 So I think the trend I'm seeing in these comments is that,
22 number one, try a species sensitivity distribution if you can, even if it doesn't
23 work. You at least get to see the spread of the data, and that makes us all feel
24 more comfortable. You want to use as much data that's out there as you possibly

1 can. If you took this question to the National Academy, I would almost
2 guarantee you they would come back with a comment like that.

3 You just don't want to -- you can -- it makes a logical
4 sense to take the most sensitive species and draw your line there. But you
5 always wonder about is there a quality issue? Is it an outlier? Is it representative
6 of most of the other information that we do have data for?

7 Dr. Schlenk mentioned the absence of developmental data
8 from medaka. There's also some developmental data for native amphibians that
9 really wasn't discussed at all. Fundamentally -- and I will let my colleagues
10 comment on this -- I don't think the numbers are out of line. I think the numbers
11 are good. That is my comment. I just don't think they're well supported.

12 There's also a field study out there, however, where
13 actually PCE was added to a natural pond at concentrations around 0.44 mgs per
14 liter and 1.2 mgs per liter where numbers of daphnia declined to zero within one
15 day and a higher concentration with about four days. And so I didn't see that
16 referenced at all, not even to the section where the systematic review was done.

17 There were a lot of studies that were deemed acceptable, I
18 thought, that I saw based on the systematic review. But we really didn't see
19 them in the DRE. There are other comments that suggested that -- shoot. I just
20 lost my train of thought. Sorry about that. Yeah. There's a lot of comments that
21 actually provide specific references for some studies that they didn't see listed.

22 Another comment we see here -- and we've seen it before
23 with the other chemicals -- is that there may be one or two -- actually, one of the
24 other outside reviewers had a comment similar to this where some studies were

1 eliminated because it was unacceptable. And I understand the logic behind
2 making the study unacceptable. However, sometimes there is some valuable
3 information there somewhere, and you hate to throw the baby out with bath
4 water.

5 There may be some information in a corroborative sense
6 that still could be useful. Even though you wouldn't want to develop a pod with
7 that data, that data still might help corroborate a pathway, a mechanism or
8 something about toxicity to another species that you didn't consider. So
9 sometimes totally excluding studies might not be the way to go.

10 There's still some comments here about terrestrial
11 vertebrates or invertebrates, but there was a study that I found where they looked
12 at terrestrial vertebrates in functionally confined spaces, burrowing mammals at
13 Air Force Institution -- this was a peer reviewed study -- and concentrations in
14 the part per billion ranges where they didn't see adverse effects. You could point
15 to that to help support that point if you want to make it. We also -- there are also
16 some issues, I believe, with the -- let me see if I can find that exact comment.
17 I'm scrolling through five pages here to find that one point in particular where I
18 believe LC50 and EC50's were averaged together in a geometric mean.

19 You really can't average sublethal and lethal endpoints
20 together. It's inappropriate. However, it is appropriate to average a LOAEL and
21 a NOAEL geometrically within a study because there you know that,
22 theoretically, hypothetically, the threshold's somewhere between the NOAEL
23 and the LOAEL. How do you get there? Well, you take the geometric mean.
24 That makes sense. But to take the geometric mean of the median lethal

1 concentration and the median effective concentration isn't really appropriate
2 unless you can show that that sublethal endpoint would logically lead to
3 mortality in a natural environment.

4 I think we kind of said the same thing with TCE last go
5 round where it caused narcosis. It could cause a developmental fact where there
6 is extreme teratoma of the backbone or some other areas where you know that
7 individual probably wouldn't last long. That's becoming prey to other
8 organisms. That would be okay to do so. But we didn't see that information
9 being displayed.

10 I think without getting into the details, there were some
11 other comments about whether or not to use a safety factor or not. I think what
12 most of us were suggesting is that you want to start with a species sensitivity
13 distribution. If you can't do that, then at least share the data in some kind of
14 spatial scattered diagram-like format. That way, it gives people more confidence
15 that the endpoint and the effects you're looking at in these different species is
16 reasonable, that no one's cherry picking the data here. Here's where the data fall
17 out. Here's where we're drawing our line. And therefore, it gives much more of
18 a transparent situation of where the threshold may be for not just a species of
19 concern by for other species.

20 It's a shame you only have that one algal study. I think
21 that the big thing is you really want to protect aquatic plants, not just algae.
22 Some would argue that algae's a problem in some ecosystems because over-
23 nutrification. But if you had some other plant species, duckweed for example,
24 lemma would be excellent to show if you had that information. And I think I'm

1 going to stop right there and let my colleagues a chance to voice and if I missed
2 anything in particular.

3 **DR. KENNETH PORTIER:** Thank you. I will mention,
4 Dr. Barone, I can hear you typing. You need to mute yourself. Let's see. Dr.
5 Blystone?

6 **DR. SHERI BLYSTONE:** As usual, Mark did a great
7 job again. I have nothing to add at this point.

8 **DR. KENNETH PORTIER:** Okay. Dr. Cobb?

9 **DR. GEORGE COBB:** Okay. I have a couple of things
10 to add. Mark did a great job, just a couple of things. In full disclosure, he said
11 he had five pages of comments. I think at least half of those were mine. So
12 thanks, Mark, for going through things.

13 I guess you start on page 249, perhaps. In my estimation,
14 you've got 10 studies there that have been included or could have been included
15 from the problem formulation, including some amphibian data. But many of
16 those were excluded or somehow paired down in this risk assessment. I think
17 it's be preferable if you, again, did that species distribution and looked at all of
18 those species in that study.

19 I'll also make the comment that Table 3.1 contains data
20 from studies that were generate by testing programs that EPA was undertaking at
21 the time. And they're exactly the kind of testing programs that EPA must
22 implement to effectively address the questions that we're going through now.
23 And part of the reason for that is while those testing programs were great, they
24 were using the standard methods of the time, and all of the toxicity data for this

1 assessment are based on nominal exposure concentrations. And if I'm wrong on
2 that, please correct me. But I could not find a measured concentration anywhere
3 in these toxicity assessments.

4 So the entire hazard assessment is based on nominal
5 concentrations, which is in direct contradiction to the EPA's exclusion criteria.
6 So you could make the argument that there are no toxicity data in this
7 assessment. On that basis, I think you almost have to open this up to reasonable
8 quality studies, even if they're missing one type of data quality factor that you
9 would like to have.

10 I'll also point out that one of the studies actually utilized is
11 from Niederlehner-- I can't pronounce that -- that actually shows a superior
12 approach for developing safety factors for these types of compounds, especially
13 for these low molecular weight compounds. And I think Dr. Schlenk brought
14 this up months ago when we were talking about another compound that works on
15 general narcosis mechanism very likely for environmental systems.

16 Also, on page 253, the acute COC for invertebrates is
17 listed as 1342 micrograms per liter. If you go back to the problem formulation,
18 that same acute COC was 800 micrograms per liter. Some determination of how
19 that occurred should be provided. I think it had something to do with the way
20 that the data out of Horne, Call, and Ahmad assessments for these that are
21 actually listed in the DRE were handled in this DRE versus the problem
22 formulation. And I've got a table to kind of address that a little bit.

23 And then, again, I think the assessment factor of five for
24 daphnia and perhaps the one of ten for the invertebrates are low -- excuse me,

1 five for daphnia are low. And even an assessment factor of ten might be low.
2 And I've talked about the hundredfold adjustment factor in the Kinsler reference.
3 It would seem to be more appropriate for protecting aquatic species. But going
4 back to the original comment that Dr. Johnson made, if you use a species
5 distribution, you get away from the need for some of these assessment factors.
6 And with that, I'll be done.

7 **DR. KENNETH PORTIER:** Thank you, Dr. Cobb. Dr.
8 Davies?

9 **DR. HOLLY DAVIES:** Hi. Mark mentioned a lot of
10 what I put in. I just wanted to emphasize again that there seem to be a lot of hits
11 in ecotox that weren't included and a lot of other toxicity studies that weren't
12 included that we'd like to know more about why and just kind of issues with the
13 systematic review where some of the criteria seem to be inconsistently applied.
14 And as Dr. Cobb mentioned, when one criterion is unacceptable, the whole study
15 gets thrown out, even though some of these studies seemed useful. With that, I'll
16 sign off.

17 **DR. KENNETH PORTIER:** Thank you. Dr. Doucette?

18 **DR. WILLIAM DOUCETTE:** Yeah. I think my
19 concerns have been adequately addressed by the other panel members, so I won't
20 add anything.

21 **DR. KENNETH PORTIER:** Dr. Schlenk?

22 **DR. DANIEL SCHLENK:** Yeah. Just to follow up on a
23 couple things Mark mentioned. I don't know whether the Agency's had a
24 chance to get back with me regarding the question I had earlier about the

1 Spencer et al 2002. The reason why I bring that one up is because it's a
2 developmental assay that actually puts the LOEC -- or actually allows a COC to
3 actually approximate what we have for algae. I know there's a big concern that
4 algae are always too sensitive and always too sensitive. But this would actually
5 be a vertebrate value that actually would be in the same ballpark.

6 If you take their LOEC, which is 1.5, divided by two to
7 get the NOEC, you're going to get 0.75. You slap a tenfold safety factor on it.
8 You're getting right in the same ballpark that we're seeing with invertebrates.
9 So to have a vertebrate number I think would strengthen the case. Obviously,
10 the specie sensitivity distribution would be a lot better.

11 But one thing I would like to highlight, which Mark
12 mentioned, was nowhere do we see a weight of evidence approach in any of
13 these studies that I've looked at, at least in terms of the eco side of things. We
14 see it in the human health determinations all over the place. But maybe the
15 HCBd one there was a weight of evidence discussion, but I didn't -- I never see
16 that mentioned at least in the eco side of things. And it definitely should be
17 there, particularly at least in the risk characterization aspect. I'll beat a dead
18 horse.

19 At least use some form of partnering of the human health
20 with the eco side of things. If you see developmental tox in the human health
21 side of things, fish are vertebrates and amphibians are vertebrates. So typically,
22 you are going to see some form of similarity in mode of action that's conserved
23 among vertebrates in that particular case.

1 It also goes to mention that a lot of the data was not
2 shaded because sometimes the concentrations didn't exceed a 20-day period, for
3 example, because that's when the assays were taking place. Again, if you use a
4 developmental assay, those windows are hours. The field study that Mark
5 mentioned, daphnia being dead within a day, you don't need 20 days to actually
6 see an effect. So consequently, again, you're using conservatism there in terms
7 of potential risks that could be sort of highlighted a little bit more by using at
8 least a weight of evidence approach and/or at least using endpoints that are,
9 again, more sensitive in that particular case.

10 I mentioned in my previous comments about the
11 sediments. Again, I think that's been, again, sort of -- for some reason, there
12 seems to be a disconnect between the problem formulation and the assessment.
13 Obviously, this compound goes down in the water column. It actually is very
14 likely with a log K_{oc} and a log K_{ow} of three. I mean, that's 1,000 times more
15 likely that it's going to be in a certain media.

16 So consequently, I do believe that you are going to see
17 sediment as a media that is going to be impacted. And there are hazard data for
18 sediment for this compound. There's actually, again, a sediment quality
19 objective for the state of California that's been proposed for this compound, for
20 low effects threshold and the high effects threshold. So again, I'm still puzzled
21 why there's this disconnect between the problem formulation and the DRE that
22 is present there.

23 And I already mentioned similarly the inhalation aspect at
24 least for aqueous mammals and avian species is something that, again -- if

1 volatility is what's happening, which I'm not -- again, based on George's
2 comments, it sounds like maybe this stuff goes back in the water. But if you are
3 proposing a volatility component or movement, then there needs to be at least
4 some sort of hazard side of that to make that assessment, again, maybe even in
5 the uncertainty section discussions in the characterization aspects. But again, it
6 just seems to be a disconnect between what's presented in the problem
7 formulation and what's actually adhered to in terms of the DRE. So with that,
8 I'll let everybody go.

9 **DR. KENNETH PORTIER:** So Dan, this is Ken Portier.
10 So for this particular DRE I did a general search on weight of evidence, and I
11 was just trying to understand the models for establishing weight of evidence
12 because I think we've brought this topic up, especially on the ecotox side. And
13 you're right. I didn't find anything that really talks about weight of evidence or
14 establishing weight of evidence for toxic causality in environmental because a lot
15 of the discussion centers around the kind of Bradford Hill concepts: timely,
16 relevance, et cetera.

17 Do you know of any or does anyone on the Committee
18 know of any discussions of a model of this? I suspect it's because for
19 environmental you do a lot of experimentation. You're not having to depend on
20 this epidemiological data, which has a lot more kind of uncertainty that's
21 association based rather than experiment based. Somebody was going to
22 comment. I'll stop.

23 **DR. MARK JOHNSON:** Ken, this is Mark. I just want
24 to chime in real quick. Yeah. There's basically two different things we're kind

1 of conflating, and that's evidence integration and strength or weight of evidence
2 that we have. I would say when you think about evidence integration, you
3 basically have three lines. Maybe you have epi or field data in eco. You have
4 mechanistic. You may have -- actually, four kinds -- in vitro and controlled
5 animal data.

6 Controlled animal data you feel pretty confident,
7 particularly if you have a dose response because that is controlled. And you
8 might have -- and it includes kinetics and dynamics. And you may have enough
9 information to develop a number from which you can branch off of as to your
10 point of departure. But then you have mechanistic information to say, okay --
11 well, like the point Dan brought up. Is it relative? This effect that I'm seeing in
12 mammals, is it relative to fish? Is it relative to -- how does it lend itself to what
13 I'm seeing is not a false positive or false negative? And how relevant is it in
14 terms of extrapolating across species?

15 Then there's other questions you have. And then in terms
16 of adverse outcome pathways, that kind of also lends itself to that. That's part of
17 your weight of evidence. But the other issue you have is variability. And the
18 variability is study quality, and that's where -- well, it also could be differences
19 in species and kinetics there that maybe you don't know about. That's the
20 uncertainty aspect of it, too. But the variability is a lot of things that could affect
21 that.

22 And if you have a lot of vectors all pointing at the same
23 area in that general order of magnitude, then you feel a lot more confident about
24 the value you've chosen, if that all makes sense. But I know the EPA folks are

1 working that from the IRIS side, this term of evidence integration. And then
2 they combine that with the weight of evidence, which is like Keith brought up,
3 the Bradford Hill sort of criteria but also some other things that NTP outlined in
4 their systematic review. And you combine both.

5 **DR. DANIEL SCHLENK:** Yeah. This is Dan, Ken, and
6 Stan's going to love this. But again, the adverse outcome pathways, that's what
7 it was made for was to try to connect the dots so to speak in terms of
8 mechanisms to eco level effect. So I know I'm beating a dead horse on that one,
9 but that's what the purpose of it was for was to try to link those hierarchies in
10 terms of mechanism to whole animal to population impacts.

11 **DR. KENNETH PORTIER:** Thank you. That helps.
12 Anyone else want to comment on Question 3? I know we're going to have a
13 good write up on that, but any issues that you thought up that haven't been at
14 least mentioned here? I'm not seeing any hands go up. I'll turn to EPA. Do you
15 have any questions on the comments that the panel had presented or clarifying
16 questions?

17 **DR. STANLEY BARONE:** No, not at this time. I do
18 find the discussion of AOPs and the weight of the evidence important and would
19 look to the Committee to provide some more suggestions -- actionable
20 suggestions other than just -- we all agree it's a good thing. And again, it's what
21 data do we have available to us. On the Spencer study, we're still looking at
22 that. So hopefully we can get back to you later about that.

23 **DR. KENNETH PORTIER:** Yeah. Dr. Barone, this is
24 Ken Portier. That's kind of the way I was trained to read the literature to say

1 how can we present weight of evidence in a more concise, precise, and clear
2 way. In these DREs, there's a lot of material presented. And really, we want
3 kind of a weight of evidence structure so that the components of evidence
4 presented kind of weights assigned or quality assigned. And then it kind of gets
5 summed up or added up some way. At the end, we have more confidence in the
6 conclusions that you draw. I haven't -- I've got some suggestions on the human
7 health side, but I have a lot less confidence on the environmental hazard side.
8 I'll have to go look at the AOP model again and think about that.

9 **DR. STANLEY BARONE:** Again, the more concrete
10 recommendations you can give us the better.

11 **DR. KENNETH PORTIER:** Yeah. No, I understand,
12 and I think the panel understands that as well. We're looking at actionable
13 recommendations, even though this report is looking like the previous three
14 reports. And we're going to probably end up with about 120 recommendations.
15 Okay.

16 I don't see any additional comments. We've covered the
17 material that I'd planned to cover today. We're a little bit short, but that's
18 surprising but good. I appreciate Dr. Johnson hanging around a little bit after his
19 break time to lead us through Question 3. At this point, I'm going to turn it over
20 to Tamue for any final comments before we break for the day. Tamue?

21 **MS. TAMUE GIBSON:** Well, the only final comment I
22 have is same time at 10:00 a.m. tomorrow morning. We'll begin Day 2 for our
23 deliberations and discussions. And again, just keep in mind of the best practices
24 when logging on to Webex and ensure that, you know, you're connected through

1 your phone as well as keep your phone muted until you're ready to provide any
2 comments. And also note that we will continue a recording and transcribing of
3 this meeting. And that's all I have.

4 **DR. KENNETH PORTIER:** Thank you, Tamue. And
5 I'll also remind the Committee that we have a different phone number tomorrow
6 morning, I mean, a different link.

7 **MS. TAMUE GIBSON:** That's right.

8 **DR. KENNETH PORTIER:** So definitely look at the
9 memo that Tamue sent where she's got the different links for the different days
10 and click on the right link. Otherwise, the meeting may not be there. Tomorrow,
11 our concentration is going to be on exposure. It's going to be a full day of
12 discussions of exposure. So with that, I'll call this meeting adjourned for today.
13 And I look forward to more discussion tomorrow morning.

14 **MS. TAMUE GIBSON:** Yes, we will adjourn for today.

15 **DR. KENNETH PORTIER:** This meeting is ended.

16 **MS. TAMUE GIBSON:** Yes. Thank you. Thank you
17 all.

18
19 **[MEETING ADJOURNED FOR DAY]**
20

OPENING OF MEETING DAY 2

MS. SARA WILSON: Good morning. Welcome to day two of the meeting of the U.S. EPA peer review of the draft risk evaluation for Perchloroethylene. Patel is an EPA contractor providing meeting support for this series. This event is being recorded. Please be aware that the host may use Webex chat to share announcements with all attendees, but all attendees will not be able to respond to the chat. I will now introduce Tamue Gibson, the Designated Federal Official.

DR. KENNETH PORTIER: Tamue, you're muted in Webex.

MS. TAMUE GIBSON: Can you hear me now? I'm sorry. Good morning. Can you hear me?

DR. KENNETH PORTIER: Yes. Yes. We can hear you.

MS. TAMUE GIBSON: Okay. Great. Good. Thank you. Good morning. I am Tamue Gibson. And as the Designated Federal Official it is my pleasure to open the second day of the four-day meeting of the TSCA SACC review of EPA's draft risk evaluation for Perchloroethylene.

I must say, yesterday's Webex host meeting went very well. However, I would like to state that if you encounter any problems with the audio or video you may go to our EPA website for TSCA SACC which is TSCA-peerreview-review. As noted in my opening comments yesterday, as a reminder that peer reviewers please send a note to myself and the Chair

1 indicating if you must step away for a short time. Let us know when you've
2 come back.

3 In a minute we will do a check in roll call and then start
4 today's meeting. And therefore, I am turning the meeting over to Dr. Portier and
5 thank you.

6 **DR. KENNETH PORTIER:** Thank you, Tamue. And
7 thank you to all of the committee for returning for day two of this peer review of
8 the EPA draft risk evaluation for Perchloroethylene or PERC. We're going to
9 start this morning by establishing who on the committee's here through a roll
10 call. I'm Ken Portier, Chair of the committee and I'm here. Dr. Anderson.

11 **DR. HENRY ANDERSON:** Present.

12 **DR. KENNETH PORTIER:** Dr. Barton. Dr. Bennett

13 **DR. STEVEN BENNETT:** I am here.

14 **DR. CHARLES BARTON:** And this is Chuck. I'm
15 here.

16 **DR. KENNETH PORTIER:** Okay, Dr. Barton.

17 **DR. CHARLES BARTON:** -- button off.

18 **DR. KENNETH PORTIER:** Dr. Blystone.

19 **DR. SHERI BLYSTONE:** Yes. I am here.

20 **DR. KENNETH PORTIER:** Dr. Bruckner.

21 **DR. JAMES BRUCKNER:** Morning.

22 **DR. KENNETH PORTIER:** Good morning. Dr. Cory-
23 Slechta. I see Dr. Cory-Slechta --

1 **DR. DEBORAH CORY-SLECHTA:** Yes. I'm here.

2 Sorry.

3 **DR. KENNETH PORTIER:** Yeah. Now you're
4 unmuted. Thank you. Dr. Davies.

5 **DR. HOLLY DAVIES:** Here.

6 **DR. KENNETH PORTIER:** Dr. Doucette.

7 **DR. WILLIAM DOUCETTE:** Virtually present.

8 **DR. KENNETH PORTIER:** Dr. Gilbert.

9 **DR. KATHLEEN GILBERT:** I'm here.

10 **DR. KENNETH PORTIER:** Dr. Johnson.

11 **DR. MARK JOHNSON:** I'm here.

12 **DR. KENNETH PORTIER:** Dr. Kaufman.

13 **DR. ALAN KAUFMAN:** I'm here.

14 **DR. KENNETH PORTIER:** Dr. Kissel.

15 **DR. JOHN KISSEL:** Here.

16 **DR. KENNETH PORTIER:** Dr. Rowlands.

17 **DR. CRAIG ROWLANDS:** Yes. Here.

18 **DR. KENNETH PORTIER:** Ruthann Rudel.

19 **MS. RUTHANN RUDEL:** Yes, I'm here

20 **DR. KENNETH PORTIER:** And Dr. Schlenk.

21 **DR. DANIEL SCHLENK:** Here.

22 **DR. KENNETH PORTIER:** That's the chartered
23 committee all present. Dr. Apte.

24 **DR. UDAYAN APTE:** Here.

1 **DR. KENNETH PORTIER:** Dr. Cobb.

2 **DR. GEORGE COBB:** Here.

3 **DR. KENNETH PORTIER:** Dr. Daniels.

4 **DR. MICHAEL DANIELS:** Here.

5 **DR. KENNETH PORTIER:** Dr. Grant. Dr. Hossain.

6 **DR. MUHAMMAD HOSSAIN:** Good morning. I am
7 here.

8 **DR. KENNETH PORTIER:** Dr. Lash.

9 **DR. LAWRENCE LASH:** Hi. This is Larry Lash. I'm
10 here.

11 **DR. KENNETH PORTIER:** Dr. Lin.

12 **DR. ZHOUMEG LIN:** Hello everyone. This is
13 Zhoumeg Lin.

14 **DR. KENNETH PORTIER:** Let's see. I'm not sure if
15 Dr. Meliker is singing in this morning. I see him logged in. Dr. Meliker.

16 **DR. JAYMIE MELIKER:** Yes. Present.

17 **DR. KENNETH PORTIER:** Good. I couldn't tell
18 whether you were going to be absent on eastern time or other time. So I realize
19 you're going to have to step out some time today. Dr. Roby.

20 **DR. KATHERINE ROBY:** Yes. Good morning. I'm
21 here.

22 **DR. KENNETH PORTIER:** Dr. Vorhees. Dr. Willhite.

23 **DR. CALVIN WILLHITE:** Here.

1 **DR. KENNETH PORTIER:** Let's see. Dr. Vorhees is
2 muted.

3 **DR. CHARLES VORHEES:** I'm here.

4 **DR. KENNETH PORTIER:** There he is.

5 **DR. CHARLES VORHEES:** Yep. I'm here.

6 **DR. KENNETH PORTIER:** And Dr. Pennell.

7 **DR. MICHAEL PENNELL:** I'm here.

8 **DR. KENNETH PORTIER:** Good. Dr. Grant. Has Dr.
9 Grant joined us?

10 **DR. STEPHEN GRANT:** I'm here.

11 **DR. KENNETH PORTIER:** I see. There he is. Okay.

12 All present and accounted for. Okay. Yesterday we actually -- while we got
13 behind on our agenda, we covered everything we had hoped to cover on day one
14 discussing questions one, and two, and three. I wanted -- at this point I'd like to
15 open it up to see if there are any follow up issues or discussions from the
16 previous day. And I think, Dr. Johnson you had indicated that you wanted to
17 kind of clarify or read into the record a clearer expression of part of your
18 presentation on Question 3.1 yesterday.

19 **DR. MARK JOHNSON:** Yes. Yeah. I would like to.

20 Thank you. I'll begin currently. The current approach on systematic review and
21 data evaluation is focused on a selection of a critical study from which dissolve a
22 toxicity benchmark.

23 There's logic in selecting data from the most sensitive species to be protective of
24 others.

1 However, the selection of a single study also introduced --
2 or risks introducing the perception of biases, subjective professional judgement
3 decisions that are often questioned, particularly for data from studies that are
4 outside the range of other data. In these cases the committee recommends a
5 much greater scrutiny of those data to defend their use in driving benchmarks.
6 The process that the EPA currently uses is appropriate for the critical study
7 approach and has utility for chemicals where few data are available.

8 However, in a case of relatively data-rich substances, such
9 as the case for PCE, the committee suggests the EPA considers using as much
10 available data as possible when developing these benchmarks. Evaluation of
11 multiple lines of evidence provides plausibility, coherence, corroboration, and
12 allows for patterns in these observations that reduces the influences of biases and
13 variability of these measurements, and any perceived subjectivity in benchmark
14 derivation.

15 It should also provide further support for the cause-effect
16 relationships that tend to be less sensitive to influences of study designs, fiscal
17 error, and quality issues. This pleniv biology is fundamentally founded on a
18 search for patterns. That's generally accepted by the scientific community for
19 interpreting relatively robust toxicity data sets including the use of scatter
20 diagrams where exposure's plotted relative to effect levels. These figures
21 provide a transparent view of large data sets at a glance and give reviewers
22 confidence in the toxicity benchmarks designed to be protective for multiple
23 species and endpoints.

1 Another approach that uses refined toxicity data when
2 sufficient data are available are species sensitivity distributions. Typically SSD's
3 apply -- employ effective concentrations of contaminants and aqueous media,
4 water, for multiple species. And from there, an effective concentration at five
5 percent is developed to be protective of population level effects for 95 percent of
6 population.

7 No adjustment factors are considered necessary in these
8 cases. SSD's can be constructed with lethal LC-50 or sub-lethal endpoint EC-50,
9 but generally should not be mixed. In other words, you don't want to mix acute
10 and chronic simultaneously. When there are insufficient data for species to
11 construct an SSD, scatter diagram provides the transparent support for the
12 critical study approach.

13 It is important that developers pay particular attention to
14 the outliers and cause and effect relationships. Both can be supported by using
15 the current quality approach that the EPA is using with the addition of data from
16 other studies previously not considered appropriate or potentially excluded for
17 benchmark derivation. These would include mechanistic or adverse outcome
18 pathway information, data from field or epidemiological studies or other
19 information, such as in vitro, that would support the selected observed endpoint
20 found in the critical study.

21 This information could also be used to support the
22 derivation of other toxicity benchmarks across species if it is for conserved
23 biological pathway in a qualitative sense, dependent upon the availability of
24 information adjustment factors can then be used. There are some references that

1 describe the expected variation in response for differences in time and
2 concentration that can be used to support their magnitude. We have a couple
3 references to that effect. And that's all I have.

4 **DR. KENNETH PORTIER:** Thank you. Does anybody
5 -- anyone want to add to this?

6 **DR. DANIEL SCHLENK:** Yeah. Ken, this Dan
7 Schlenk. Just -- I was going to add a reference to that -- to the AOP aspect that
8 was provided back in last year's HBCD conference that Ed Perkins had outlined.
9 I thought he did a pretty good job of outlining how to use AOP's in a qualitative
10 weight of evidence approach. So put that reference in.

11 **DR. KENNETH PORTIER:** Good. Thank you.
12 Anything else? Okay --

13 **DR. GEORGE COBB:** Ken, this is --

14 **DR. KENNETH PORTIER:** -- I'm --

15 **DR. GEORGE COBB:** -- Ken --

16 **DR. KENNETH PORTIER:** -- turning it to EPA --
17 yeah --

18 **DR. GEORGE COBB:** Ken, this is --

19 **DR. KENNETH PORTIER:** -- Dr. Cobb.

20 **DR. GEORGE COBB:** I just wanted to reiterate what
21 Mark said and I concur. And the other thing I'd like to say, several of the
22 comments I made yesterday about increased uncertainty factors or adjustment
23 factors are really only pertinent if the Agency doesn't take the recommendations
24 that Mark was making just now. And so that's -- that's kind of an either/or. The

1 preference would be what Mark was just saying. And then if the Agency decides
2 that's not the way to go, then the uncertainty factors start to kick in. And so
3 that's all I have.

4 **DR. KENNETH PORTIER:** Good. We'll try to make
5 that clear in the minutes where we write this up that that option's available. Any
6 additional comments? I don't see any hands up. Maybe I could turn to EPA and
7 say, have you had any -- has the team had any questions that came up from
8 yesterday's discussion that you might want to little bit of clarifying? We have a
9 few minutes.

10 **DR. MARI LEE:** Hi. This is Mari. No, I don't think we
11 have any questions at this moment.

12 **DR. KENNETH PORTIER:** Good. Well, Dr. Lee, I
13 think it's time to move on to Charge Question 4. The task before the panel today
14 is primarily to discuss the occupational and consumer exposure portion of the
15 draft risk evaluation. So this should be interesting.

16 Please read in -- I think what I'd like you to do is read in
17 Questions 4.1, 4.2, and 4.3 as a set and then we'll -- and then the committee will
18 take the questions in turn. But they kind of work together as a set. So, Dr. Lee.

19
20 **CHARGE QUESTION 4: OCCUPATIONAL AND CONSUMER**
21 **EXPOSURE**
22
23

1 **DR. MARI LEE:** Sure. This is Mari Lee with EPA.

2 Question number 4, Occupational Exposure. EPA quantified occupational
3 exposure as via the inhalation route for both workers and occupational non-users
4 using a combination of monitoring data and modeled exposure pathways. EPA
5 quantified occupational exposure via the dermal route for workers only
6 accounting for the effect of volatilization, high evaporative loss from skin
7 resulting in reduced absorption. EPA assumed that workers and ONUs would be
8 adults of both sexes by age 15 and older.

9 Question 4.1, please comment on the approaches and
10 estimation methods, models, and data used in the occupational exposure
11 assessments in section 2.4.1.

12 Question 4.2, specifically, please comment on the
13 occupational near-field/far-field models and their input parameters.

14 Question 4.3, please provide any specific suggestions or
15 recommendations for additional data or estimation methods that could be
16 considered by the Agency for conducting the occupational exposure assessment.

17 **DR. KENNETH PORTIER:** Thank you. We'll scroll
18 back a slide. The -- we have the one group from the committee that's been
19 assigned to all three of these questions, Dr. Davies with support from Drs.
20 Anderson, Kissel, and Willhite. And Dr. Davies has the lead on this. Dr. Davies
21 take it away.

22
23 **CHARGE QUESTION 4 (4.1)**
24

1 **DR. HOLLY DAVIES:** Hi. I'm going to go through and
2 summarize the comments that I've received from everybody before seeing if
3 anyone else wants to say anything. I'm also going to start with general
4 comments that are applicable to all of the worker exposure assessment and then
5 comments on specific uses. And more details including references will be in the
6 written document.

7 So there's five general comments that we have. The first
8 is flaws in the systematic review process. Systematic review is so important
9 because it underlies the sources of information and we'll comment on some
10 specific examples. The second is inappropriate assumption of personal
11 protective equipment and the use of protection factors. I'd also like to mention
12 comments from Ture (phonetic) in Massachusetts about the inconsistent and
13 improper use of PPE that they have observed.

14 Three is the lack of description or comparative use of data
15 available from OSHA inspection database or data from international programs
16 similar to OSHA. Four, not considering aggregate exposure of inhalation and
17 dermal exposures as well as multiple uses underestimates worker's exposure.
18 EPA's approach to risk evaluation is to set levels of exposure that's without risk
19 and compare it with predicted worker exposure from only a single use, assuming
20 no other PERC exposure from other -- any other sources.

21 We had a comment on the eight hour being converted to
22 24 hours, which I think EPA addressed yesterday. And also, co-exposures to
23 other similar central nervous system depressing solvents, the effects are likely to

1 be additive. And the risk evaluation should provide data to indicate if facilities
2 using PERC also used other CNS depressing and SIP inducing solvents.

3 And the fifth, not considering all exposures in estimates
4 including community drinking water and air exposures. I know we had talked
5 about this yesterday also, but the Agency has said that other statutes adequately
6 assess and effectively managed these exposures without giving us details on
7 those. And those draft risk evaluations refer us to a (Inaudible) formulation
8 which also states their effectively managed by other statutes without any
9 evidence or other information.

10 So for example, the 2008 National PERC Air Emission
11 Standards for Dry Cleaning Facilities is the kind of information that would be --
12 that we're interested in to explain how other regulations are addressing PERC
13 because this requires a phase out of dry cleaners that are co-located within
14 residential buildings by the end of 2020.

15 And lastly, one committee member suggested this
16 complex document should be broken into multiple documents to make it less
17 unwieldy and confusing. So on specific uses, committee members focused more
18 deeply into one or two conditions of use to evaluate as examples. So we don't
19 have comments on all of the uses but some of the recommendations are
20 applicable to additional conditions of use.

21 So let's start with manufacturing. So the first point is the
22 small data sets that were used. In the -- page 123 of the draft risk evaluation it
23 says that a data set comprise of the combined exposure modeling -- monitoring
24 data from all studies applicable to the condition of use. However, nearly every

1 condition of use only a single or a few study exposure data appears to be used,
2 and no combined exposure data set was developed. And for manufacturing the
3 only data set that was used was from HSIA.

4 We also disagree that the HSIA data is high quality. EPA
5 expressed high confidence in this data and indicated it was highly represented in
6 geographic skill and reflective of the current operations. EPA indicates the data
7 is breathing zone data. But a review of the HSIA data document found there was
8 no indication that the samples were breathing zone and no mention of the method
9 of collection, charcoal tubes, passive dosimeters, volume of air sampled, et
10 cetera.

11 While EPA's assumptions of high quality may be
12 warranted, those data sets suffer from many of the missing information criticisms
13 EPA assigns to peer review publications graded down by the data quality
14 evaluation criteria. There's no mention of the laboratory method used in the
15 analysis or whether the sampling or laboratory methods were NIOSH or OSHA
16 compliant. The location of the plant is not mentioned and so we're not sure
17 about the geographic representations.

18 The EPA also needs to provide further explanation and
19 more closely review the data. In looking at the analytic results of Facility A and
20 B, the full shift results were exactly 8 hours or 12 hours, and that's unlikely in
21 supposition in turning pumps on and off. So this observation suggests the actual
22 length of sampling was not recorded by the industrial hygienist collecting the
23 sample or not available and perhaps added later to represent the time of a full
24 shift. Or the samples could all be from a fixed area monitor.

1 In Facility C, the sampling reporting times have lengths
2 typically seen not exactly 8 or 12 hours. And for Company A, the full shift
3 samples are for operators with work description general eight-hour exposure.
4 These could be area samples or operators in multiple manufacturing lines.
5 Without more information on how to interpret the data, using it -- well, we
6 would -- so recommendation is not to not use this data. And we'd also like to
7 thank the organization for stepping up and submitting this data, but EPA should
8 review how the manufacturing data was collected, transcribed, and whether some
9 explanations have been lost. So asking HSIA for more information on it.

10 We'd also like to comment on the definition of workers.
11 EPA seems to assume that all the employee data and limited job descriptions
12 were consistent with their definition of workers with direct handling or exposure
13 to PCE. In the HSIA document, there's no definition or description of what the
14 exposure group terms mean.

15 In looking through the listed exposure group
16 characterizations it's not clear if -- that all the workers met the EPA worker
17 definition, and some might better fit as an ONU or unexposed. Very few of the
18 task descriptions mentioned PERC. And there's different types of workers,
19 tradesmen, supervisors, laboratory analysts listed which could be ONUs in the
20 EPA categorization.

21 In Company C, there are inflators and pipe fitters who
22 indicates that the only workers reported to wear respirators. There's technicians,
23 which we don't know if that was in a separate room or a laboratory. And we

1 don't -- so generally just looking for more definition of workers and what they
2 do.

3 Some more of -- another comment on the systematic
4 review were some seemingly good studies were not used for unknown reasons.
5 So publications containing brand new factory worker exposure data that weren't
6 mentioned in the DRE were found in the reference list and the data quality file.
7 And for one example -- sorry, I'm losing my page here as I'm looking through the
8 comments. There's three additional studies that were available and reviewed but
9 not used.

10 It doesn't talk about the exposures and when looking at
11 them, they all had different exposure levels than when compared to the HSIA
12 data that was actually used. So this would be Sagey (phonetic) 1989 study
13 headed -- repeat the number but a higher geometric mean. Another Sagey 1990
14 paper, geometric mean of 17 parts per million. And then another, Dow Chemical
15 paper from 1983.

16 So all of these studies report exposure quite different from
17 the 0.03 parts per million central tendency that EPA calculated using the HSIA
18 data. And there's no explanation of why these studies were not used. And in
19 general, EPA should consider identifying publications that are considered
20 unacceptable only because of lack of metadata and then attempting to contact the
21 authors to obtain the missing information rather than just not using those studies.

22 So for comments on dry cleaning, wanted to start by
23 saying that it doesn't take into account other people that are nearby. They could
24 be considered ONUs. Yesterday, Dr. Willhite mentioned several studies on

1 PERC in apartments that are co-located. EPA mentioned the 2008 rule that
2 phases out dry cleaners that are co-located with residential buildings so I'm not
3 going to re-mention the studies again. But this rule does not address other
4 people nearby such as other businesses and service establishments.

5 In section 2.4.1.16, dry cleaning and spot cleaning, EPA
6 states the ONUs of dry cleaning facilities are employees who are not expected to
7 handle PCE, operate dry cleaning machines or perform spotting or finishing
8 operations. They include cashiers, counter clerks, and other similar employees.
9 So in essence, ONUs are bystanders who don't load solvent into dry cleaning.
10 And people who work near dry cleaners could also be considered ONUs.

11 In the 2010 King Count survey of dry cleaners which is
12 referenced in the DRE and other places, it notes that 77 percent of respondents
13 said their facility is part of a larger building. And 69 percent of the respondents
14 indicated there are businesses that sell or serve food where their dry cleaning
15 facility is located. One of the studies, Schreiber et al that examined apartment
16 buildings in New York City that contained an active dry cleaning facilities also
17 included a dry cleaner that was co-located with a daycare center.

18 And that had nine female staff and it was in a single-story
19 building separated by an interior wall from an operating dry cleaning facility that
20 used a third generation machine. So it didn't specify the ages of the students, but
21 it was -- the study was done -- it was included -- the daycare was included
22 because a parent was concerned.

23 And then, for other industrial uses, in section 2.4.1.23 it
24 only estimated getting the solvent to the facility but the tank truck and rail car

1 loading and uploading release and inhalation exposure module but didn't include
2 bottling activities after that. So EPA should model exposures from additional
3 activities.

4 So for example, PCE is used in textiles as most recent --
5 remove spinning oils, lubricants, and naturally occurring dirt and oil from yarn,
6 and also used in clothing manufacture, and is a carrier solvent for dyes in the
7 textile industry. And all of those are activities that would have exposure to
8 workers after they unloaded it into the facility. And that's the end of my
9 questions for 4.1. Not questions, comments for 4.1.

10 **DR. KENNETH PORTIER:** Thank you. Dr. Anderson,
11 do you want to add?

12 **DR. HENRY ANDERSON:** Thank you. Covered most
13 of my issues. Again, just to -- I think everybody ought to take a look at the three
14 company data from HSIA and you'll see on the job descriptions, a fair number of
15 them, I think in work descriptions describes that they're actually carbon
16 tetrachloride (phonetic) workers. And without understanding how the plot is
17 organized does -- knowing somewhat about the manufacturing process, the
18 process probably use also generates a certain amount of carbon tet.

19 And depending on temperature and pressure applied in the
20 system you'll get more carbon tet or less than the PERC. So those workers may
21 be on a separate line in a separate room. So we really -- the need for greater
22 description of the engineering design process -- sorry, my other phones started in
23 there. I'll hang that up and hope it's not an emergency call.

1 So really needs to be looked at. And, like, in Company A,
2 as I looked through that list there's only a single sample in all of those reported
3 that appears to be detectable. Well, that certainly is a -- if that's true for the plant
4 all the time that shows they've been exceedingly successful and to be
5 commended for removing all exposures from the workforce.

6 And then the listing for Company B, there's one page
7 which lists quite low measurements and then second page, those same levels
8 have a less than before them. So the question would be, are the first ones just
9 missing that less than or is it actually calculated that way? So there's lots of
10 questions that are -- it was wonderful that companies submitted that data and
11 unfortunately without a key to really understand what all these jobs are, we don't
12 know what proportion of the workforce would be in a control room.

13 These processes are under high temperature and pressures
14 so more modern companies now have most of the measurement things to look at
15 in a control room which is quite controlled. So being an operator could mean
16 you spend your day in a control room and if you notice something wrong or
17 somebody goes around to check temperature gauges they would be out on the
18 floor. But it's a pretty quiet operation and the other types of chemical plants that
19 I've visited. I've never been in one of these but maybe some others have some
20 understanding about that.

21 So seeing that high qualities measurements were
22 combined into one data set is a concern. And then if you look at all the other --
23 just a minute, I've got -- have to -- what my wife....

1 **DR. KENNETH PORTIER:** So, while Dr. Anderson's
2 taking that call why don't we move on to Dr. Kissel.

3 **DR. HENRY ANDERSON:** Sorry about that. So the
4 question would be, in many of the other user groups there isn't in the database
5 what the job descriptions are. The exception to that would be the NIOSH H
6 studies that were -- HHE studies that were used in some of the exposure
7 scenarios that have jobs listed. But otherwise the research papers that are used
8 just give the overall description of the group so that may or may not contain
9 ONUs in it.

10 And so we'll talk more about ONUs later but basically the
11 literature ONU is not a term that's used in the research arena or in the
12 occupational setting. In understanding an individual plant you need to know
13 what workers are exposed at what level so you can provide protections for them
14 that's appropriate to their exposure. But there really aren't separate groups like
15 that. So that's kind of a summary of my comments and additions as well. That's
16 it.

17 **DR. KENNETH PORTIER:** Thank you, Dr. Anderson.
18 Dr. Kissel? Dr. Kissel, I see you're muted in Webex.

19 **DR. JOHN KISSEL:** Sorry. I thought I had taken that
20 off. This first question is generic, and I focused on the dermal parts. So EPA is
21 using an approach that they have used in some of the previous risk evaluations.
22 It's the Kasting Miller 2006 as informed perhaps by the Frasch 2012
23 modifications. The calculations are shown in supplement document 16 in
24 Appendix K of that document. I did check some of the rudimentary calculations

1 of the -- they checked out. I got the same answers that EPA did of using
2 Appendix K, equation 3 is the same as Kasting Miller equation 40. And the
3 numbers check. And the physical chemical parameter inputs match what's in the
4 p.chem portion of the DRE. So all that matches.

5 The -- so this would generally be a reasonable approach.
6 It's using peer reviewed literature. As far as the calculating absorption, I think
7 it's very defensible. The -- there are a few things that I would like to check.
8 The Kasting and Miller approach uses a permeability prediction from a paper
9 that I don't use. They mention a couple of choices and then they use one that I'm
10 not as familiar with and so I kind of reserve the right to go back and do some
11 more checking on that one. But it is published work and it should be okay.

12 The issue, and this came up with TCE also, is that the
13 basic Kasting Miller approach represents competition between absorption and
14 evaporation. And as long as you have the rough relative magnitude of each of
15 those processes together then you can use the Kasting Miller approach. What's
16 not raised here, and this was this issue for TCE, is that if you -- if the solvent -- if
17 exposure to the neat solvent damages the skin then the absorption rate would be
18 faster than predicted by the standard models and that would mean that the
19 competition is not quite the same and the relative proportion of absorption could
20 go up.

21 And the same paper, there's a -- an in vivo rat study
22 published by Morgan (phonetic) in 199- -- Morgan et al 1991. EPA, I think
23 discounted that study for TCE because the methodology was perhaps a little odd.
24 It involves gluing -- using super glue to put a reservoir on the back of a rat

1 because it's an in vivo experiment, and then they monitor blood in the rat. But
2 you don't need -- the methodology should not prevent use of the overall
3 observation, the actual rates of uptake. It's rat work anyway and so you wouldn't
4 want to use that for humans.

5 But what it did show because they -- and this is the value
6 of this paper is that they compared effects of neat compound to a saturated
7 aqueous solution. And in the absence of skin damage, theoretically that's the
8 same thermodynamic driving for so you should get the same uptake. But they
9 didn't get the same uptake. The uptake was much more rapid from neat
10 compound than from aqueous solution which suggests that the solvent damages
11 the skin somehow and causes greater uptake.

12 And that caveat needs to be checked and some language
13 which -- or empirical investigation of, I don't mean doing data collection, but I
14 mean fiddling with the equations. Using alternative permeability coefficients
15 and the recalculating so that you would get yet another version of possible
16 outcomes, and that should be considered in the -- at least as a quality control
17 check on the estimates that you're doing. And I will -- I did that for -- or
18 something along those lines for TCE and I will do something along those lines
19 for PCE also.

20 So one other point that I would add to what Holly and
21 Henry said, is that again -- well actually, there's a couple of other points. The --
22 with respect to the overall approach, the -- there's no consideration of direct
23 dermal uptake for dermal, which for this compound generally using the Weschler
24 and Nazaroff approach from 2014, the contribution, if you had a person just

1 breathing air and exposed to vapor you would expect the inhalation to dominate
2 and neglect of the dermal vapor would therefore be okay.

3 However, two things. One, I would like to see dermal
4 vapor just kind of thrown in routinely as part of EPA's template, so they just do it
5 automatically. If we're making a template by which to do these evaluations, I
6 think that would be useful. Although I don't expect it to be, in the generic case,
7 to be important here. The caveat on that is that if you assume a high level of
8 respiratory protection then a relatively minor inhalation -- a relatively minor
9 direct dermal vapor exposure can actually dominate inhalation if you're wearing
10 really effective respiratory protection. So then you would want to know what
11 that number is if you're doing an estimate of risk.

12 And that brings up the -- that caveat about respiratory
13 protection also brings up the glove protection thing which Holly mentioned that
14 we have some doubts. I will note that one of the comments that we got from the
15 public, from the Halogenated Solvents Industry Association was that EPA was
16 overestimating dermal exposures because the gloves aren't actually readily
17 penetrated by the solvents. And that's true if you're wearing the right kind of
18 gloves and using them correctly.

19 But something that was ignored in those comments, and
20 it's one of the reasons that many of us who are somewhat skeptical about the
21 efficacy of PPE is that the phenomenon by which people who are dermally
22 exposed does not require that the glove material actually be permeated by the
23 solvent. There's -- glove material can be permeated if the -- if it's torn which can

1 happen in working conditions. In which case, it doesn't matter how wonderful it
2 is, if it's got a slit in it will let chemical through.

3 And actually more important is the observation -- I've
4 never been in one of these PCE manufacturing plants, so I don't really know
5 what their conditions are like. But certainly something that happens routinely in
6 agriculture is that people wearing protective gloves find that they're extremely
7 cumbersome and they stop, they get off their tractor, they have to repair
8 equipment. And they can't turn a nut with their fingers in the gloves, so they
9 take the gloves off, contaminate their fingers, and then they put the gloves back
10 on.

11 And that's -- that taking gloves on and off is actually the
12 primary concerns when it comes to glove failure and not direct permeation of the
13 glove material, which may in fact be rigorously resistant to -- if the material's
14 selected correctly the gloves may actually be rigorously protective against the
15 material if they're used with 100 percent efficiency.

16 But the observation from the real world is that laborers do
17 not use gloves with 100 percent efficiency and so therefore the glove strategy
18 can be circumvented by behavior not chemical permeation. And I think that's
19 everything I wanted to say for, kind of, the overview.

20 **DR. KENNETH PORTIER:** Dr. Anderson, you wanted
21 to add some comments.

22 **DR. HENRY ANDERSON:** Yeah. I'm sorry. One other
23 thing. The processing as a reactant worker group, surrogate data being the
24 manufacturing data was used for that. And again I would wonder whether it's

1 appropriate to consider that highly accurate and grade it as the highest quality
2 data if you're using surrogate data. And the concern would be there where
3 there's only eight manufacturing sites, which are probably large facilities that are
4 really working hard at reducing exposures.

5 There's 117 sites mentioned for processing in the reactant
6 so there's many more opportunities for different kinds of exposures to occur. So
7 I would just question whether using surrogate data from one of the other groups
8 is appropriate. Then the question becomes, what other data might one be able to
9 utilize in those kinds of circumstances.

10 **DR. KENNETH PORTIER:** Thank you. Dr. Willhite,
11 you're also listed as an associate.

12 **DR. CALVIN WILLHITE:** Can you hear me now?

13 **DR. KENNETH PORTIER:** Yes. We gotcha.

14 **DR. CALVIN WILLHITE:** Okay. I'd like to turn to the
15 public comments. And I understand of course that this TSCA group is unable --
16 it is -- and it does not consider itself to be a research organization. But I see
17 from the comment from Andrew Maier from Cardno ChemRisk. In that letter
18 they recommend EPA investigate whether empirical study of dermal exposure
19 can -- to PCE can be conducted. And second, they recommend EPA conduct or
20 solicit surveys characterizing tasks at PCE facilities to determine their duration,
21 contact volumes, contact frequencies, et cetera.

22 Now, one of the problems that is pointed out by Safer
23 Chemicals and Healthy Families they state, "the PCE draft does not combine
24 dermal and inhalation exposures even though these two routes occur

1 simultaneously for both workers and consumers." So let's just focus on workers.
2 At page 23 of their submission they state, "since inhalation and dermal risks are
3 significant in their own right for most conditions of use, the failure to combine
4 exposure across these rates results in a significant understatement of risk." Now,
5 what they're asking for is, please determine the total absorbed dose.

6 Therefore, in order to integrate PCE total absorbed dose
7 after uptake by dry cleaning workers who've historically loaded solvent, had
8 direct hand contact with PCE wet garments, and who inhaled airborne PCE in
9 this establishment, it will be necessary to reconstruct those exposures. We need
10 a dose. And a good example of this, and it's been done in detail, it was done in
11 the case of the pliofilm benzene cohort and that's Paustenbach '92 and Williams
12 and Paustenbach 2003.

13 Those reconstructed task specific, and it's important to
14 realize, in that benzene historical cohort upon which EPA based its traditional
15 cancer potency value, people had their hands in liquid benzene on the wet side as
16 compared to the dry side. That's all been looked at in detail. So those
17 reconstructed PCE exposures could be related to PCE induced adverse health
18 effects. Therefore, what we need to do is go back and look at the exposures
19 historically and try to determine total absorbed dose. Thank you.

20 **DR. KENNETH PORTIER:** Does anyone else have a
21 comment on Question 4.1? Dr. Davies, you want to move on to 4.2?

22
23 **CHARGE QUESTION 4 (4.2)**
24

1 **DR. HOLLY DAVIES:** Sure. So as the slide says, 4.2 is
2 about the occupational near-field/far-field models and their input parameters.
3 Our base of comments is about, I think, the division of workers and ONUs.
4 Near-field and far-field models are well known and have been used to
5 reconstruct individual worker's exposures. But it's overly simplistic to do what
6 EPA seems to have done, which is to say ONUs are all far-field and workers are
7 all near-field. Because most workers spend varying lengths of time working or
8 passing through near and far-field sources of exposure.

9 And also, of course, for highly volatile chemicals like
10 PERC the exposure, you know, being in the room but not handling it can have a
11 higher exposure. And this, of course, goes back to the comments earlier on the
12 job descriptions or information -- more information about the workers, what they
13 do, and where they spend their time.

14 And using the TWA approach doesn't allow
15 characterization near-field or far-field exposures unless the occupational workers
16 is in the constant near-field environment. So it's more of a composite exposure
17 from time spent near-field, far-field, and other times as, you know, break time,
18 lunch times versus shorter sampling periods near -- measuring near-field
19 exposures from specific activities. And that, well, with that I'll open it up to any
20 other comments.

21 **DR. KENNETH PORTIER:** Dr. Anderson. Dr. Kissel.

22 **DR. JOHN KISSEL:** I don't have any additional
23 comments on 4.2.

24 **DR. KENNETH PORTIER:** Dr. Willhite.

1 **DR. CALVIN WILLHITE:** Nothing to add.

2 **DR. KENNETH PORTIER:** Anyone else?

3 **DR. HENRY ANDERSON:** This is Henry Anderson
4 again.

5 **DR. KENNETH PORTIER:** Dr. Anderson.

6 **DR. HENRY ANDERSON:** Yeah.

7 **DR. KENNETH PORTIER:** Yeah. Sure.

8 **DR. HENRY ANDERSON:** I just wanted to say, I think
9 for understanding the near-field exposures the short term monitoring results that
10 -- especially in the manufacturing sector, it was clear they're sampling strategy is
11 they're really concerned about the SPEL standard. And if you can control the
12 shorter term limited exposures then of course that'll help the overall exposure of
13 the workforce.

14 So I think being able -- taking a look at the short term
15 exposures and not converting them to TWAs, but just looking at those, that
16 might help better understand near-field types of activities that are really
17 contributing to an overall exposure. Keeping in mind that I think EPA may have
18 done that, and sometimes if you just assume that you're 15 minute exposure is
19 the only exposure you've got or a worker would do that, you know, 10 times a
20 day, that's two-and-a-half hours' worth of exposure. You can then see the impact
21 of the higher peak shorter term exposures on the overall exposure. But it isn't
22 necessarily captured in a TWA.

23 **DR. KENNETH PORTIER:** So I'm just trying to, kind
24 of, understand the impact of this comment and maybe Dr. Holly and Dr.

1 Anderson can help me on this. Kind of what you're saying is, the model's okay,
2 it's a standard model. And the input parameters are the parameters there are, but
3 it's how the model is applied to this -- to specific occupational tasks or
4 occupational individuals so that the individual doesn't spend eight hours in the
5 near-field.

6 They may only spend two-and-a-half of an eight hour day
7 in the near-field, the rest of the time they're in the far-field. And has that been
8 accounted for in this -- in the exposure estimates that are generated in the draft
9 risk evaluation. Is that kind of what you're getting at here?

10 **DR. HENRY ANDERSON:** I think -- I think that's true.
11 The issue being I haven't -- I'm not a modeler so it seemed to me like they take
12 the average or the median exposure and put that data into the near-field/far-field
13 to predict what the average far-field exposure would be. When in fact, near-
14 field/far-field really is appropriate for individual activities. So you could take
15 some of the shorter term exposures, which can be an order of magnitude
16 different and then calculate what they're far-field exposure would be.

17 But as you get into the far-field in a facility where you
18 have a lot of this activity going on, you're going to end up with a general
19 confusion of the exposure in the far-field. So I've only seen it used mostly to try
20 to understand an individual worker what they're trying to reconstruct their dose.
21 What are the model parameters that are put in? Where did those values come
22 from, is kind of the question I would have. I didn't look that up.

23 **DR. KENNETH PORTIER:** Okay. I'll remind the
24 committee that if you're not speaking, please mute your -- mute your connection.

1 I'm seeing a little bit of, kind of, crossover from some non-speaking committee
2 members. Dr. Davies, did you want to add anything to this?

3 **DR. HOLLY DAVIES:** Well, I would just add that you
4 mentioned the idea that, you know, a worker might only be near-field for part of
5 their shifts. But it's also possible that what's considered an ONU in this risk
6 evaluation, someone who doesn't directly handle PERC, could also be in the
7 near-field for a significant amount of -- part of their workday also even if they're
8 not handling it. Especially since it's a volatile compound they could be getting
9 inhalation exposure -- getting more inhalation exposure than this estimate has.

10 **DR. KENNETH PORTIER:** The other reason I was
11 thinking about this is a public commenter yesterday kind of made a suggestion
12 that EPA should be looking even in finer detail to operational tasks -- excuse me,
13 to occupational tasks. And I was trying to think about how that -- what that
14 would do to the draft risk evaluation? I mean, we're already having a struggle to
15 understand some of these complicated PBPK models and how they're used to set
16 internal dose. And here we're on the exposure side and now I'm starting to think,
17 well, we're going to need these complicated workday models -- dynamic
18 workday models to try to figure out finer and finer details of occupational
19 exposure, and where's the cost benefit from that?

20 So I'm -- I was trying to figure out, what do we really
21 gain from this? Is what they're doing right now that too conservative or too
22 liberal? Are they getting too high and exposure, too low an exposure or is it just
23 the uncertainty in what we're really estimating that's the concern?

24 **DR. HOLLY DAVIES:** I don't think we --

1 **DR. KENNETH PORTIER:** Dr. Anderson. Oh, Holly.
2 Go ahead.

3 **DR. HOLLY DAVIES:** Yeah. I've got -- I was going to
4 say I don't think we know which way it is because we don't really have a
5 sensitivity analysis on this. And I liked your comments on which, what's worth
6 doing because we know that, you know, by not aggregating the dermal and
7 inhalation exposures of people who are handling PERC we're underestimated in
8 the exposure. You know, which of these is worth going into and doing and I
9 don't think we know.

10 **DR. KENNETH PORTIER:** Dr. Anderson.

11 **DR. HENRY ANDERSON:** Yeah. Kind of the way I
12 look at it, and this is probably all wrong is, part of the reason for having ONUs is
13 you'd like to remove the ONUs who have -- who should have lesser exposures
14 from the main occupationally exposed contact workers. Now, most of the data
15 that we have is all -- we can't sort those out. So there's probably ONUs in there
16 and that then reduces the average exposure or the peak exposure of the group
17 because it's diluted by people who really are not at highest risk.

18 And to -- so that, I think, is one point that we wanted. I
19 don't think we can sort it out. Which in the studies data we have, again, with the
20 exception of the HHE data where they talk about doing some measurements in
21 administrative staff, you don't want the administrative staff who have lower
22 levels to necessarily be counted as the online workforce.

23 So once you have -- if you're part of the online workforce
24 we're not trying to further go to only the people who are the most exposed but we

1 want to have people who are really, kind of, the manufacturing worker not the
2 laboratory analytics and the administrative staff, and the guards, and things like
3 that. So those people may be exposed but if we're really after, is there really a
4 reasonable risk to some workers then we need those some workers -- or we think
5 that's most likely to be are in the group that are doing the jobs that result in the
6 highest levels of exposure.

7 So I can't see a decision being made to say Company A
8 you can't have line manufacturing or processing workers, but you can have
9 workers who are administrators because there's no unreasonable risk to them. So
10 you can't be putting product into cans or bottles if you don't have the guys who
11 are doing that. So those are the ones we are most concerned about and you want
12 to be able to as accurately as possible estimate what those exposures are.

13 **DR. KENNETH PORTIER:** Gotcha. I think -- thank
14 you. I think Dr. Blystone is next and then Dr. Willhite. Dr. Blystone.

15 **DR. SHERI BLYSTONE:** Yeah. I was just commenting
16 or thinking about in general risk assessment process and whether we consider
17 this draft risk evaluation a screening level assessment. Because what we're
18 trying to do here -- what has been done is with available information and
19 supported by models were available -- that were representative of the group that
20 we're looking at, you evaluate that and determine if there's -- if the data is
21 suggesting that there's a problem. And then, like you were saying, Ken, is then -
22 - that could direct you to further refine the assessment to tweak -- tease out those
23 areas that are really -- is that really a problem or now and -- or how -- or can we
24 define it better?

1 So the question is that we seem to be struggling with is,
2 this document is supposed to do that or is it just a screening level assessment
3 that's saying, you know, this is what we've got? We're asking some questions
4 about the models and is this representative, but it's pointing us in a direction of
5 this is where the problem is. And are we expecting this document to then do that
6 further refinement as well. And I'm -- I guess I'm suggesting that's probably not
7 -- I don't know that EPA can do that with these documents.

8 **DR. KENNETH PORTIER:** Yes. This is Ken Portier
9 again. I -- yeah -- I -- while we're not supposed to talk about risk management,
10 that detailed kind of assessment of who's exposed highly and who's not exposed
11 probably occurs at the plant when they're required to look more closely, right? I
12 mean, this draft risk evaluation helps EPA kind of see which conditions of use
13 potentially have risk. And I think the -- what Dr. Anderson said, you know, kind
14 of in my mind translates to the meat in this draft risk assessment to increase our
15 confidence that when they're talking about workers who are actually handling
16 product that the estimate of their exposure is not contaminated by workers -- by -
17 - in the set used to set it -- set that exposure level by workers who are not
18 handling product.

19 And I think what I -- what I'm kind of hearing is we need
20 more insight into the data set. And I think that was the original comment. We
21 need more insight into the -- how the data was generated, who's included in what
22 set so we have confidence that that estimate is -- a worker exposure is a good
23 estimate. Dr. Willhite and then I noticed that Dr. Cobb's got his hand up and
24 Ruthann Rudel's got her hand up. So, Dr. Willhite.

1 **DR. CALVIN WILLHITE:** Yes, sir. I hope I'm coming
2 in loud and clear.

3 **DR. KENNETH PORTIER:** Yes.

4 **DR. CALVIN WILLHITE:** We have an important set of
5 missing parameters here that have to do with peak exposures. Now, it could well
6 be as it was the case with benzene, it's the high peak exposures that contribute in
7 great measure to the total absorbed dose. So it's episodic exposures not
8 necessarily your TWA. That's why we have ceilings on lots of materials -- well,
9 a lot of those apply to sensory irritants but the important this is, you look at those
10 high peak exposures.

11 Second, as far as dry cleaning workers, we do have
12 excellent data summarized by Lois Gold some years ago about -- and the peak
13 exposures are on the order of, like, 150 parts per million. Now, if we're going to
14 have adverse health outcomes, ordinarily we'd expect the dose makes the poison
15 and the higher the exposures, the greater the response.

16 Therefore, we do have good, solid historical data. And we
17 do have, despite the EPA's assertion that they want to throw away the apartment
18 building data, those are -- as far as exposure data those are reliable for near-field,
19 like the daycare center. So what we can do is, we can use those data with a bit
20 more inspection to try to come out with more reliable exposure estimates for
21 occupational exposure and enhanced risk. Thank you.

22 **DR. KENNETH PORTIER:** Thank you. Dr. Cobb.

23 **DR. GEORGE COBB:** Thank you, Ken. I'd just like to
24 quickly concur with some things that Dr. Davies and Dr. Blystone said. They --

1 the uncertainties, we really aren't sure which way they would make the
2 assessment come out and there's lots of missing information. And to my mind,
3 that means that this evaluation is pointing towards the places that more data are
4 needed. I understand the Agency may have to make a determination but as we
5 go forward in this process or the Agency goes forward in this process, I think it's
6 really important to use these early assessments, or early formulations to decide
7 where data is needed so that the Agency doesn't end up in this conundrum time,
8 and time, and time again. With that, I'm done.

9 **DR. KENNETH PORTIER:** Thank you. Ruthann.

10 Your still muted in Webex.

11 **MS. RUTHANN RUDEL:** Thank you. I just wanted to
12 reinforce points that -- well, so I don't really understand still why the OSHA
13 enforcement data aren't really used to set exposure point concentrations with the
14 exception of dry cleaning and even then it's limited to facilities that specify the
15 type of machine. And I just wanted to make the additional point that since this
16 risk evaluation is the -- is the first step and to bring conditions of use into risk
17 management.

18 So it's best to capture conditions of use that are risky using
19 OSHA enforcement data is one good way to do that. In the risk evaluation
20 process -- risk management process, EPA has the opportunity to fine tune
21 exposure scenarios, can get more information and more detail about exposures,
22 and then may learn that some uses may not be so risky. And then those can drop
23 out of risk management. But if this risk evaluation underestimates exposure then

1 there's really no opportunity to capture those risky exposures and protect those
2 workers. Thanks.

3 **DR. KENNETH PORTIER:** I agree. Dr. Willhite, your
4 hand's still up. Did you want an additional comment? Thank you. I do think it
5 would, you know, based on Dr. Cobb's comment, you know, I think it would be
6 useful for this question if we could somehow identify what the next level of
7 information that's needed to improve the evaluation. Specifically, on these
8 models and input parameters. If, as Dr. Cobb mentioned or we're missing input
9 parameters, are we missing some parameters? It would be nice if we could at
10 least identify some of them that EPA should go after.

11 And that brings us to Question 4.3. So why don't we go
12 ahead and look at any specific suggestions or recommendations for data
13 estimation methods or whatever to improve the DRE. Dr. Davies.

14
15 **CHARGE QUESTION 4 (4.3)**
16

17 **DR. HOLLY DAVIES:** Hi. So some of these have been
18 mentioned before in 4.1 and 4.2 as the benchmark comments. And so, some
19 additional comments are that the -- reviewing -- EPA should review the COU
20 data used, the exposure data used to see if some of the data attributed to workers
21 are actually ONU exposures. And as we discussed, the short-term sampling
22 rather than -- and the peak exposures rather than the TWA approach. We've
23 already talked about OSHA enforcement that Ruthann just brought up.

1 And there doesn't seem to have been a systematic review
2 of international exposure from countries that have similar exposures to the U.S.,
3 like Germany. Sorry, just kind of going through the comments here. And
4 looking at how the systematic data review was done for the data quality, and
5 which studies that were rejected or downgraded and not used that might have
6 useful information.

7 Some of the studies are graded downward because the data
8 is older. And especially for dry cleaning studies, looking at age rather than what
9 typed of machines are used. And that it might not be the best idea to only use
10 studies with current machine technology because that doesn't capture the full
11 industry. And it also doesn't look at the early exposures that people have when
12 we're looking at lifetime exposure. And I think that's everything I have for now
13 so I can open it up to everybody else.

14 **DR. KENNETH PORTIER:** Dr. Anderson.

15 **DR. HENRY ANDERSON:** Yeah. The only thing I
16 would add to that is, again, lifetime issue, especially when we're looking at
17 carcinogenesis, and this would almost be a question to EPA and TSCA. It seems
18 that we're only including current circumstances in the assessment where the --
19 trying to predict cancer risks is a lifetime of exposure. Well, is it a lifetime that
20 starts now moving 40 years into the future or do we take the 85 percent of the
21 workforce who's likely to have already 10 or 20 years of exposure in? And
22 therefore, those earlier studies become important when trying to estimate what
23 the lifetime exposures are likely to be for the workforce going forward, if we can
24 control up to the current technology.

1 So accommodating those earlier studies might be useful to
2 better understand what is the risk for the current workforce. And we have in a
3 number of industries you remove the person from exposure, not after their full
4 year but after they start to show signs and symptoms of things. So I don't know
5 if that's relevant there if we have TSCA statues specifically say only to address
6 issues going forward when we're assessing the impact of the workforce, is it only
7 added impact?

8 So those are -- there's a lot of earlier studies that certainly
9 would have -- or do have higher exposure. You can see that again in the
10 manufacturing. One of the reasons for eliminating some studies it's
11 characterized how old the data is. And really, the highest score goes for those
12 that are less than 10 years, but some of the manufacturing data that was in the
13 file was 2007 so that's already 13 years old. But I would not throw that data out.
14 I thought it was very useful to have.

15 So those are kind of questions as to when you're dealing
16 with lifetime exposures. Do we take into account your current status? Or are
17 those considered high risk or unusual exposure part of the best group of people,
18 and therefore that ought to be mentioned that many of the workers have accrued
19 or have accumulated exposures under more highly exposed circumstances, and
20 therefore that group is considered to be a sentinel group of people to worry
21 about? So those are all questions I would have.

22 **DR. KENNETH PORTIER:** Thank you. Dr. Kissel.

23 **DR. JOHN KISSEL:** Yeah. So I didn't really have much
24 to add here. The -- but I wanted to -- I neglected under 4.1 to mention aggregate

1 exposure. That's something that we've talked about a lot through these various --
2 or the previous reviews. And want to thank the other members of the community
3 who picked up on that and mentioned it. So I just want to -- I think there's
4 probably a very strong majority for doing aggregate exposure which we keep
5 recommending. So that's it. Thank you.

6 **DR. KENNETH PORTIER:** Dr. Willhite.

7 **DR. CALVIN WILLHITE:** Nothing more to add save
8 what Henry Anderson and Dr. Kissel have enumerated. I concur 100 percent.

9 **DR. KENNETH PORTIER:** Thank you. Ruthann.

10 **MS. RUTHANN RUDEL:** I don't have anything further.
11 I just forgot to put my hand signal down. Sorry.

12 **DR. KENNETH PORTIER:** Okay. You know, one of
13 the --

14 **DR. HENRY ANDERSON:** Let me --

15 **DR. KENNETH PORTIER:** -- one of the comments
16 that we --

17 **DR. HENRY ANDERSON:** Let me just add --

18 **DR. KENNETH PORTIER:** Yeah. Henry.

19 **DR. HENRY ANDERSON:** -- to the -- I also did --
20 neglected to say about aggregate exposure. I think there's a -- there's a paragraph
21 early on in the first 40 pages or so of the document where EPA explains why
22 they don't do aggregate. And the statement is because the uncertainties may
23 result in higher or low -- you know, lower estimates of risk.

1 And I would say it would certainly -- you could say they
2 will if you don't consider the combination of the two, I can't see how combining
3 them would result in a lower exposure than combining them. So you could say it
4 will result we just can't say how much lower it will be.

5 **DR. KENNETH PORTIER:** Thank you. I wanted to
6 make a remark on the -- on the use of the OSHA compliance data. We've
7 mentioned in the past that, you know, going into that data set there's an
8 assumption or acknowledgment that the data would be supposedly biased to the
9 high end, right? I mean, OSHA goes in because there's a suspicion that the
10 workplace is not safe or that some part of their process is not being controlled
11 properly. Henry, you want to comment on that?

12 **DR. HENRY ANDERSON:** Yeah. I think less than 15
13 percent are actually triggered responses. The others are all scheduled in
14 advance. And again, the complaint may not be about the exposure. It may be
15 about other things. So you really have to look at -- it's like NIOSH going into
16 places or the HHEs. Some of the ones that were used here, the workers were
17 concerned about, you know, reproductive issues not necessarily related to
18 exposure. So I think it's unfair to characterize that all of the OSHA inspections
19 are done because of exposure complaints. Really needs to --

20 **DR. KENNETH PORTIER:** Well, that was -- that was -
21 - that was going to be my question. You know, and I think we should at least
22 add something like that. If we're going to mention use of the OSHA data we
23 should mention the fact that that preconception is maybe not correct, and
24 therefore they should look more carefully at that data. And even if they throw

1 out the 15 percent that are, you know, high end exposure complaints, there's still
2 data left there that would be useful to compile and potentially utilize in this draft
3 risk evaluation.

4 **DR. HENRY ANDERSON:** I guess I think even if they
5 are high end, they could be used for that sentinel kind of issue for estimating the
6 high end and calculating what they -- the extent or how we want to characterize
7 is that an unreasonable risk if they're into some plants or -- I don't think we need
8 to have a -- talk about the average exposure in the plant. So I think it's good.

9 What I think is missing in a lot of this is just the
10 understanding of the variability in exposures and then how you want to use that.
11 It's descriptive, so we're missing a lot of descriptive information that would be
12 useful to understand, kind, of, what's going on. And there's always going to be
13 problems but you don't have to say, you know, you're going to base your
14 assessments solely on problematic data.

15 But it's very useful to see how does that data that they
16 have compare to the research study data that you have. And if it seems to be
17 very similar that really is -- then, gives you greater confidence in the database
18 you're using that it's an appropriate database. So I'm -- I've -- I like to use all of
19 the data more in a qualitative understanding of exposures. The focus here is on
20 picking something for a quantitative assessment.

21 **DR. KENNETH PORTIER:** Yeah. I think I get --

22 **DR. SHERI BLYSTONE:** This --

23 **DR. KENNETH PORTIER:** -- I get your point. Dr.
24 Blystone.

1 **DR. SHERI BLYSTONE:** Yeah. I just wanted to weigh
2 in briefly on the aggregate exposure, which I also agree is useful provided there
3 is a generally accepted standardized methodology for doing that. Which might
4 be a good topic for this team going forward.

5 **DR. KENNETH PORTIER:** It's on my list. Dr. Barone,
6 I see your hand. I just want to ask if anyone else on the committee has a
7 comment before we turn to EPA for their clarifying questions or comments. I
8 don't see anyone. Dr. Barone.

9 **DR. STANLEY BARONE:** Dr. Portier, I wanted to
10 follow up on a couple of the comments and questions with regard to the dose
11 reconstruction issue versus the exposure assessment issue. And I think in some
12 cases some of this discussion is sort of conflated those two concerns or two
13 issues.

14 EPA is concerned about past exposures. We are
15 concerned about the dose reconstruction. We are evaluating the studies and what
16 the appropriate dose and dose response is in the epidemiological findings. So
17 that is critical for the -- on the hazard side and dose response side.

18 I think the committee is also discussing what other
19 information could be used, or would be used, and what we could do better on the
20 exposure assessment side. There's rarely a case where we have that wonderful
21 perfect study which is both for exposure assessment and for hazard assessment.
22 And at least in the PERC database, I don't think we have that kind of study.

23 So again, I think there's distinctions between the exposure
24 assessment and its general applicability across conditions of use versus -- well, in

1 the hazard assessment side where we can use studies and generally apply them
2 because of the toxicity and the dose reconstruction across conditions of use. So I
3 think there are two different things. I just wanted to make sure we're clear about
4 that.

5 **DR. KENNETH PORTIER:** Yeah. I had -- I had
6 similar thoughts about that when Dr. Willhite mentioned, well, it's the peak that's
7 important. Whereas, you know, on the hazard side we're looking at area under
8 the curve and maybe those two concepts don't work out. And they are related to
9 each other.

10 The other thing I thought of is that, you know, part of the
11 issue with the draft risk assessment is that there's a focus most on kind of what I
12 might call confirmatory kind of strong data and supporting weaker data. And
13 what may be missing is a discussion and acknowledgment that there is a lot more
14 supportive weaker data out there that isn't discussed in the DRE.

15 So, you know, I have fair confidence that EPA looked at
16 the OSHA data but decided it's not the strong data we're looking for, it's weak
17 supportive data. But then you didn't go back and kind of incorporate that into the
18 discussion to, in a sense, help address some of the uncertainties that come up in
19 just focusing on this strong data that's going to move forward into establishing an
20 exposure level. So that was just kind of my take on this discussion.

21 I think it's been a good discussion. Any additional
22 comments on these three questions before we kind of take a 15 minute break? I
23 don't know about you guys, but I really need another coffee this morning. So I

1 have 11:27. Let's go ahead and take a 15 minute break return at 11:45 eastern.

2 So we're in break for 15 minutes.

3
4 (Break)

5
6 **DR. KENNETH PORTIER:** Thank you. I have 11:45.
7 I'd like to reconvene. I think we're ready to move on to Questions 4.4, 4.5, and
8 4.6. Dr. Lee would you please --

9 **DR. MARI LEE:** Yes, I will.

10 **DR. KENNETH PORTIER:** -- read them --

11 **DR. MARI LEE:** Question --

12 **DR. KENNETH PORTIER:** -- into the record?

13
14 **CHARGE QUESTION 4 (4.4)**

15
16 **DR. MARI LEE:** Yes. Question 4 - Occupational
17 Exposure continued. Submit ONU inhalation exposure EPA considered
18 available personal monitoring data, area monitoring data, and modelled far-field
19 exposure concentrations. When exposures to ONUs could not be quantified,
20 EPA considers a central tendency from worker personal breathing zones to
21 estimate ONU exposures.

22 Question 4.4, please comment on the assumptions and
23 uncertainties of this approach. 4.5, are there other approaches or methods for
24 assessing ONU exposures to a specific condition of use? And 4.6, please

1 comment on this and provide any suggestions and or data for assessing dermal
2 exposure to ONUs.

3 **DR. KENNETH PORTIER:** Dr. Davies, it seems like
4 we're still with you here.

5 **DR. HOLLY DAVIES:** Yes. Three down and two to go.
6 So for Question 4.4 I wanted to mention that the response to the previous
7 questions on, you know, 4.1 to 4.3 also commented on the assumptions and
8 uncertainties in estimating ONU exposures and I'm not going to repeat those
9 here.

10 So a few additional comments. Section 2.4.1 is
11 reasonably presented with the assumptions and uncertainties. Another -- the next
12 comment is that we'd like to highlight that the wipe cleaning solvent and the
13 metal stone polish exposure estimates may be unreasonably high. The data you
14 used don't seem representative and these are very high exposures, so we
15 recommend consideration of greater uncertainties that the risks moving forward
16 with these exposures.

17 I think we've talked before about the difficulty of
18 separating employees into workers and ONUs and how that's done with far-field
19 and near-field. It's also uncertain -- it's unclear how EPA used the area
20 monitoring data. And then some comments on the employee -- number of
21 employee estimates. Not clear how these estimates are used in hazard
22 assessments.

23 And on -- and also, on the Table 2.13 the last entry on that
24 table, which is a table of number of worker estimates is not -- doesn't -- that is a

1 public comment. It doesn't actually have information about number of workers
2 in it. So we recommend that that be taken out of that table. And that's all I have
3 to -- so you can open it up to everybody else.

4 **DR. KENNETH PORTIER:** Good. I'm going to want
5 to come back to this area monitoring data issue. I'm not quite sure what that
6 means but let's see if other want to discuss it. Dr. Anderson.

7 **DR. HENRY ANDERSON:** Yeah. I'm -- area
8 monitoring is mentioned in the question and in the -- and in the text, but I didn't
9 see any area monitoring data presented in the parts that I read. And I would
10 suggest that area monitoring really is just the general air in the facility and would
11 be generally considered to be more background plant wide exposure. So I'm not
12 sure area monitoring, unless you know where the monitor's located, would be
13 helpful.

14 We don't know that the area monitor is in the, you know,
15 far zone versus the near zone. So I don't -- I think that just confuses the issue a
16 little bit. And again, I don't believe there's any personal monitoring data for job
17 categories that are ONUs. And it would be probably helpful if EPA gives some
18 examples of what they would consider to be ONUs. And some of those like
19 administrative staff, they're probably not within the far-field, they may in a
20 totally different room. So it's how do you characterize the workforce by how
21 close they are to a point source of exposure. It's problematic in some of these
22 worker categorizations.

23 So -- and then using the central tendency data is, you
24 know, that -- if you have nothing else I suppose it's good and may well

1 overestimate but it really suggests that the ONUs are in fact part of the overall
2 workforce. And they may in fact be counted twice because they may be part of
3 the central tendency description of the exposure assessment.

4 So if they're not -- if you can't remove the ONUs from the
5 workers and separate -- clearly delineate between the two groups, what's likely to
6 happen is the ONUs are -- or some of them are going to be in the worker group.
7 And you're now just further reducing their exposure by using a central tendency
8 of a database. And that's not well characterized as to, are they actual hands-on
9 workers or are they ONUs.

10 So I'm not -- not over -- more that I've looked at these over
11 the various projects, I don't really know how -- what having a category called
12 ONUs really contributes to the understanding on the hazard. Unless we are able
13 to clearly distinguish, keep only those who meet the worker definition are in the
14 data -- in the exposure database we're using. Otherwise, it's a general workforce.
15 And of course, workers change jobs on and off so there's more apt to be a mixing
16 of ONUs with workers as a workforce moves forward. So I think there's perhaps
17 more confusion and complexity added by having an ONU category than just
18 having the worker category when we don't have any real ONU data.

19 **DR. KENNETH PORTIER:** Thank you. Dr. Kissel.

20 **DR. JOHN KISSEL:** So I have really only one comment
21 here on -- in this -- for this particular chemical. I think we have good data which
22 suggests that there's another category that is not the traditional occupational non-
23 user as EPA has -- is defining it. I think we have occupational bystanders in this
24 scenario. We have people that live in buildings above dry cleaners. And I think

1 there's enough data in the literature to say that those exposures, well one, they're
2 chronic. And they're not captured by the bystander notion that well. Somebody
3 used glue in the -- in the house and that's distributed and so therefore, for some
4 episodic event you get some exposure which is the consumer bystander version
5 that we have here.

6 But I think there should be occupational bystanders here
7 because we know there are people who are breathing air in buildings that are co-
8 located with dry cleaners and so I think we need another category. And that's my
9 primary comment here.

10 **DR. KENNETH PORTIER:** Seems to be a good point
11 John. Can you think of a situation other than the dry cleaner where occupational
12 bystander -- I mean, you know, in the pesticide stuff we talk about bystander and
13 risk analysis as well but I hadn't even thought about it here so I was wondering if
14 any of the other COUs might use that kind of designation.

15 **DR. JOHN KISSEL:** Well, there's -- you know, there's
16 always the possibility of an owner operator living above a shop of some kind. I
17 don't know how well that's characterized. The dry cleaner issue has been
18 identified and then there's empirical data. There probably are other cases where
19 people are doing things but they're just less obvious and less well quantified.

20 **DR. KENNETH PORTIER:** Yeah. Dr. Meliker. We
21 get a new voice here in the discussion.

22 **DR. JAYMIE MELIKER:** Yeah. Can you hear me?

23 **MS. RUTHANN RUDEL:** Oh, this is Ruthann --

24 **DR. KENNETH PORTIER:** Yeah.

1 **MS. RUTHANN RUDEL:** -- can I just -- can I just --
2 can I just jump in on that -- just on the thread that you guys were talking about?
3 I think another scenario, I think John's suggestion is good. And another scenario,
4 you know, would be being next to certain kinds of shops that are often within
5 residential areas. That could include like automotive repair shops and some
6 other light industrial where PERC is -- can be used. Dry cleaners, obviously, are
7 the biggest example.

8 **DR. KENNETH PORTIER:** Yeah. And I see Dr. Apte,
9 you have your hand up.

10 **DR. UDAYAN APTE:** Yeah. So I'm just wondering
11 about the dry cleaner thing too. And this might be covered already but, you
12 know, the way my dry cleaner works especially, is they have a factory
13 somewhere where they bring the clothes to a shop and pick them up. And the
14 lady who gives them to me, stays there eight, nine hours a day with all those
15 clothes, you know, right there next to her. And so I was wondering, people like
16 that, are they ONUs? And are they covered in this?

17 **DR. KENNETH PORTIER:** Yeah. I think they're
18 considered ONUs because they're not handling the material. But I think you'd
19 have to look at the DRE to understand. Dr. Meliker.

20 **DR. JAYMIE MELIKER:** Yeah. I mean, I agree with
21 everything people have said. I think, thinking about bystanders especially close
22 to dry cleaners, there's good literature there that we can generate estimates on.
23 And I feel for EPA because they've done a lot of work. I -- this is -- it's really
24 hard work to try to build these exposure estimates.

1 But I guess my main point is that some of these estimates
2 for different activities and different industries are better than others. Yet I don't
3 get a sense from the document that that type of uncertainty in the exposure
4 assessment is propagated forward in any way. And I'm not necessarily talking
5 about a quantitative propagation. I think in an ideal world that would be the
6 case, but I know that takes a long time.

7 But I think at a minimum some type of table or figure that
8 ranks the confidence that EPA has in these different -- in their exposure
9 estimates for these different types of activities for workers, for occupational non-
10 users, for occupational bystanders, and so on so that -- and then to base their risk
11 assessment in some way based on where they're -- where they're most confident.
12 You know, at least factor the confidence in -- in some capacity. So that -- I'd say
13 that's my overarching comment on the exposure assessment section here.

14 **DR. KENNETH PORTIER:** So the use of low, medium,
15 high kind of general descriptive but you're looking at something a little bit more
16 granular maybe is the right word?

17 **DR. JAYMIE MELIKER:** No. I think even low,
18 medium, high is okay. But then when you get to the risk assessment at the end, I
19 don't remember seeing low, medium, high discussed in terms of where they're
20 most confident versus least confident. You know, like, propagating it through,
21 not just saying here's the -- here's the exposure assessment, here's low, here's
22 medium, here's high and then not talking about it again. I don't remember it
23 being talked about again. Does that make sense? Propagating it through.

1 **DR. KENNETH PORTIER:** Yeah. You might be --
2 you might want to look at the risk characterization section, kind of where they
3 put together exposure hazard and then kind of get back to the confidence in the
4 final risk estimate. But I'd have to go back and check. I'm not sure. I thought
5 there was some discussion on certainty assessment low, medium, high on
6 exposure but I may be wrong. Dr. Willhite, did you have anything to add?
7 Calvin, your cell phone might be muted, or your phone might be muted.

8 **DR. CALVIN WILLHITE:** Yes. I have dyslexia here.
9 The bystander suggestion I would say is excellent. It's difficult to consider the
10 neighbors per se as ONUs but I don't know what else you'd call them. But the
11 important thing is to not throw away the data that we have for the near-field.

12 And we -- and if you look at the data, we not only have the
13 indoor air for different times like day and night that would be active during the
14 day, probably not so much at night. But we also have personal air collection.
15 And for the PERC levels in the indoor air, we have values to as high as 5,000
16 micrograms per cubic meter. And for personal air you're looking at about 1,000,
17 948. So -- and we have -- so in these studies the first is *Environmental Health*
18 *Perspectives* 110, page 655. The other is *Environment Health Perspectives* 2005
19 page 1,336.

20 We have, I would say, as good a data as you're going to
21 get. So therefore, I would not make the risk management decision based on
22 some purported regulation that was passed what have you, about different
23 mixed-use buildings. These are the data. And they're as good as we're going to
24 get for the ONU population as far as I can see. That's number one.

1 And then I'd like to go back and just speak to one thing
2 about what the EPA said that they didn't have, like, a significant sentinel study
3 on say health outcome related to, like, carcinogenicity or any other adverse
4 effects as we have with benzene.

5 So in order to address that problem, and this is beyond the
6 scope of where we are here, if EPA in cooperation with halogenated solvents et
7 cetera, followed the tac of the National Cancer Institute and UC Berkeley that's
8 one team. The second is the A -- American Petroleum Institute and Rob
9 Schnatter at Exxon is another. They went to China and they followed people and
10 they followed their tasks. They examined them.

11 And so the thing this, in a prospective way, and there's
12 about -- there's at least 40 papers that come out of those efforts on concentration
13 response, mode of action for benzene and it's not exactly what we used to think it
14 was. So there's a whole rich potential for defining PERC adverse health effects
15 because of the giant *n* associated with benzene. So I'd say, don't throw away
16 these Schreiber and McDermott (phonetic) papers with their data because they're
17 as close as I think we're going to find for bystander/occupational non-user.
18 Thank you.

19 **DR. KENNETH PORTIER:** Do we have additional
20 comments on the assumptions on uncertainties, under occupational exposure?
21 Okay. I'm not seeing any. Let's go onto 4.5 other approaches or methods for
22 assessing ONU exposure. And I think that's Dr. Kissel has the lead on 4.5.

23

CHARGE QUESTION 4 (4.5)

MS. RUTHANN RUDEL: Oh, we've switched. It's Ruthann. And Dr. Kissel is going to do 4.-- you promised me you were going to forget and you did. So that's good.

DR. KENNETH PORTIER: I got it written down in front of me, but it wasn't on my computer screen. Darn. Okay. Back to -- I mean, Ruthann Rudel has the lead on 4.5. Dr. Kissel has the lead on 4.6. Ruthann. I told you to correct me anyway and you did. Thank you.

MS. RUTHANN RUDEL: No worries. So the question about is, you know, are there other approaches or methods for assessing ONU exposure for specific conditions of use. And of course many of the specific -- many of the comments are echoes of things that we have already talked about but I want to -- so some of them I won't go into in a lot of detail if I feel like we've talked about them before.

One of them is using the OSHA enforcement data to represent exposure point concentrations would -- there's not a good reason that that wasn't used. And it's certainly -- represents exposures of some workers and possibly of many workers.

There are a couple comments from other members just on the concept of the ONU and that it's -- it seems forced and not to fit within actual the way workplaces are set up. And that it's not a term that's used, you know, in other parts of the literature of public health or industrial hygiene. So it's kind of -- stands out in that way. The suggestion that EPA should more clearly define

1 worker tasks and where ONUs might be in relation to the solvent rather than just
2 assuming all workers are near-field and all ONUs are far-field.

3 Another comment that -- and again, I think we've -- we
4 heard which is that the approach -- the inhalation exposures is given that there's a
5 low confidence in the ONU inhalation estimates it would be useful to propagate
6 that uncertainty through the analysis.

7 And the final comment I think building on what one of the
8 public commenters from NRDC, I just wanted to -- there's many conditions of
9 use where ONUs are determined to have to unreasonable risk. And so it's very
10 important to make sure that risks for these scenarios are not underestimated.
11 And the risk that it's important -- I mean, the reason that that's important, as I've
12 said, is because once that determination is made EPA won't revisit those risks
13 and states will be preempted from stepping in to protect those workers, or in
14 some cases maybe their neighbors too.

15 And honestly, to me it looks like there are many ways
16 throughout the risk evaluation that EPA is underestimating risks. And these
17 include not using OSHA enforcement data for exposure concentrations, filling
18 the PERC risk bucket with these workplace exposures, and not accounting for
19 other exposures that may occur from other jobs, from consumer uses, from
20 contaminated drinking water or air.

21 Also, skimping on uncertainty factors. For example,
22 there's no database uncertainty factor, no additional uncertainty factor for
23 susceptibles, for example, with polymorphisms and CYPs. Also, for not
24 considering PERC exposures in conjunction with exposures to other solvents that

1 have similar effects and, in some cases, correlated exposures. So I just hope that
2 the SACC and the public understands the stakes are high if EPA makes an
3 erroneous finding of no unreasonable risk. That's all I have.

4 **DR. KENNETH PORTIER:** Thank you. Dr. Anderson.

5 **DR. HENRY ANDERSON:** Yeah. I only have one
6 thing to add to that. While we've spoken a lot about the OSHA enforcement
7 database, there's also an OSHA consultation program that every state has that is
8 voluntary that businesses call them and ask for assistance and evaluation. And
9 that is targeted to smaller sized businesses.

10 Well, small isn't 10 or less people, it's 500 or less
11 employees kind of a thing. So I think that's a database that might well be more
12 representative because companies who don't have the resources or staff to do
13 monitoring or other things call the OSHA consultation program. And they go in
14 and the do it and so they will have job descriptions and information like that in
15 each of their evaluations.

16 So that's a database. They used to be separate. I think
17 they may be combined now so -- but you can determine which are from the
18 consultation program which is really not enforcement at all. They have no
19 enforcement authority. While it is true because I oversaw our one in Wisconsin
20 for quite a while. Companies who are worried that the OSHA enforcement may
21 come in can call and have the consultation program come in and then OSHA
22 enforcement will defer to the consultation program to provide the assistance to
23 see if anything needs to be done. But I think that's another database. We kind of

1 tend to put all OSHA together but there's really those alternative programs that
2 really should be looked at or could add more information to this.

3 **DR. KENNETH PORTIER:** Thank you. Dr. Davies.

4 **DR. HOLLY DAVIES:** Ruthann did a good job of
5 summarizing all of the comments. I also just wanted to echo Andy's mentioning
6 the state programs. Washington state also has a program that's separate from the
7 enforcement in our labor and industries department. So that's a good place to
8 look for more information.

9 **DR. KENNETH PORTIER:** Dr. Meliker.

10 **DR. JAYMIE MELIKER:** Yeah. I have nothing else to
11 add.

12 **DR. KENNETH PORTIER:** Dr. Willhite.

13 **DR. CALVIN WILLHITE:** I hope I'm getting better at
14 phone operation.

15 **DR. KENNETH PORTIER:** Perfect.

16 **DR. CALVIN WILLHITE:** I'd like to note the
17 California Department of Industrial Relations and under CALOSHA has had one
18 of those consultation programs since the -- certainly the late 1970s. And so what
19 you could certainly do is actually they're working from home now so you
20 probably -- this is a good time to contact the California Department of Industrial
21 Relations, dig down inside there and find the CALOSHA consultation program
22 for dry cleaners. Thank you.

23 **DR. KENNETH PORTIER:** I added Dr. Kissel to the
24 end of this list just in case you had something to add.

1 **DR. JOHN KISSEL:** I don't have anything further.

2 **DR. KENNETH PORTIER:** Okay. Dr. Blystone.

3 **DR. SHERI BLYSTONE:** Yeah. Just a quick comment.

4 I've heard several times throughout all of these meetings about data that states
5 may have that is relevant and that EPA should go and ask for it. But I think it
6 should be the other way around, right? When these scoping documents and
7 problem formulations are put out and states have relevant information, they
8 should submit it to EPA proactively.

9 **DR. KENNETH PORTIER:** Well, I know EPA asks for
10 it. We don't know if the states actually offer it back again. Dr. Anderson.

11 **DR. HENRY ANDERSON:** Yeah. I -- most of the state
12 programs are in different locations and the mail coming in, I'm not sure they're
13 really all that involved with the program. It's nice to say it. It's the same as
14 saying, gee, you've got all of these companies out there. And other than the
15 manufacturers I haven't -- it doesn't appear that any of the other facilities have
16 submitted data. Yet there's a fairly large industrial engineering and industrial
17 hygiene workforce out there that are providing consultation and are in and out of
18 various committees.

19 So I think it really behooves EPA to reach out and trying
20 to look through -- I couldn't do a search on the database of whatever thousands
21 were there to see how many of those were kind of gray literature reports from
22 states. I don't know who EPA contacted in the state. Did they go the
23 consultation programs individually and say, we're looking for this -- basically do

1 a data call in? And that's what some of the EPA and other programs do go out
2 specifically or OSHA or NIOSH attempts to do that as well to get data.

3 So I think it would be helpful in the doc- -- I mean, if we
4 want a recommendation, I didn't see a good description of the extent of the EPA
5 effort to obtain data. And I think if they were to say, we sent out 350 letters to
6 all sorts of different state agencies and nobody responded, that's kind of a sort of
7 statement in there that would then raise somebody's question that well, why
8 aren't they -- why aren't the states or why aren't the companies participating?
9 Possibly assume that people will send in the information, but we have to be sure
10 that it went to the right program that might have that data.

11 **DR. KENNETH PORTIER:** Dr. Davies and then Dr.
12 Willhite.

13 **DR. HENRY ANDERSON:** I think one more option is
14 there, is a state and territorial epidemiologist which has members from every
15 state. There's Conference of State and Territory, CSTE, to contact that group and
16 they routinely on behalf of NIOSH and some of the others can do surveys. So
17 could do a survey just to ask states what data do they have, and what format it is
18 in. And the next step would be to see from the -- you know, like that, it's pretty
19 inexpensive to do. You could find out what health departments and labor
20 departments, what data they have and for what kind of industries. And then get
21 the -- they're description of their databases.

22 **DR. HOLLY DAVIES:** Hi. This is Holly Davies. I just
23 wanted to add onto what Dr. Anderson was saying. And another possible thing
24 for EPA to do would be for EPA to contact the state's environment agencies and

1 then those agencies within the states could contact their sister agencies like the
2 Department of Health and the worker agency to get more information.

3 **DR. KENNETH PORTIER:** Well, in a minute I'm
4 going to ask EPA for clarification. But Dr. Willhite.

5 **DR. CALVIN WILLHITE:** Yes. I think Dr. Holly
6 Davies underestimates the bureaucracy here in California. You have enough
7 trouble trying to go to the Department of Motor Vehicles to try to get something.
8 However, what I would say is, if I were in the EPA headquarters shoes given this
9 time crunch and these comments, I would to the regions.

10 For example, Region 9 in San Francisco. Find out what
11 they have. They -- you've -- or the California Water Resources Control Board.
12 The regional water control boards handle all those places where the
13 Perchloroethylene was dumped or leaked underneath the facilities. They'll not
14 only have that, but they'll have near-field, they'll have next door data. So there's
15 a lot of places you can look but to just go to CAL EPA and try to ask them what
16 they have, I think that's probably a fruitless search. Thank you.

17 **DR. KENNETH PORTIER:** Henry. Dr. Anderson.

18 **DR. HENRY ANDERSON:** Yeah. I would echo that,
19 that it's problematic getting to the right person. One thing the regional offices
20 have and all the other EPA enforcement programs they have a very large EPA
21 state cooperative agreement. So there's a -- because I know on the health
22 department we always tried to get them to build into those agreements which
23 cover all of the water testing, all of the air testing, where they put the monitors

1 for air and all of that kind of thing, or the waste side investigation, there's a lot of
2 EPA money that goes to states.

3 We always complained that we would send in requests and
4 our state agency, sister agency, would rate ours lower and say go get your own
5 money. But in fact, going forward, the TSCA program could perhaps work with
6 the regions to build in some requirements into those agreements so that the states
7 then -- because they would getting -- would be part of that agreement would then
8 be really motivated to help out more than they perhaps are doing now.

9 Again, that's the kind of thing going forward. And given
10 the short turn around and quick times this first 10 has had is something to think
11 more for the future. And in later questions here I think it'd be helpful to have a
12 kind of after actions review of this first ten to see what kind of commonalities
13 each of them have and then, can those be addressed by longer term commitment
14 programs as it goes forward rather than just say, well we -- what's easily
15 available is what we're going to have to use.

16 And that's certainly was what had to be done for these first
17 ones, but we could certainly strengthen the data and the coordination of going
18 forward with having some more infrastructure in place to know what -- we know
19 what -- we already know what the set of chemicals are going to be and there
20 could be an ask to develop programs for that right now.

21 **DR. KENNETH PORTIER:** Thank you. Dr. Willhite,
22 do you have your hand up? Do you want to add a comment? And it went down.
23 Any additional comments on other approaches or methods for assessing ONU
24 exposures? Dr. Barone, you want to address some of this?

1 **DR. STANLEY BARONE:** Yes. I've heard some great
2 recommendations, some of which are, again, take time and resources. And I
3 think committee's recognized that. We do try very hard to do outreach to the
4 states for data. Our risk management division facilitates that and Tyler Lloyd,
5 who's part of our team, might be able to speak to that more in detail.

6 But the big challenge, and I think this discussion brought
7 it out is, who are the data keepers, data holders? Many of the -- many times what
8 we find is that there's no electronic or quote/unquote web-based databases.
9 There are a few exceptions. Most of the time it's in some file drawer, paper
10 folder, and we've had access issues or difficulty in trying to access those except
11 on rare occasions.

12 And who, again, who is the holder? Who's the point of
13 contact has been somewhat difficult. So we're hoping that with the publication
14 of our scopes, and the submission for the next 20, and submission for
15 information in the public docket will get more of that information as folks learn
16 about its criticality, and as you bring attention to the importance of these issues
17 in the peer review recommendations.

18 **DR. KENNETH PORTIER:** Did anyone else on the
19 EPA team want to comment? Dr. Barone, I hear that kind of a question as to
20 whether you go through the regions, so the risk management teams are regional
21 based or is that national based?

22 **DR. STANLEY BARONE:** We do have some
23 interactions with our regional. We have cooperative agreements. Yes, that's
24 correct. Most of that has focused on our pesticide program and our superfund

1 program. There has -- there has been less emphasis in the past on TSCA. That's
2 something we're working on with, again, with our regional offices. And your
3 suggestions, again, bring new light to this particular issue. It is a resource issue
4 as well.

5 **DR. KENNETH PORTIER:** Yeah. This is Ken Portier.
6 One of the frustrations I always find is I'm more familiar with what EPA's done
7 on the pesticide side. And there's just so much more data there, so much more
8 opportunity to get data, especially monitoring data that exposures are much
9 better measured and these TSCA assessments just seem to be data poor
10 assumption rich.

11 And I think part of our conversation here has been the
12 committee's reaction to that fact of life at this point. Any final comments from
13 the committee? Let's move on to Question 4.6 which Dr. Kissel is the lead on.
14 Dr. Kissel? I see that you're not on mute but we're not hearing you. Your phone
15 might be muted.

16
17 **CHARGE QUESTION 4 (4.6)**
18

19 **DR. JOHN KISSEL:** Can you hear me?

20 **DR. KENNETH PORTIER:** Yes.

21 **DR. JOHN KISSEL:** Sorry. I had phone issues. So 4.6,
22 this question involves dermal exposure to ONUs which is actually excluded so
23 presumably the question is, could EPA somehow include ONU dermal
24 exposures? The first thing that I would mention as I've said before is that I think

1 assessment of dermal vapor -- direct dermal vapor uptake should be included. I
2 also mentioned that for this compound for people not wearing respiratory
3 protection dermal vapor -- direct dermal vapor's not likely to be important.

4 But I think -- I think it's good to get in the habit of doing it
5 and I think reporting low numbers is okay if the numbers turn out low. You
6 know, it completes the risk characterization to say we looked at this problem and
7 we got low numbers and here they are. And then if somebody doesn't like the
8 way the calculation was done, they can argue about it. So I think as a default the
9 dose calculation should be shown.

10 The -- then the rest of the discussion -- I got relatively
11 limited comments from the other members and they reiterate much of the
12 discussion that we've already had. There's, I think, a general consensus that there
13 are people that don't have -- that are sufficiently remote from active use that they
14 don't have direct dermal exposure to liquids. And so that's okay.

15 The problem becomes actually defining and then we get
16 into the whole question of who are the ONUs and how well do we actually know
17 what they're doing? And so there's a large amount of uncertainty. And there's
18 the comments go so far as to say, well, we should stop trying to define ONUs
19 and just list employers -- or employees. Everybody's a worker and then have a
20 larger range of potential exposure. So I will -- I -- with that I'll just open it up if
21 anybody else wants to say anything.

22 **DR. KENNETH PORTIER:** Dr. Anderson.

1 **DR. HENRY ANDERSON:** Yeah. There's always a
2 problem with being an A at the top of the alphabet. Let's go for -- this example -
3 -

4 **DR. KENNETH PORTIER:** You know I was just
5 thinking the same thing Dr. Anderson. I should have jumped to Dr. Kaufman
6 and give you a break. But it's too late.

7 **DR. HENRY ANDERSON:** Yeah. Well that -- and this
8 just probably compounds the issue with getting data from states or external
9 bodies, but I would be interested in and it doesn't say anywhere -- so what does
10 the European Union or what was Japan or individually, what does Germany do
11 as it related to ether dermal exposure, assessing that? This kind of goes on the
12 data access issue as well.

13 Sending a letter through the State Department to external
14 governments is not going to get you much in a 90-day period. But again, going
15 forward, I would think that there may be some data there that would be helpful to
16 know how do they even evaluate dermal exposures and do then do summing of
17 exposures or how do they approach that. It's unclear what the -- our international
18 partners and some of the owners of the manufacturers here I'm sure are
19 international as well. So that's one recommendation to maybe see what is done
20 there.

21 The other way is if you take the literature that we have
22 you can quickly get a list of who are the lead authors and those lead authors all
23 have, usually at the Journals, have an address. So it would seem to me that if we
24 look at some of these -- well, for example, again I focused on manufacturing.

1 There were a few individuals at research institutions who have done multiple
2 studies or are busy studying for other purposes some of these plants and these
3 workforces.

4 Early on you could query them, one to see -- not try to get
5 their necessarily underlying data because of all the confidentiality and other
6 issues, but you could ask them are they aware -- does their enforcement agencies
7 or others have data from facilities in their countries? So that might be another
8 way to potentially access information. Or, by the time you get your journal
9 article published often times it's been cut down on the number of words and the
10 sections to be far more focused and concise than we would like to see.

11 So now, with the online publishing you could have your
12 data or tables electronically available but just not in the publication itself. So I
13 think there's potential ways to reach out to those who've been involved in the
14 research. Even if it's 10 years ago, those individuals may still be around or
15 somebody there that could -- is interested and could be helpful on addressing the
16 issue of dermal exposure and characterizing ONUs that may be unusual. That's
17 it.

18 **DR. KENNETH PORTIER:** Thank you. Dr. Bennett.

19 **DR. STEVEN BENNETT:** Yeah. Good morning or
20 good afternoon. You know, I -- as we look -- go through this discussion I don't
21 have a lot to add onto it. I think it's, you know, an interesting question but I'm
22 not sure, you know, similar to John I'm not sure how far it would expand the
23 understanding of the consumer exposures -- or excuse me, the occupational
24 dermal exposures.

1 I get, you know, it doesn't appear to be a significant route
2 or significant contributor to the overall exposure, certainly from the occupational
3 non-user perspective. But you know, it would be -- it also would be nice to have
4 information supporting that hypothesis. But that's all I want to put in.

5 **DR. KENNETH PORTIER:** Thank you. Dr. Kaufman.

6 **DR. ALAN KAUFMAN:** Hi. Yeah. First of all, I want
7 to commend the EPA staff. As I looked through the risk evaluation it is, you
8 know, it's clear to me that the sheer number -- or the ubiquity of this chemical
9 and the sheer number of use cases had to make this extraordinarily challenging
10 from a data acquisition standpoint. This -- this -- and trying to in some cases
11 separate one use case from another because the, you know, there are some that
12 are very similar to others.

13 Having said that, you know, the comments that I've got --
14 let me see if I can find my comments here. You know, first of all, I think, not to
15 belabor points that have been brought up, I think, you know, the issue of whether
16 PPE is used as regularly as assumed is a concern. You know, the --even, you
17 know, if -- in terms of glove use, I think the issue of aggregate exposure is one
18 we certainly need to look at.

19 You know, if you think about it, some of these ONUs may
20 have some element of dermal and inhalation exposure, and also possible oral
21 intake from drinking water. So I think we need to at least look at that from that
22 perspective.

23 Beyond that, the concerning thing for me is that when you
24 look at the ONU dermal exposure, there seemed to be a lot of areas where it is

1 either there's no data available, there are data gaps or it's assumed there's no
2 dermal exposure. And I don't know that that's the case in every single use case.
3 I have to believe, for instance, in paint or adhesive manufacturing even someone
4 who's not directly involved in the process of, you know, compounding that
5 product, you know, may have some dermal exposure.

6 And in some cases -- I think in that particular use case it's
7 indicated there, you know, there are either no data or it's assumed that there is no
8 dermal exposure. So I think those would, you know, those would be my
9 concerns with, you know, with what I've read. I think that's it. Thank you.

10 **DR. KENNETH PORTIER:** Thank you. Let's see, who
11 else? Dr. Meliker.

12 **DR. JAYMIE MELIKER:** Hi. Yeah. I don't have much
13 to add either. It's really, I mean, this is hard. You have very little data. EPA has
14 very little data here and they're making assumptions. And they might be
15 reasonable, but they might not. But we don't know and I'm not -- I think the
16 suggestions that have been made are worth pursuing.

17 I don't know if they'll be fortuitous or not, but I think it
18 seems like we're really -- we need to have better data to be able to know whether
19 or not the estimates are good or not. And unfortunately, I think we just -- we're
20 not sure at this point. But the approach seems reasonable given the data that are
21 available.

22 **DR. KENNETH PORTIER:** Let's see, Dr. Willhite.

23 **DR. CALVIN WILLHITE:** Certainly, from where I sit,
24 this document as Dr. Portier summarized previously, we have some empirical

1 data, but we have lots and lots of assumptions. In the case of this particular
2 point, I think the Agency is better off to just admit they have insufficient data
3 and to write an eloquent paragraph to be inserted that says, we just don't know. I
4 think honesty is probably the best policy here. Thank you.

5 **DR. KENNETH PORTIER:** Yeah, Calvin, my only
6 problem is I'm not quite sure the legislation allows them to get away with that.
7 Dr. Anderson, before I go to Dr. Davies as clean up, Dr. Anderson.

8 **DR. HENRY ANDERSON:** I don't have any -- oops, I'm
9 sorry. I should have had my down. Missed it.

10 **DR. KENNETH PORTIER:** Okay. I just say your and
11 up there.

12 **DR. HENRY ANDERSON:** I just left it up.

13 **DR. KENNETH PORTIER:** Dr. Davies.

14 **DR. HOLLY DAVIES:** I don't have anything to add.

15 **DR. KENNETH PORTIER:** Ruthann Rudel, did you
16 want to add anything? You're kind of in this group.

17 **MS. RUTHANN RUDEL:** I've got nothing to add.
18 Thank you.

19 **DR. KENNETH PORTIER:** This is Ken Portier. While
20 we were talking, I was looking back at the risk evaluation and I realized that
21 Table 1-3, you show a number of international risk assessments that were done.
22 But if you -- if you search for any reference to these risk analyses in the rest of
23 the document they don't seem to be cited. Which suggests that the lessons
24 learned from some of these international risk assessments may not be fully

1 integrated into the rest of the draft evaluation, which means some of that good
2 occupational exposure information that we've been talking about may be in those
3 reports and just hasn't been extracted and pulled out into the discussion.

4 So I would, I kind of would add a recommendation that
5 we look at that and at least acknowledge whether those risk evaluations do have
6 data that would address any of these issues including the dermal exposure for
7 ONUs, whether they even address the concept of an ONU or how they handle the
8 idea of an ONU. I just don't think it's moved forward. Some of the international
9 risk evaluations are hazard evaluations and that information is captured into the
10 kind of questions we're going to talk about tomorrow on hazard, but I don't know
11 that literature. I'm hoping EPA knows that literature, but I don't see that
12 integrated.

13 Any final questions on -- or any final comments on 4.4,
14 4.5, 4.6? Not hearing any I think I'm inclined to go ahead and break for lunch at
15 this point. I have about a quarter 'til, a little bit -- 17 'til, something like that,
16 1:00 eastern. Let's go ahead and reconvene. We're supposed to reconvene at
17 1:45. I would say, let's go ahead and reconvene on time at 1:45 and take a one
18 hour lunch break.

19 And we have a lot to discuss this afternoon, and even then,
20 today's probably our short day. Tomorrow's going to be a long day so I'm going
21 to give you your lunch break so you can have 10 minutes to eat and 50 minutes
22 to do email and all the other things that you need to do today. So we're going to
23 break at this point and reconvene at 1:45. Thank you.

24 **MS. TAMUE GIBSON:** Okay. Thank you.

(Break)

DR. KENNETH PORTIER: Good afternoon, everyone.

Except those on the pacific coast. It's 1:45 here in eastern time and it's ready to reconvene. As we do every day, I'm going to do a quick roll call of the committee this afternoon. I know at least one panel member has had to step out. Let's see how many have returned from lunch at this point. Dr. Anderson. Can anyone hear me?

MS. TAMUE GIBSON: Yeah. We can hear you.

DR. KENNETH PORTIER: Okay. Good. Just wondering. Barton, Dr. Barton.

DR. CHARLES BARTON: Here. Here.

DR. KENNETH PORTIER: Thank you. Dr. Bennett.

DR. STEVEN BENNETT: I am here.

DR. KENNETH PORTIER: Dr. Blystone.

DR. SHERI BLYSTONE: I am here.

DR. KENNETH PORTIER: Dr. Bruckner.

DR. JAMES BRUCKNER: Still here.

DR. KENNETH PORTIER: Dr. Cory-Slechta. Dr. Davies.

DR. HOLLY DAVIES: Here.

DR. KENNETH PORTIER: Dr. Doucette.

DR. WILLIAM DOUCETTE: Virtually here.

1 **DR. KENNETH PORTIER:** Dr. Gilbert. Dr. Johnson.

2 Dr. Kaufman.

3 **DR. ALAN KAUFMAN:** I'm here.

4 **DR. KENNETH PORTIER:** Dr. Kissel. Dr. Rowlands.

5 **DR. CRAIG ROWLANDS:** I'm here.

6 **DR. KENNETH PORTIER:** Ruthann Rudel.

7 **MS. RUTHANN RUDEL:** I'm here.

8 **DR. KENNETH PORTIER:** Dr. Schlenk, can you hear
9 me?

10 **DR. DANIEL SCHLENK:** Here.

11 **DR. KENNETH PORTIER:** Was that Dr. Gilbert? Dr.
12 Apte.

13 **DR. UDAYAN APTE:** I'm here.

14 **DR. KENNETH PORTIER:** Dr. Cobb.

15 **DR. GEORGE COBB:** I am here until the hail and
16 lightening knock our power out.

17 **DR. KENNETH PORTIER:** Oh, the joys of living in
18 Texas. Dr. Daniels.

19 **DR. MICHAEL DANIELS:** Yeah, I'm here.

20 **DR. KENNETH PORTIER:** Dr. Grant.

21 **DR. STEPHEN GRANT:** I'm here.

22 **DR. KENNETH PORTIER:** Dr. Hossain.

23 **DR. MUHAMMAD HOSSAIN:** I am here.

24 **DR. KENNETH PORTIER:** Dr. Lash.

1 **DR. LAWRENCE LASH:** I'm here.

2 **DR. KENNETH PORTIER:** Dr. Lin.

3 **DR. ZHOUMEG LIN:** Hi. I'm here.

4 **DR. KENNETH PORTIER:** Dr. Meliker is out this
5 afternoon. Dr. Roby.

6 **DR. KATHERINE ROBY:** I'm here.

7 **DR. KENNETH PORTIER:** Dr. Vorhees.

8 **DR. CHARLES VORHEES:** I'm here.

9 **DR. KENNETH PORTIER:** Dr. Willhite. Dr. Pennell.

10 **DR. MICHAEL PENNELL:** Here.

11 **DR. KENNETH PORTIER:** Dr. Pennell, you're last on
12 my list. For some reason you got left off the list and I had to add you in. So I
13 apologize for having you last. Let me go back and check. Dr. Anderson, is that
14 who joined us?

15 **DR. HENRY ANDERSON:** I'm here.

16 **DR. KENNETH PORTIER:** Thank you. Dr. Cory-
17 Slechta?

18 **DR. DEBORAH CORY-SLECHTA:** Yes, I'm here.

19 **DR. KENNETH PORTIER:** Dr. Gilbert. I hear
20 something click on and off but I'm not quite sure.

21 **MR. MARTIN ALVARADO CORTES:** Dr. Portier,
22 Dr. Gilbert's experiencing some audio issues. She messaged me. We are
23 working on reconnecting her, but she is here.

1 **DR. KENNETH PORTIER:** Okay. Thank you. Dr.
2 Johnson.

3 **DR. MARK JOHNSON:** Yeah. I'm here.

4 **DR. KENNETH PORTIER:** Good. Everybody's here.
5 Let's continue. Are there any thoughts on this morning's discussions that we
6 need to revisit, or shall we move on? You can raise your hand I guess if you've
7 got a comment you wanted to add. I'm not seeing any so let's move on to charge
8 Questions 4.7, 4.8, and 4.9 at this point. I should have checked if Dr. Lee was
9 on. Dr. Lee, I see you on but muted.

10 **DR. STANLEY BARONE:** Dr. Portier, I'd be happy to
11 read the questions. Dr. Lee may have childcare issues.

12 **DR. KENNETH PORTIER:** Yeah. Well, she had issues
13 yesterday afternoon too right after lunch. So it may be the time of day for those
14 who are connected by --

15 **DR. STANLEY BARONE:** It's a unique time.

16 **DR. KENNETH PORTIER:** Yeah. Go ahead, Stan.

17
18 **CHARGE QUESTION 4 (4.7)**

19
20 **DR. STANLEY BARONE:** Question 4, Consumer
21 Exposures. EPA estimated consumer inhalation and dermal exposures to PCE
22 containing products using Consumer Exposure Model (CEM), consumer dermal
23 exposures for dry cleaning -- for the dry cleaning COU using CEM and the
24 consumer inhalation for dry cleaning COU using the Multi-Chamber

1 Concentration Emission Model, the MCCCEM. Product specific consumer
2 monitoring information was not identified in the literature therefore model inputs
3 related to consumer use patterns are based on data from a comprehensive
4 national survey --

5 **UNIDENTIFIED FEMALE:** -- for the first time. So
6 you're saying added. This had never happened before. Back checking....

7 **DR. KENNETH PORTIER:** Hello?

8 **DR. STANLEY BARONE:** Hello?

9 **DR. KENNETH PORTIER:** A little cross feed there.

10 **DR. STANLEY BARONE:** I'm not sure. The Westat
11 1987 survey as described and referenced within the PCE draft risk evaluation.
12 Weight fractions of PCE within products are based upon safety data sheets and
13 default model values are based on literature reviewed as part of the model
14 development as well as the exposure factors handbook. Next slide.

15 The Consumer Model Exposure, Question 4.7, please
16 comment on the overall approaches, models, exposures or use information and
17 overall characterization of consumer inhalation exposures for users and
18 bystanders for each of the identified conditions of use. EPA's asking what other
19 additional information, if any, should be considered and this is found in section
20 2.4.2 of relevant documentation.

21 Question 4.8, please comment on the approaches, models,
22 exposure or use information and overall characterization of consumer dermal
23 exposures for each of the identified conditions of use. And this is also found in
24 section 2.4.2.

1 **DR. KENNETH PORTIER:** Let's leave it right here and
2 we'll -- let's address these two questions first. Okay? So 4.7 and 4.8. Dr. Kissel
3 you have a read on 4.7?

4 **DR. JOHN KISSEL:** Yeah. So I didn't get comments on
5 all of the different conditions of use. I got more generic comments that are --
6 that are consistent with what we heard before lunch. Generally, people felt like
7 the inhalation approaches are reasonable. Modeling emission rates and making
8 estimates of duration and concentration is fine as far as it goes. But there was --
9 varying degrees of concern were expressed over data deficiencies.

10 So specifically, consumer behaviors, housing variables
11 including ventilation, and use of products. And various members expressed
12 various degrees of alarm over that. Some with a, well, it's probably okay
13 approach. And some with -- to the other end would be, well, we don't really
14 know enough to be saying this. The modeling is okay structurally, but the inputs
15 are so unknown that we have a problem. And so that's the overview and I will
16 let anybody who's listed as an associate fill that out if they are so inclined.

17 **DR. KENNETH PORTIER:** And I think what I'm going
18 to do is start with Dr. Bennett on this one. Give Dr. Anderson a break. Dr.
19 Bennett, do you want to add?

20 **DR. STEVEN BENNETT:** Sorry. It took me a -- took
21 me a second to unmute myself. I'm so used to not having to -- not doing that.
22 You know, I would generally agree with John's comments. I think the, you
23 know, the -- certainly, some of the conditions of use are very well described but
24 then there are others that aren't so much. I think part of that goes back to the

1 Westat study where it looked at some of these particular conditions of use that
2 are not -- so again,

3 I'll reiterate some of my thoughts -- concerns with Westat
4 study and, you know, a, you know, a need to look at some of those conditions to
5 better -- make sure that they adequately support the variety of conditions of use.

6 Looking at one particular use, I think the bright cleaner
7 use would be enhanced with either an outdoor modeling incorporated into that or
8 to expand the description similar to what was done with the marble polish
9 condition of use. Because that was done, you know, both for a -- both for a
10 utility room and for a -- for the kitchen use. Sorry. I was interrupted by my son
11 and -- coming back in from a water battle. The merits of working from home.

12 So I think that would be that particular condition use
13 would be -- would be enhanced by incorporating that. I would expect that to be a
14 much lower exposure in compared to doing it into the garage as it was modeled.
15 But I think it would be useful to incorporate that into the discussion. So I think
16 that's all I have for the big pictures from the inhalation perspective for now.

17 **DR. KENNETH PORTIER:** Dr. Davies.

18 **DR. HOLLY DAVIES:** Hi. My -- a lot of my comments
19 were about, kind of, inhalation and dermal together. As John said, consistent to
20 what we were talking about with occupational exposures earlier today. One
21 comment being, you know, dermal and inhalation estimates should be
22 aggregated to get a more accurate estimate of consumer's exposures. And
23 getting a better picture of the total exposure by looking at other exposures like
24 drinking water.

1 As also was mentioned earlier, I guess on yesterday, some
2 consumers have chronic exposures to PERC and EPA should estimate chronic
3 exposures for some consumers. And looking at section 2.4.2.5.1, new clothing
4 and textiles, it seems like EPA could model inhalation and dermal exposure for
5 those consumer products like they did for dry cleaning clothing. And just to --
6 also, just another general comment, as John said, generally seems reasonable and
7 reasonable assumptions around just looking at inhalation and dermal and not
8 estimating the ingestion.

9 Oh, and one more comment, on the Westat survey, we've
10 talked about this before in other reviews. Don't have any particular things to
11 point out with the Westat survey, but in general it would be nice for EPA to think
12 about doing a new survey to get more up to date information on product use.

13 **DR. KENNETH PORTIER:** Thank you, Dr. Davies.
14 Dr. Kaufman.

15 **DR. ALAN KAUFMAN:** Hi. Some of my comments are
16 going to echo what Dr. Davies said. And, you know, I think it was difficult for
17 me also to separate 4.7 from 4.8. Especially because I think that, you know, in
18 some use cases particularly dry cleaning, aggregation of exposure between
19 dermal and inhalation makes a great deal of sense and that was not done. But
20 other than that, you know, the model does seem reasonable. I do have concerns
21 about, you know, the data gaps, you know, and the assumptions that were made.

22 The -- let me pull this up here so I've got it in front of me.
23 The other thing is, when I look at, you know, consumer exposure I have a hard
24 time thinking of a consumer exposure which is not a low intensity use. In other

1 words, I think if you're a medium or high intensity user it's probably in an
2 occupational setting.

3 You know, you're either in an auto repair shop or a carpet
4 cleaning service or -- you know, how often does a consumer really need to clean
5 their brakes? I mean, I think that would be a very sporadic type of thing. So,
6 you know, that I have some concerns about. In other words, that, you know, we
7 may be overestimating the exposure for some of those users, you know, because
8 they, you know, those use cases may or may not really exist.

9 I think that's really about it. You know, some of these
10 comments -- I'll just save most of my comments for 4.8 since I'm going to lead
11 on that because -- but they will also apply here on 4.7. Thanks.

12 **DR. KENNETH PORTIER:** Okey-doke. Dr. Willhite.

13 **DR. CALVIN WILLHITE:** I will defer to Alan
14 Kaufman and his presentation. And he has comments from me on this section
15 regarding consumer products.

16 **DR. KENNETH PORTIER:** Okey-doke. Dr. Anderson.

17 **DR. HENRY ANDERSON:** Yeah. I don't have much to
18 add and -- or that would make too much of a difference. Seems to me compared
19 to the Westat, I mean, one issue would be so, for a given product who's likely to
20 be the user of that product? Kind of separating out by gender if it's a spray can
21 of paint or a stripper or whatever it's going to be then it might be either one.

22 I think that -- it is dealt with the detached garage versus
23 the attached garage. I think building stock is probably different from the

1 information that Westat had. So that's one thing just to think about and to
2 support why it might be worth doing another study.

3 And then the other is, just as a descriptor, the proportion
4 of homes who are likely to have small children or newborns in them because that
5 would then represent a special group of people. It may also be exposed to maybe
6 more sensitive. Especially if it's a product that's apt to be used by women
7 frequently they'll have a young child will be with them in the room or if they're
8 in a utility room or somewhere else if they're working. I'm not sure they would
9 exclude the child from being there while they're working.

10 And then the last one again is to detached or attached
11 garage, if you're working on an automobile and you're spraying or going to be
12 using rags then an issue would be how you dispose of rags now. They will,
13 because of the volatility, won't stay around that long but you have a longer
14 exposure period depending on what is done with rags or other materials that you
15 may use to use the -- a product or clean up -- use a product to clean up before it
16 completely evaporates.

17 **DR. KENNETH PORTIER:** Thank you. One of the
18 things -- I forget who said it, about thinking about who's using the product. In --
19 in some of the other reviews when we've talked about consumers that --
20 consumer exposures especially to volatile chemicals in the home we've worried
21 about the high-end hobbyist. Do we have the same kind of concerns with these
22 consumer COUs? Do any of you see the high-end hobbyist or something like
23 that? I was looking through these. I don't see very many products that -- with
24 the exception of maybe adhesives that a hobbyist might be using. Liquid

1 primers, sealants, I don't think those are the ones that hobbyist would be using.

2 But maybe metallic overglazes?

3 **DR. HENRY ANDERSON:** The only group I --

4 **DR. KENNETH PORTIER:** Anybody?

5 **DR. HENRY ANDERSON:** The only group I would
6 think of is you have automobile collectors that then go to shows who spend a
7 great deal of time cleaning their cars so they're really as pristine as possible. So
8 it could be rather than you don't use -- how often do you clean your brakes?

9 Well, they will clean their brakes every time before they go to a show.

10 Especially if the brake drums are exposed or cleaning the engine and things like
11 that. So there's a lot of -- they have to -- a set group of people may -- especially
12 certain time of the year be using it more than one would traditionally use it.

13 **DR. KENNETH PORTIER:** Anyone else comment?

14 Dr. Doucette.

15 **DR. WILLIAM DOUCETTE:** Ken, just to follow up on
16 that comment about consumer products, I got involved in a study that really
17 started out as a vapor intrusion study but ended out -- ended up as an indoor
18 source study. And this was around an air base here in Utah, and we kept finding
19 the same PCE adhesive giving background indoor air concentrations. And that
20 particular adhesive was -- at least according to the SDS sheet associated with it,
21 contained 85 to 95 percent PCE.

22 And the reason I bring this up is that actually, we were
23 able to measure concentrations of PCE in the indoor air that that was the source.
24 And it didn't matter, once it was opened it still emitted. So in other words if you

1 -- if you assume that it's only admitting during the use, that's not correct because
2 the seal is not perfect, and it continues to be a long-term emitter over time.

3 And the emissions, you know, obviously for a PCE
4 containing product, it's 85 to 95 percent PCE, will continue to be a source
5 indefinitely until that -- until all the PCE is volatilized from that tube. So there
6 are those sorts of things and the -- I don't have the paper in front of me and the
7 report that we published. But the -- but the levels of the PCE in the room where
8 that was used and or stored were near the action levels that the air force used at
9 that particular site. Just thought I'd throw that out there.

10 **DR. KENNETH PORTIER:** I think it would be nice if
11 you could find that report and add it to the -- add it to the discussion.

12 **DR. WILLIAM DOUCETTE:** Yes. I can provide a
13 reference and a report.

14 **DR. KENNETH PORTIER:** Yeah. Provide it to Dr.
15 Kissel.

16 **DR. WILLIAM DOUCETTE:** Okay. Thank you.

17 **DR. KENNETH PORTIER:** Any additional comments?
18 You throw out a net and you're never quite sure what you're going to get back in
19 these discussions. Okay. Why don't we move to Question 4.8? Dr. Kaufman.

20
21 **CHARGE QUESTION 4 (4.8)**
22

23 **DR. ALAN KAUFMAN:** Yes. It just -- not to, you now,
24 not to beat a dead horse but again, you know, I think, you know, consider -- you

1 have to consider the dermal and the inhalation together. And I think aggregate
2 exposure in some of these use cases probably makes more sense than not. And,
3 you know, I think, for instance I mentioned dry cleaning.

4 You know, I also, I think when you look at the high and
5 medium intensity, you know, users, I think for some of these use cases I, you
6 know, it didn't make a lot of sense to me that there would be other than a low
7 intensity user. At least at a consumer level. You know, certainly at a, you know,
8 at an occupational setting there might be but not at a consumer level.

9 There was concern -- one of the panel -- one of the team
10 members indicated that that -- the dermal exposure model was reasonable and --
11 but with the inhalation example, the exposure estimate seemed to be very high
12 and again they mentioned the medium and high intensity users. The assumptions
13 being made seemed reasonable, but I think there's a concern we may be
14 overestimating the exposures for some of those groups, you know, or we may be
15 propagating an error.

16 Let's see, and then, we have lots of comments here. It,
17 you know, it -- in addition to aggregating the dermal and inhalation exposure, I
18 think there's a potential exposure through drinking water. Some consumers
19 have, you know, therefore have that chronic exposure to PERC, which I think
20 was just mentioned when we were talking about the last one. We, you know, we
21 looked deeply at dermal exposure to dry cleaned articles and inhalation exposure
22 to dry cleaned articles. They seemed reasonable.

23 Dr. Davies mentioned new clothing textiles. That's
24 another one where there is some potential exposure. And, you know, there really

1 -- at least for some of the studies for other consumer used, like the Children's
2 Safe Product Act and some of the state reporting statutes, there doesn't seem to
3 be a lot. The few reports we did see appear to be either an error -- a drop down,
4 you know, somebody selecting out of a drop down box and they made a wrong
5 selection or they over reported just to make sure they were reporting even if they
6 didn't know something was there. Because it was popping up in places where it
7 didn't make any sense, like in a lipstick.

8 So the other comment, Dr. Willhite provided voluminous
9 comments here so I'm going to try and summarize rather than try to go through
10 them. The exposure data for the consumer piece, and I think Dr. Willhite's
11 mentioned some of this. There's California Air Resources Board(ARB) studies
12 from 1991. PCE Area Concentration for Residential Indoor Air, there's a
13 background level that needs to be taken into account.

14 Concurrent outdoor air samples. Contains some but there
15 was obviously a difference. Indoor air was considerably higher than the outside
16 air. Breathing zone PCE concentrations, you know, when they were collected
17 during the night were somewhat higher compared to outdoor nighttime PCE
18 concentrations. So I think the ARB results are something that certainly needs to
19 be taken into account here. I think that is it. Although, Dr. Willhite, you might
20 want to elaborate on some of the comments because I want to make sure we've
21 captured everything.

22 **DR. KENNETH PORTIER:** Dr. Kaufman, when you
23 said that some of the COUs expected to be low, do you have a list? Are you
24 going to be able to provide a suggestion that these are the ones that may be

1 overestimated and these are the ones in the collective experience of the panel
2 members who comment on this, which ones might be low, which ones might be
3 underestimates, which ones might be overestimates?

4 **DR. ALAN KAUFMAN:** We didn't get specifics, but we
5 can certainly do that in our written comments because there were some that. For
6 instance the one that stood out to me was, you know, cleaning your brakes. You
7 know, not -- a consumer is not likely to do that very often, you know, even
8 someone who works on their car on a regular basis. On the other hand, you
9 know, there may be some people who are exposed at the medium or high levels.
10 But that's -- again, that's -- I think that's going to be more likely in the
11 occupational setting. We can certainly put together a list of the ones that we, you
12 know, we would have some questions about and would like EPA to kind of go
13 back and double check.

14 **DR. KENNETH PORTIER:** Dr. Willhite, do you want
15 to follow up on this?

16 **DR. CALVIN WILLHITE:** Certainly, Mr. Chair. I
17 think one of the main concerns that I had is consumer use of small quantity
18 carpet cleaner and fabric cleaner. If you've got a spot of tar that's stuck on your
19 stairs, why, you can go over to Home Depot and get a product -- and I included
20 the safety data sheet as an example -- Renown carpet cleaner, there's another
21 example that I have in there that's -- one's a liquid and one's an aerosol.

22 Now, what will happen, assuming we use the U.S. EPA
23 cancer potency factors based on rodent data that are advocated currently, for
24 those individual small short duration uses, there is a finite cancer risk that can be

1 calculated based on quantity used, duration used and frequency used. If in fact
2 we don't have a conclusion about these products, even though it appears EPA is
3 loath to do that, I fear that what will happen is this will cause an open door, if
4 you will, for a bounty hunter and personal injury attorneys.

5 Unless there is a cancer risk estimate associated with
6 those, and if that conclusion is not de minimis, I anticipate that we will have
7 those problems. So I included those examples and instructions for use as well as
8 disclaimers by retailers et cetera. But I view that as a significant omission.
9 Thank you.

10 **DR. KENNETH PORTIER:** Calvin, I just wanted to
11 make sure you didn't misspeak. But you're speaking about an acute exposure
12 cancer risk here. Is that correct?

13 **DR. CALVIN WILLHITE:** Less than lifetime -- yes,
14 less than lifetime --

15 **DR. KENNETH PORTIER:** Okay. Yeah. I
16 understand. I just want to double check make sure I understood you correctly.

17 **DR. CALVIN WILLHITE:** Thank you, Mr. Chair.

18 **DR. KENNETH PORTIER:** Dr. Doucette, your hand's
19 up.

20 **DR. WILLIAM DOUCETTE:** Sorry. Forgot to put it
21 down after the last comment.

22 **DR. KENNETH PORTIER:** Okey-doke. Let's see,
23 where are we? Dr. Anderson.

1 **DR. HENRY ANDERSON:** Yeah. I don't have much
2 more to add. The only thing I saw here that has a standalone, I would agree that
3 overall risk is probably not going to get it into the significantly hazardous range
4 with the exception of perhaps the cancer issue. But what I would look at is, there
5 are so many of these products and will of these COUs that the aggregate
6 exposure that you add consumer -- I mean, a lot of the workers that I know or see
7 in clinic, they're taking their products that they're manufacturing home. So you
8 may well have more use of certain products by the people who are
9 manufacturing them because they are provided free by their company or
10 whatever. And therefore you have somewhat of an aggregate issue here where
11 you have both a worker and ONU exposure plus a consumer neighborhood type
12 exposure.

13 The likelihood of workers living in the neighborhood
14 where their factory is, is relatively high for a lot of people so they're more likely
15 to have neighborhood or consumer type exposures. So I think that's one thing to
16 try to think about. If EPA is going to move or is willing to move to looking at
17 aggregate exposures, you have many more for this particular compound to
18 consider than you do for many of the other compounds that we've dealt with.

19 **DR. KENNETH PORTIER:** Thank you. Dr. Kissel,
20 your hand's up.

21 **DR. JOHN KISSEL:** Yeah. So I have -- I have multiple
22 issues with the methodology here. And I will note that EPA told us yesterday
23 that they considered their consumer dermal dose estimates to inoperative because
24 they were using a method that they acknowledge is flawed. And so the numbers

1 that we're looking at are not the real numbers, which are to be provided at some
2 future date, which makes review kind of difficult. But there are additional
3 procedural issues here.

4 So this is a -- consumer dermal exposure is done doing a
5 permeability-based model with an experimental value from the Kine (phonetic)
6 1999. The Kine paper is from diluted aqueous solution and is, you know, fine
7 enough for that purpose but then it's repurpose -- and this is the error -- it was
8 repurposed for things that are basically neat solution, or neat compound or
9 something close.

10 The text -- pardon my confusion here, it's just it's just hard
11 to figure out what actually was done for a variety of reasons. In the DRE on
12 page 210 there's reference to P_DER2b which is the code name for a particular
13 EPA model that's in the CEM. And I've raised this issue before, is that the
14 numbering of those models has changed with version of CEM. So the text says
15 on page 210 that they're using P_DER2b, Table 2.64 on page 212 references
16 P_DER1b but no P_DER2b.

17 And if you go look at the CEM version 2.1 which I think
18 is the one that's referenced, there's no P_DER2b there or there or -- I'm sorry
19 there's no P_DER1b. Actually now my notes are scribbled here, and I can't
20 remember which. But the notation that's in the DRE isn't internally consistent
21 and it doesn't -- also doesn't match well with what's out there in the EPA
22 guidance documents.

23 There's two supplemental documents, one of which is
24 Supplement 20, which is the textual description and it doesn't mention -- there's

1 no mention of P_DER2b in that supplement even though the DRE says that that's
2 the model that's being used. And there's also in the supplement there's no clear
3 statement of what the model actually is so you're supposed to go to CEM to get
4 the model. It would be nice if it was actually just written down.

5 And then Supplement 19 is an Excel file which is labeled
6 The Results. The problem is that all the guts of that file are actually hidden
7 columns and I don't know if the problem is a PC/Mac incompatibility or if it's
8 because the sheets are protected, but I wasn't able to unhide the hidden columns
9 so I couldn't see what was done. I couldn't see the assumptions and basically, it's
10 just a table of results which is not at all satisfactory.

11 So the -- in some ways it doesn't matter too much because
12 EPA's going to change all those numbers anyway. But I would mention that
13 there are a bunch of pitfalls associated with changing the results. And the mere
14 fact that they're going to use an appropriate KP doesn't mean that they actually
15 will.

16 I just reviewed a paper that was citing directly a European
17 safety agency document that both were completely wrong and they were -- as an
18 example of how people can take the KP approach and really screw it up, they
19 were using the concentration of an agent in an acetone solution before it was
20 deposited on skin in in vitro cells. So that's a transitory concentration that goes
21 away and doesn't exist in the real world.

22 And using that concentration as driving forces is
23 scientifically absurd and I hope that as EPA changes their methods and thinks
24 harder about using KPs that they will be very careful how they do that. Because

1 there is -- there are documents in the peer reviewed literature which are
2 absolutely wrong and unambiguously stupid. So, you know, as you do the fix
3 you might want to ask somebody who actually knows how to do this kind of
4 work.

5 And that's -- I would add to -- that's my primary comment.
6 And I would add that although I think it's cited, at least tangentially in the
7 document, that the TEAMS data from the early '80s showed pretty clearly that
8 indoor Perchloroethylene data could be much higher than outdoor
9 Perchloroethylene measurements even in industrial locations. So that's not a -- an
10 odd phenomenon. That's something that people understand consumer product
11 use. There is background exposure to lots of VOCs and TEAMS showed that
12 very clearly. Okay. I'm done.

13 **DR. KENNETH PORTIER:** So John, something you
14 said, you know, a couple of times we've mentioned the neat and aqueous PERC.
15 But when I look at a lot of these consumer products, it almost looks like some of
16 them are in oils or oily bases like a paint or a coating. What's the impact of that
17 on dermal exposures and do any of these models address that kind of --

18 **DR. JOHN KISSEL:** Generally --

19 **DR. KENNETH PORTIER:** -- that kind of would it --
20 matrix I guess is the word. Right?

21 **DR. JOHN KISSEL:** Generally, the literature's
22 dominated by aqueous solutions because it's something people are familiar with
23 and they work with. The -- when you get into mixtures the chemistry gets a lot
24 more complicated. So ultimately, what you want to know is what's the thermal

1 dynamic activity of the compound in the solution. And that changes with the
2 vehicle.

3 So EPA's approach has been to just -- to take the density
4 of the compound, which would be the concentration of the pure compound and
5 multiply by a fraction, which is very crude and largely -- or oftentimes incorrect
6 because the relative activity depends upon what the matrix is. If the -- if a -- if
7 you had something -- so the aqueous solubility is ostensibly 200 parts per million
8 or so. So if you change from a 75 percent PCE water -- 25 percent water mix to
9 a 50 percent PCE water mix the thermodynamic activity shouldn't change
10 because you're still super saturated.

11 But that's assuming ideal solutions and lots of things are
12 not ideal solutions. So it gets really messy and really complicated when you're
13 dealing with mixtures that are not well defined mixtures. And at some point, you
14 know, you're probably better off looking for data and seeing whether it's -- it
15 makes sense, you know, empirical data. And just use empirical data instead of
16 trying to predict. If you're not willing to do pretty high-powered chemical
17 solution theory kind of calculations, which the vast majority of people who are
18 publishing are not willing to do.

19 **DR. KENNETH PORTIER:** Okay. I think I understood
20 that John. Thank you. Dr. Willhite, your hand's up. Calvin, your phone might
21 be muted.

22 **DR. CALVIN WILLHITE:** Not again. Now I'm back?

23 **DR. KENNETH PORTIER:** You're back.

1 **DR. CALVIN WILLHITE:** This is a comment for Dr.
2 Lash, and it regards the comments from Dr. Kissel, which are extraordinary. We
3 need to get Dr. Kissel on the Toxicology Applied Pharmacology editorial board.
4 But at the same time please never send any of my manuscripts to Dr. Kissel
5 because I don't know how I would respond to a reviewer's comment that says,
6 absolutely wrong and completely stupid. So therefore, that's my comment.
7 Thank you.

8 **DR. KENNETH PORTIER:** You mean you haven't
9 gotten those comments on some of your papers? I would dare say most of us
10 have seen comments like that.

11 **DR. CALVIN WILLHITE:** Only a few.

12 **UNIDENTIFIED MALE:** I was going to say, John
13 needs to learn to say what he means, huh?

14 **DR. KENNETH PORTIER:** Okay. Where are we?
15 Let's see. Dr. Bennett, did you want to add anything?

16 **DR. STEVEN BENNETT:** Sorry, not at this point.

17 **DR. KENNETH PORTIER:** And I -- I'm trying to
18 remember, Dr. Davies on this topic?

19 **DR. HOLLY DAVIES:** I don't have anything to add
20 right now.

21 **DR. KENNETH PORTIER:** Okay. I think I'll open it
22 up at this point. Does anyone else want to add discussion on these topics? I
23 have about 12 things that were mentioned under this particular topic, Dr.
24 Kaufman. So there's a lot that's gone on here.

1 **DR. ALAN KAUFMAN:** Absolutely.

2 **DR. KENNETH PORTIER:** At this point -- yeah. At
3 this point I'll open it up to maybe EPA for clarifying questions or comments.

4 **DR. STANLEY BARONE:** Is Dr. Lee on? Dr. Portier --

5 **DR. KENNETH PORTIER:** Dr. Lee looks to be -- Dr.
6 Lee looks to be connected to a computer with earphones and she's muted.

7 **DR. STANLEY BARONE:** Yeah. Maybe we should --

8 **DR. MARI LEE:** Hi.

9 **DR. STANLEY BARONE:** Go ahead.

10 **DR. MARI LEE:** I have a child in my lap at the
11 moment. I've been asked other people please to step in for me.

12 **DR. STANLEY BARONE:** Yeah. I was going to
13 suggest, can we come back at the end of the day for clarifications from Dr. Lee?

14 **DR. KENNETH PORTIER:** Certainly. Not a problem.
15 We'll move on to 4.9 and 4.10. Stan, are you going to read these in?

16 **DR. YVETTE SELBY-MOHAMADU:** Hi. Sorry, this
17 is Yvette SELBY-MOHAMADU and I can read the questions. So --

18 **DR. KENNETH PORTIER:** Sorry, Dr. Mohamadu, I
19 had forgotten you're the backup.

20

21 **CHARGE QUESTION 4 (4.9)**

22

23 **DR. YVETTE SELBY-MOHAMADU:** Oh, no

24 problem. No problem. So 4.9 is, please comment on whether there are dermal

1 models which would be appropriate to address evaporation during use and or the
2 amount of product absorbed into the skin during use when evaporation is not
3 hindered. What other additional information or modeling approaches, if any,
4 should be considered? And this is within section 2.4.2.

5 And then Question 4.10 is, please provide any other
6 suggestions or recommendations for additional approaches, dermal methods,
7 models, or other information which may guide EPA in developing and refining
8 the dermal exposure estimates. Also in section 2.4.2.

9 **DR. KENNETH PORTIER:** Lead on 4.9 is Dr. Davies.

10 **DR. HOLLY DAVIES:** Hi. I did not get any comments
11 from the associates on different dermal models which would be appropriate, but I
12 have not heard from Dr. Kissel yet. So I was hoping that he would have
13 something.

14 **DR. KENNETH PORTIER:** Well, let's just jump right
15 to Dr. Kissel then. Dr. Kissel.

16 **DR. JOHN KISSEL:** Yeah. I did have comments. So I
17 think what this question is referring to is that these consumer exposures mostly
18 would involve potentially evaporation as do the occupational exposures where
19 they've used the methodology.

20 So the obvious first answer is why not just use the
21 approach you're using? Some variation -- so you've got the Kasting Miller 2006
22 paper, the 2012 Frasch paper and the 2014 or '15 Frasch/Bunge paper which are
23 all variations on that theme. And that approach could be applied to consumer
24 uses as well as to occupational uses.

1 So there's always been this question of why are using one
2 approach for consumer and one for occupational? Why not use the same
3 approach for both? So that's the first option. The other options of -- at least for
4 this compound and a couple of the other VOCs there's a paper by Kezic and --
5 hello?

6 **DR. KENNETH PORTIER:** I think that was just some
7 cross talk. Go ahead, John.

8 **DR. JOHN KISSEL:** Okay. So second option is that for
9 this compound and some VOCs there's a paper from Kezic in 2001 where they
10 did short term exposures to human volunteers. And you could take results
11 directly from that as an indication of potential exposure.

12 And the third option is that the permeability coefficient
13 approach that EPA is using for consumer has a non-steady state version, so the
14 standard version is that you assume steady-state so the external driving force is
15 constant. But the mathematics for a declining external driving force has -- or a
16 finite dose kind of approach is out there also. Or if things that are so short term
17 that the steady state is never established, the mathematics is a little more
18 complicated. The dependents wind up being square root of time instead of time.
19 But that methodology exists and the EPA regs, the superfund dermal guidance,
20 has got the case worked out for aqueous solution and by analogy you could
21 extend it to non-aqueous solutions. So that's at least three options for dealing
22 with evaporation in the consumer models.

23 **DR. KENNETH PORTIER:** That sounds good. Dr.
24 Bennett.

1 **DR. STEVEN BENNETT:** All right. I go on two
2 screens. So I don't have much to add to John -- Dr. Kissel. I did have a
3 difficulty distinguishing between the intent of Question 4.9 and 4.10. That was
4 one of the pieces but I -- we'll deal with that in a minute. But I think that -- I
5 won't have -- nothing additional to add.

6 **DR. KENNETH PORTIER:** Dr. Kaufman.

7 **DR. ALAN KAUFMAN:** Hi. Nothing to add at this
8 point. Thank you.

9 **DR. KENNETH PORTIER:** Dr. Willhite.

10 **DR. CALVIN WILLHITE:** Nothing to add.

11 **DR. KENNETH PORTIER:** Dr. Anderson.

12 **DR. HENRY ANDERSON:** Just for my edification
13 since I'm not familiar with these. When we're talking about evaporation, is that
14 evaporation in the sense that it reduces exposure through the skin or are we
15 including inhalation of the amount of product that's evaporated? So really this
16 becomes an aggregate exposure of skin plus inhalation or are we just looking at
17 evaporation and therefore it doesn't go through the skin directly into the body?
18 And then it would seem to me that evaporation rate would also depend on the
19 temperature of the environment where the product is being used.

20 **DR. JOHN KISSEL:** So the context here is the dermal
21 dosing and evaporation competes with absorption and reduces it.

22 **DR. HENRY ANDERSON:** Okay.

23 **DR. JOHN KISSEL:** So the inhalation is a separate
24 consideration.

1 **DR. HENRY ANDERSON:** Okay. Thank you. That's
2 what I thought, but I thought I would ask.

3 **DR. KENNETH PORTIER:** But that declining dose
4 that comes off the skin becomes a component of inhalation potentially if they
5 wanted to do that in an aggregate setting. Right? I mean, these models probably
6 give you an idea what is lost from the skin.

7 **DR. HENRY ANDERSON:** Right.

8 **DR. KENNETH PORTIER:** So, Dr. Davies. Oh, John,
9 go ahead.

10 **DR. JOHN KISSEL:** Yeah. The calculation that you do
11 -- that was done for the occupational is the fraction of doses absorbed and the
12 fraction that's evaporated. So both of those numbers are generated when you do
13 the calculation. I actually thought of something else here because of Henry's
14 question. We haven't talked about -- because there's this bifurcation between
15 consumers and workers, and this is kind of another spin on the -- on the
16 occupational bystander, is that we haven't talked about the take home pathway.

17 And there's implicit or explicit in this analysis. There is
18 you bring home dry cleaning and it de-gasses and that contaminates your house.
19 But spurred by Henry's question it dawned on me that it's also true that if
20 somebody works in a dry cleaning establishment all day, when they come home,
21 they de-gas also. They exhale so that would be another indoor source. If you
22 cohabit with an employee who is exposed to VOCs that person is a -- is an
23 indoor source for you.

1 **DR. KENNETH PORTIER:** As would likely be their
2 clothes, right?

3 **DR. JOHN KISSEL:** Yes. Both.

4 **DR. KENNETH PORTIER:** Yeah. That's a good point.
5 Dr. Davies.

6 **DR. HOLLY DAVIES:** Hi. I have two things. One is
7 just to add onto what Dr. Kissel just said. It's kind of like expanding the ONUs
8 to include co-located businesses and such with dry cleaners and any other
9 facilities. Because I would think that the take home pathway is just -- it reminds
10 me more of an extension of the occupational exposure rather than being a
11 consumer exposure if we want to kind of work up recommendations on that.

12 The other question I had was that Dr. Kissel mentioned
13 three different approaches. And I'm wondering which one he would recommend.
14 What is the best approach or are there pros and cons to each of them?

15 **DR. JOHN KISSEL:** So, John Kissel again. So I would
16 start with the approach that EPA is using for occupational, which is based
17 originally on the 2006 Kasting Miller document and then I would check it against
18 the Kezic empirical results and other empirical results. So my answer is always
19 going to turn out to be both. You know, any time you have a model, if you can
20 find any biomonitoring data to check it against, you want to do that.

21 **DR. KENNETH PORTIER:** Holly, was that all of your
22 comments?

23 **DR. HOLLY DAVIES:** Yes.

24 **DR. KENNETH PORTIER:** Dr. Anderson.

1 **DR. HENRY ANDERSON:** Yeah. I just wanted to add
2 an interesting parenthetical. I once had an occupational case where the wife of a
3 worker who was exposed to benzene consistently complained about her
4 husband's odor sleeping in bed with her at night. And actually doing some
5 measurements and finding that eight hours or night hours where he was exhaling
6 onto his wife and she was breathing it. It actually produced a pretty good dose
7 and she developed leukemia.

8 So that was really the questions, could a bystander
9 approach like that being so close breathing somebody's exhaled breath cause a
10 problem, and it certainly can. Totally different just it's late in the afternoon.

11 **DR. KENNETH PORTIER:** Wow. I wouldn't have
12 thought of that, Henry. That's interesting. That was a smart lawyer.

13 **DR. HENRY ANDERSON:** Yeah. You got to face
14 away though when you're sleeping. Look the other direction. You got to have
15 an agent that smells.

16 **DR. JOHN KISSEL:** Or you've got to keep the ceiling
17 fan on. Yeah.

18 **DR. KENNETH PORTIER:** Any additional comments
19 on 4.9? Dr. Bennett let's move onto 4.10.

20
21 **CHARGE QUESTION 4 (4.10)**

22
23 **DR. STEVEN BENNETT:** All right. Thank you. Yeah.
24 This one was challenging. I didn't get much feedback onto it because it fell out

1 of most of the other member's expertise and it's not really that good in my
2 perspective. I think that the approach that the Agency took was looking at the
3 different uses of where there would be likely, or potentially for dermal
4 exposures, I think that was focusing in on this particular condition of use was the
5 right approach.

6 You know, there's certainly, the brake cleaning, and the
7 spent rags and some the other methods where that's more likely where you'd
8 have the occluded uses which could lead to the dermal exposures was the right
9 approach. It's certainly going to put some degree of uncertainty into those
10 particular conditions of use.

11 But I think that's probably the best approach they can take
12 without a little bit better understanding of the data. You know, without -- with
13 the lack of data. You know, that's probably as far to go on. Hopefully, you
14 know, John -- and I think some the approaches John mentioned might be
15 applicable in here in the -- with respect to the previous one but, you know, I don't
16 many suggestions beyond there.

17 **DR. KENNETH PORTIER:** Okay. Well, I'm going to
18 continue down the list see if anyone else had thought of something since you
19 asked them. Dr. Barton.

20 **DR. CHARLES BARTON:** I have -- can you hear me?

21 **DR. KENNETH PORTIER:** Yeah.

22 **DR. CHARLES BARTON:** Okay. I have nothing more
23 to add. Thank you.

24 **DR. KENNETH PORTIER:** Okey-doke. Dr. Davies.

1 **DR. HOLLY DAVIES:** I don't have anything to add at
2 this time.

3 **DR. KENNETH PORTIER:** Dr. Kissel.

4 **DR. JOHN KISSEL:** So I think my comments of 4.9
5 apply also to 4.10. The one thing I would mention in addition, and Calvin
6 Willhite already brought this up, but there is in the public comment from a
7 representative of the Halogenated Solvents Industry Association(HSIA)
8 something that sounds like an offer to do experimental work, which might be a
9 win-win. I, you know, we've run into this problem, EPA doesn't have a budget
10 to research but if industry associations were willing to foot the bill you would
11 need supervision by somebody not being paid by the industry but that's, you
12 know, that might be worth pursuing on EPA's part.

13 **DR. KENNETH PORTIER:** Good point. Dr. Willhite.

14 **DR. CALVIN WILLHITE:** I take back --

15 **DR. KENNETH PORTIER:** Calvin, your phone might
16 be muted. Yeah. There you go.

17 **DR. CALVIN WILLHITE:** Not again. Okay.

18 **DR. KENNETH PORTIER:** Now you're back. I think
19 you muted it. You were here.

20 **DR. CALVIN WILLHITE:** Now I'm back.

21 **DR. KENNETH PORTIER:** There you go.

22 **DR. CALVIN WILLHITE:** Okay. Thank you, sir.

23 Regarding the last comment about possible industry participation, in that
24 comment from Andrew Maier Cardno ChemRisk it says quote, "recommending

1 EPA investigate whether empirical study of dermal exposure to PCE can be
2 conducted." Recommending that EPA go do it.

3 Second one was, "recommending EPA conduct or solicit
4 surveys characterizing at facilities to determine task duration, contact volume,
5 contact frequencies et cetera." It sounded like from that letter, and it would be
6 worthwhile to get clarification from the public commenter, whether they
7 recommend that EPA go do it or can this be a cooperative joint effort to try to get
8 some of these exposure data to more accurately characterize Perchloroethylene.
9 Thank you.

10 **DR. KENNETH PORTIER:** You know, Calvin, this is
11 one of the reasons I sometimes think overestimation is not bad because it's in
12 industry's best interest then to get the right estimate put in place to -- if their goal
13 is to reduce risk. There's always a cost to getting data but sometimes, I guess in a
14 regulatory setting you have to set a cost for not getting data as well. Dr.
15 Anderson.

16 **DR. HENRY ANDERSON:** Yeah. My -- I don't recall
17 all of this but it seems -- I seem to recall that the dermal modeling was done
18 assuming no use of gloves. And what I -- if that's the case, what I'm wondering
19 about if inappropriate gloves by the consumer that just grabs a pair of cloth
20 gloves to put on so you end up with occluded exposure to the skin, is that
21 considered in there? Because that would add to the dermal exposure as opposed
22 to mostly, we've been considering the use of gloves as protectant.

23 **DR. KENNETH PORTIER:** That's a point we've made
24 before on the other chemicals.

1 **DR. HENRY ANDERSON:** That may be why --

2 **DR. KENNETH PORTIER:** Any additional comment?

3 Yeah. Any additional comments from the panel --

4 **DR. JOHN KISSEL:** Uh --

5 **DR. KENNETH PORTIER:** -- on any --

6 **DR. JOHN KISSEL:** -- this is John Kissel.

7 **DR. KENNETH PORTIER:** Yeah, John,

8 **DR. JOHN KISSEL:** I just -- actually just dawned on me

9 that I injected occupational exposure into this 4.10 which is about consumer

10 dermal and so my comment which then generated further comment was maybe a

11 little off point for this particular question. So apologies for that.

12 **DR. KENNETH PORTIER:** I was trying to figure out
13 which comment you made that might be inappropriate.

14 **DR. JOHN KISSEL:** So the HSIA offered to do
15 sampling. That's occupational.

16 **DR. KENNETH PORTIER:** Oh. Okay. You're right.

17 **DR. JOHN KISSEL:** There's --

18 **DR. KENNETH PORTIER:** You're right.

19 **DR. JOHN KISSEL:** No one has offered to do sampling
20 in consumer residences so far as I know.

21 **DR. KENNETH PORTIER:** Yeah. Good point. Any
22 additional comments? I'm not seeing any hands raised at this point. We're at the
23 end of Question 4 and at the end of the task that we wanted to do today. I'll turn

1 to EPA and ask if there are any comments or clarifying questions on the material,
2 we've covered this afternoon. Dr. Barone or Dr. Lee?

3 **DR. MARI LEE:** I can just say that there are a typo and
4 I'm sorry for that in Table 6 -- 264 that it should be 2b, P_DERM2b not 1b.
5 That's the permeability model in CEM.

6 **DR. KENNETH PORTIER:** Okay. Dr. Barone, any --

7 **DR. MARI LEE:** Can I also just state it's --

8 **DR. KENNETH PORTIER:** -- follow up?

9 **DR. MARI LEE:** -- unfortunately given -- I know this is
10 unusual working circumstances. It's been very difficult for me to listen to this
11 part of the presentations. But I am very happy if anyone could send me specific
12 questions, they want to send to Tamue to have them emailed to me, I will do my
13 best to respond today and tomorrow. So I'm sorry if I'm not able to give
14 responses on time but I'd be very happy to respond to any specific questions you
15 email. It's just been a -- an unusual working circumstance.

16 **DR. KENNETH PORTIER:** Not a problem, Dr. Lee.

17 **DR. MARI LEE:** Thank you.

18 **DR. KENNETH PORTIER:** Tomorrow morning they'll
19 be -- if the EPA team comes up with any questions or clarifying -- to clarify what
20 we've discussed there's a -- there will be an opportunity first thing tomorrow
21 morning to kind revisit some of this. At this point --

22 **DR. STANLEY BARONE:** Thank you, Dr. Portier.

23 **DR. KENNETH PORTIER:** Yeah. At this point, we're
24 kind of at the end of the material we wanted to cover today. Tomorrow we're

1 going to start in on the discussion of human health hazard and I really don't want
2 to kind of break that discussion because I think it's going to be a full day and an
3 exciting day tomorrow. But to kind of break the discussion would kind of maybe
4 break the flow of the information.

5 So my desire at this point I think is to adjourn the meeting.
6 But before the panelists and before the committee signs off I want to have a short
7 administrative meeting -- virtual meeting here in Webex once we officially close
8 the public meeting. The Webex administrator will move us all into a private
9 space so we can talk about some logistic issues. Since we're halfway through the
10 meeting this is a good time to talk about how we will organize report writing.

11 So at this point I want to adjourn the meeting and I'm
12 going to turn it over to Tamue Gibson, the DFO for any final remarks. Tamue.

13 **MS. TAMUE GIBSON:** Okay. Thank you. Thank you
14 again. This is Tamue. I am your DFO. I want to thank the SACC peer
15 reviewers and the public for listening online. Thank you all. This does conclude
16 our peer review activities for the agenda today and we will reconvene tomorrow
17 morning for day three at 10 a.m. eastern. So today's session is now adjourned
18 and thank you all. Have a great evening.

19 **DR. KENNETH PORTIER:** And panelists hold on for
20 the transfer so we can have this discussion. **[MEETING ADJOURNED FOR**
21 **THE DAY]**
22

OPENING OF MEETING - DAY 3

MS. SARA WILSON: Good morning and welcome to Day 3 of the meeting of the U.S. EPA Peer Review of the Draft Risk Evaluation for Perchloroethylene. Battelle is an EPA contractor providing meeting support for this series.

This event is being recorded. Please be aware that the host may use Webex Chat to share announcements with all attendees, but attendees will not be able to respond to the chat. I will now introduce Tamue Gibson, the designated federal official.

MS. TAMUE GIBSON: Hi. Thank you, and good morning. It is my pleasure again to open the third day of the four-day meeting for the Science Advisory Committee on Chemicals Peer Review of EPA's Draft Risk Evaluation for Perchloroethylene.

So Tuesday and yesterday's Webex host meetings went very well. I do want to note that this is a virtual meeting, meaning that the audio is provided by telephone or over your computer and that graphics are presented by the Webex online internet platform.

If, for any reason, the Webex platform or audio transmission encounters any technical difficulties, you will find additional information to refer to our TSCA website. It's epa.gov/tsca -- T-S-C-A -- -peer-review. Overall, the sessions are going very well. So, I would like to thank everyone for their contributions as well as the participation by the public. And at this point, I turn the meeting over to our chair, Dr. Portier.

1 **DR. KENNETH PORTIER:** Thank you, Tamue. This
2 is Day 3 of the U.S. EPA Peer Review of the Draft Risk Evaluation for
3 Perchloroethylene. This is the Science Advisory Committee on chemicals. This
4 is a FACA meeting. I'm pleased that we have public listening in and we have a
5 full committee here.

6 And as we've done every day, I'm going to start the
7 meeting by doing the roll call just to establish who's on the call. Dr. Anderson?

8 **DR. HENRY ANDERSON:** I'm here.

9 **DR. KENNETH PORTIER:** Okay. Dr. Barton?

10 **DR. CHARLES BARTON:** I'm here.

11 **DR. KENNETH PORTIER:** Thank you. Dr. Bennett?

12 **DR. STEVEN BENNETT:** I am here.

13 **DR. KENNETH PORTIER:** Dr. Blystone?

14 **DR. SHERI BLYSTONE:** Good morning.

15 **DR. KENNETH PORTIER:** Dr. Bruckner?

16 **DR. JAMES BRUCKNER:** Good morning.

17 **DR. KENNETH PORTIER:** Dr. Cory-Slechta? Dr.
18 Cory-Slechta, you're muted in Webex.

19 **DR. DEBORAH CORY-SLECHTA:** I'm here. Sorry.

20 **DR. KENNETH PORTIER:** Now you got it. Dr.
21 Davies?

22 **DR. HOLLY DAVIES:** Here.

23 **DR. KENNETH PORTIER:** Dr. Doucette?

24 **DR. WILLIAM DOUCETTE:** Present.

1 **DR. KENNETH PORTIER:** Dr. Gilbert?

2 **DR. KATHLEEN GILBERT:** I'm here.

3 **DR. KENNETH PORTIER:** Dr. Johnson?

4 **DR. MARK JOHNSON:** I'm here.

5 **DR. KENNETH PORTIER:** Dr. Kaufman?

6 **DR. ALAN KAUFMAN:** I am here.

7 **DR. KENNETH PORTIER:** Dr. Kissel?

8 **DR. JOHN KISSEL:** Here.

9 **DR. KENNETH PORTIER:** Dr. Rowlands?

10 **DR. CRAIG ROWLANDS:** I'm here. Good morning.

11 **DR. KENNETH PORTIER:** Good morning. Ruthann

12 Rudel? I don't see MS. Rudel yet this morning. Dr. Schlenk?

13 **DR. DANIEL SCHLENK:** Here.

14 **DR. KENNETH PORTIER:** Dr. Apte?

15 **DR. UDAYAN APTE:** Here.

16 **DR. KENNETH PORTIER:** Dr. Cobb?

17 **DR. GEORGE COBB:** I'm here.

18 **DR. KENNETH PORTIER:** Dr. Daniels?

19 **DR. MICHAEL DANIELS:** Here.

20 **DR. KENNETH PORTIER:** Dr. Grant?

21 **DR. STEPHEN GRANT:** Here.

22 **DR. KENNETH PORTIER:** Dr. Hossain? Dr. Hossain,

23 I'm not hearing you. Your phone may be muted. Dr. Lash?

24 **DR. LAWRENCE LASH:** Good morning. I'm here.

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DR. KENNETH PORTIER: Dr. Lin?

DR. ZHOUMENG LIN: Good morning. I'm here.

DR. KENNETH PORTIER: Let's see. Dr. Meliker?

I'm not sure if he's here this morning. Yeah, he should be here. Dr. Meliker?
Dr. Meliker is not on. Dr. Roby?

DR. KATHERINE ROBY: Good morning. Here.

DR. KENNETH PORTIER: Dr. Vorhees?

DR. CHARLES VORHEES: I'm here.

DR. KENNETH PORTIER: Dr. Willhite?

DR. CALVIN WILLHITE: Here.

DR. KENNETH PORTIER: Dr. Pennell?

DR. MICHAEL PENNELL: Here.

DR. KENNETH PORTIER: Thank you. Let me check
to see if Ruthann's on yet. Ruthann? I don't hear you.

MS. RUTHANN RUDEL: Yep, I'm here. Can you hear
me now?

DR. KENNETH PORTIER: There you go. Okay. Yes,
I can hear you. Thank you.

MS. RUTHANN RUDEL: Okay. Thank you.

DR. KENNETH PORTIER: Dr. Hossain? You're
muted in Webex, Dr. Hossain. There we go.

MS. TAMUE GIBSON: Dr. Portier?

DR. KENNETH PORTIER: I still don't hear you.
Yeah?

1 **MS. TAMUE GIBSON:** Dr. Meliker will be on at 1:00
2 p.m. today.

3 **DR. KENNETH PORTIER:** Okay. Okay, at 1:00.
4 Thank you. Dr. Hossain, I can see you're here but we can't hear you. Your
5 phone may be muted. Okay. Well, let's move forward.

6 **DR. MUHAMMAD HOSSAIN:** I'm here.

7 **DR. KENNETH PORTIER:** Ah, there he is. Good.
8 That's good. Okay. First order of business is we need follow-up. One minute
9 please.

10 **MS. TAMUE GIBSON:** Dr. Portier, it appears that your
11 line --

12 **DR. KENNETH PORTIER:** Yeah, I'm here. I just had
13 to step offline for a minute.

14 **MS. TAMUE GIBSON:** Oh, sorry. Okay.

15

16 **FOLLOW UP FROM THE PREVIOUS DAY**

17

18 **DR. KENNETH PORTIER:** I'm sorry. Okay. Ready
19 to go. Ready to go. Yes. Follow-up from yesterday -- are there any additional
20 comments on the material that we covered yesterday? All related to Question 4
21 on Occupational and Consumer Exposures.

22 Does EPA wish to ask clarifying questions or comment on
23 yesterday's discussion? We kind of left it open just in case EPA wanted to come
24 back. Dr. Lee or Dr. Barone? Let's see. Is Dr. Lee on?

1 **DR. YVETTE SELBY-MOHAMADU:** Sorry about
2 that. I was on mute. This is Yvette Selby-Mohamadu.

3 **DR. KENNETH PORTIER:** Yeah.

4 **DR. YVETTE SELBY-MOHAMADU:** And we did not
5 have any follow-up questions from yesterday.

6 **DR. KENNETH PORTIER:** Okay. Good.

7 **DR. YVETTE SELBY-MOHAMADU:** Thank you.

8 **DR. KENNETH PORTIER:** And Dr. Mohamadu, I
9 don't see Dr. Lee on yet this morning. So, I'm assuming you're going to be
10 reading questions for today.

11 **DR. YVETTE SELBY-MOHAMADU:** Yes. I'll be
12 reading the questions. They're fixing her system to get her on, but I'll start off
13 with the questions today.

14 **DR. KENNETH PORTIER:** Thank you. Well, I think
15 we're ready to move on to the questions on human health which is the topic of
16 today's conversation almost all day. Hopefully we'll get to some risk
17 characterization later today, but we've scrolled up Question 5 on Human Health
18 Hazard. Would you please read in Question 5.1?

19

20

21 **CHARGE QUESTION 5: HUMAN HEALTH HAZARD**

22

23 **DR. YVETTE SELBY-MOHAMADU:** Yes. Question
24 5, Human Health Hazard -- EPA used PODs and cancer slope factors -- i.e.,

1 human equivalent concentration, inhalation unit risk, and dermal slope factor --
2 for evaluating the non-cancer and cancer risks respectively, from chronic
3 exposures to Perchloroethylene. PODs were derived from both animal and
4 human studies.

5 Question 5.1: Have the most scientifically robust critical
6 health effects and corresponding PODs been identified for PCE? Are there
7 additional data regarding other health effects for PCE that EPA needs to
8 consider? If data gaps exist in the PCE database, how could the uncertainty
9 about sensitive health effects and critical windows of exposure be better
10 accounted for in the hazard characterization? And this is all in Section 3.2.

11 **DR. KENNETH PORTIER:** Thank you. We have a
12 long list of associates that Dr. Gilbert, the lead, has been drawing on. Dr.
13 Gilbert, do you want to lead off the discussion?

14
15 **CHARGE QUESTION 5 (5.1)**
16

17 **DR. KATHLEEN GILBERT:** Thank you. So I guess I
18 have received lots of comments from the associates. Question 5.1 is, I think,
19 supposed to consider both cancer and non-cancer health hazards. And I was
20 hoping that we could move the cancer hazard identification to Question 5.5,
21 which I'm also lead on, that is designed to look at cancer MOA?

22 That way, we can separate all the comments into non-
23 cancer hazard identification in Question 5.1 and cancer identification in 5.5. Is
24 that okay with you, Dr. Portier?

1 **DR. KENNETH PORTIER:** Yeah. I think that that
2 makes a lot of sense. I know the committee's had some conversation back and
3 forth on that via email, and I think that's a reasonable way to respond. So, 5.1
4 will focus on non-cancer. And which one is it? 5.5?

5 **DR. KATHLEEN GILBERT:** Um-hm.

6 **DR. KENNETH PORTIER:** Or 5.3?

7 **DR. KATHLEEN GILBERT:** 5.5.

8 **DR. KENNETH PORTIER:** 5.5, we'll then -- yeah. So,
9 after lunch, we'll focus on the cancer hazard. So, why don't you proceed with
10 the non-cancer discussion?

11 **DR. KATHLEEN GILBERT:** Okay. So I have tried to
12 compile and summarize the many comments and have tried to generate
13 recommendations from the comments. Many of the more minor editorial
14 comments, like requests for clarification of a term or suggestions for better
15 wording, will be confined to the written comments. So I will leave it up to the
16 discussants to tell me whether I misinterpreted or inadvertently admitted their
17 comments and to tell me whether the recommendations derived from those
18 comments are correct and sufficient.

19 And if Dr. Portier agrees, I would like to pause after the
20 description of each health hazard and invite comments. There's so much to
21 cover that I'm afraid if we waited until the end, we would have kind of a jumbled
22 discussion.

23 **DR. KENNETH PORTIER:** That sounds reasonable,
24 Kathleen. Let's just go ahead and do that.

1 **DR. KATHLEEN GILBERT:** Okay. Thank you.

2 Starting off with the non-cancer hazard identification, we're going to start with
3 some general concerns the discussants had regarding systematic review and
4 material presentation in the Draft Risk Evaluation.

5 Most of the sections that describe the non-cancer hazards
6 were relatively concise and well organized and summarized the findings in a way
7 that made it easy to extract the necessary information. There were a couple of
8 exceptions, but we'll talk about those later.

9 However, one fairly common problem in that human
10 hazard identification section was data referencing, and the heavy and sometimes
11 inappropriate use of what are essentially review articles. As an example, on
12 Page 261, the agency states there is sufficient evidence from controlled human
13 exposure studies that acute duration inhalation exposure to PCE induces
14 symptoms of CNS depression and prolonged visual potency latencies.

15 They reference the ATSDR Tox Profile, the U.S. EPA
16 IRIS assessment and then two individual studies, one which was published in
17 1990 and one in 1977. And I didn't really know what to take from that. If you
18 don't list the individual studies, it's hard to get a sense of the weight of the
19 public published evidence. And when you have two individual studies, it wasn't
20 clear. Were those studies somehow omitted from those other reviews? Or were
21 they, in fact, the studies that were discussed in those reviews?

22 It would've been much more helpful if they had said there
23 were -- if you don't want to put the individual papers in there -- which I
24 understand, if you have a lot of papers, that's not practical. But at least say there

1 were at least a dozen articles that discuss blah, blah, blah. Because the way this
2 is written, it's really hard for me to know what the actual evidence is.

3 And then the other thing that they did which I found really
4 irritating is there were numerous instances when the Draft Risk Evaluation was
5 discussing what was clearly an individual study, but the only reference is the
6 review article. That means, if I wanted to find out what was in that article, I had
7 to go to the EPA IRIS assessment, find out where the section is that I was
8 interested in, go there, and sort of wade through the data and hope that I could
9 figure out what paper the DRE was referring to.

10 So I think that's something that really needs to be fixed.
11 At least two discussants also noted that the agency heavily relied upon studies
12 considered in previous IRIS and ATSDR assessments and reviewed several
13 newer studies published after these assessments.

14 While the newer epidemiological studies were subjected to
15 a systematic review of relevance and quality in accordance with the TSCA
16 systematic review principles, none of the previous IRIS and ATSDR
17 epidemiological studies were evaluated under the TSCA systematic review
18 principles and guidance. Therefore, by assessing the quality and relevance of
19 only new studies but not all the studies considered in the risk evaluation, a
20 significant source of bias can be introduced that prevents an objective weight of
21 evidence conclusion to be reached.

22 So, for this section, in terms of recommendations, the
23 agency should evaluate the quality and relevance of key studies in accordance
24 with the TSCA systematic review principles that the agency relies on for

1 understanding other relevant epidemiological evidence considered in its weight
2 of evidence. The study referencing needs to be overhauled.

3 One member provided a recommendation for data
4 evaluation that we had not discussed much, if at all. They noted that the
5 agency's evaluation of the health effects for PCE is mainly focused on animal
6 and human studies with some in vitro studies related to immunogenicity.
7 However, EPA should also consider high-throughput in vitro assays from the
8 ToxCast, Tox21 database.

9 Currently, there are 235 assay results for PCE of which 2
10 were positive and 23 assays were negative. At this stage, it may not be possible
11 to derive PODs from these high-throughput in vitro assays, but the agency
12 should at least discuss these studies and consider the mechanistic insights from
13 these studies. This is important from a future perspective as multiple agencies
14 have recommended the use of high-throughput in vitro assays coupled with in
15 silico models for next generation risk assessment. EPA also plans to phase out
16 animal toxicity testing by 2035.

17 So that's what I had for the systematic review and data
18 presentation for this section. I didn't know if anybody wanted to chime in at this
19 point.

20 **DR. KENNETH PORTIER:** I won't call all of the
21 associates. Anyone who wants to comment on that, please just go ahead and
22 chime in, or raise your hand and I'll call you. Dr. Lin?

23 **DR. ZHOUMENG LIN:** Hello, everyone. I just want to
24 have one clarity basically about the in vitro ToxCast, Tox21 database. Currently,

1 there were was 235 assay results in this database on PCE. There were 2 assays
2 that report positive results, and there were 233 assays that are negative. I just
3 want to clarify the number. Dr. Gilbert has made a very nice summary report of
4 endpoints. Thank you.

5 **DR. KENNETH PORTIER:** Thank you.

6 **DR. DEBORAH CORY-SLECHTA:** Hi. I didn't know
7 how to raise my hand, Dr. Portier. This is Dr. Cory-Slechta. Can I just comment
8 on that as well, this issue of using the ToxCast data?

9 **DR. KENNETH PORTIER:** Sure.

10 **DR. DEBORAH CORY-SLECHTA:** Personally, I think
11 that anything that's used from there would have to be validated first. So, if you
12 can show me an assay that's actually validated, I would say that would be fine in
13 terms of maybe guiding us to mechanisms. But in the absence of that, it's hard
14 to know what the outcomes mean. Thanks.

15 **DR. KENNETH PORTIER:** Dr. Vorhees?

16 **DR. CHARLES VORHEES:** Yes. I wanted to comment
17 on the EPA's description or summaries of some of the neurotox studies that they
18 cite because I found it rather confusing in a number of places. For example, they
19 cite a study by Lucas comparing 50 dry cleaning workers exposed to PCE to 95
20 controls. And they looked for things like CNS depression, dizziness, sleepiness,
21 nausea, headache, GI symptoms. Well, the study's completely negative. They
22 found no association. So, I'm not clear why this study is even cited. And having
23 it be cited and the results described, it seemed just distracting to me.

1 They cite a study by Bove. It's a big study looking for
2 carcinogenicity primarily, comparing 150 thousand marines and seamen who are
3 stationed at Camp LeJeune versus another 150 thousand who, comparison group,
4 stationed at Camp Pendleton. It turned out that the Camp LeJeune people,
5 between 1975 and 1985, were exposed to contaminated drinking water that
6 contained PCE but also contained TCE, vinyl chloride, and benzene. So, it's a
7 complicated exposure, although most of the exposure was to PCE. But then they
8 cite this study --

9 **DR. KATHLEEN GILBERT:** Can I just jump in?

10 Sorry. I was going to hold all that stuff until we got to the neurotox.

11 **DR. CHARLES VORHEES:** Oh, you are? Okay.

12 **DR. KATHLEEN GILBERT:** Yeah. No, I haven't
13 ignored that part or anything. I just was going to include that when we talked
14 about the neurotox. This is sort of just general presentation and issues that you
15 might have. Is that okay?

16 **DR. CHARLES VORHEES:** Okay. Okay. Yeah, that's
17 okay. I'll wait.

18 **DR. KENNETH PORTIER:** Dr. Grant, anything on the
19 general stuff?

20 **DR. STEPHEN GRANT:** Yeah. I'm speaking from the
21 carcinogenicity point of view, but it is something that will come up. I felt that
22 there was indiscriminate citation of work, and I just put in a note that basically
23 said studies that had negative results, while interesting, are much more important
24 when you're looking at an endpoint that has previously been reported as positive.

1 Then you can actually say, well, why did this not validate?
2 But we don't expect PCE to have every toxic endpoint in the world and listing all
3 the ones that it doesn't show is a footnote rather than something that this
4 committee has to consider.

5 **DR. KENNETH PORTIER:** Back to you, Dr. Gilbert.

6 **DR. KATHLEEN GILBERT:** Yeah. That's an issue
7 that's been raised a couple of times. So, we'll probably end up talking about that
8 some more too. Okay. So moving on to the specific health hazards, including
9 neurotox where we'll hear some more from Dr. Vorhees, in terms of acute
10 toxicity, neurotox was selected as the main human health hazard.

11 There is sufficient human and animal evidence that
12 exposure to PCE for under 24 hours induces symptoms of CNS depression and
13 reduced amplitude of visual evoked potentials. And there is actually little
14 evidence of other types of acute toxicity. To derive a POD for acute
15 neurotoxicity, the agency used a medium-quality paper -- Altmann from 1990 --
16 in which human male volunteers inhaled 50 parts per million PCE, or 10 parts
17 per million PCE as a control group, for four hours every day for four days. The
18 results were compared to Day 0.

19 Alterations and visually evoked potentials, VEP, were
20 noticed after Day 1 of exposure and were maintained for the duration of the four-
21 day experiment. VEP tests the function of the visual pathway from the retina to
22 the occipital cortex. The section on neurotox for the acute toxicity endpoint, and
23 the selection of the study used to calculate the POD, seemed appropriate. I think

1 one of the members -- I think Dr. Johnson -- had a concern about this paper and
2 its used of VEP and maybe he will talk more about that later.

3 In addition, one of the discussants noted that the human
4 acute neurotox data seemed more uneven than the DRE indicated. And they
5 quoted a paper, Lucas et al from 1995, which compared the dry cleaning workers
6 to the controls and they tested for CNS depression, sleepiness, dizziness, and so
7 on, and found no effects. So, as we've heard before, they were wondering about
8 the value of citing this study.

9 And then we're going to talk about chronic neurotox. In
10 terms of non-cancer hazard from a chronic exposure, the neurological effects of
11 PCE have received the most attention and have been well documented in human
12 and animal studies. Although most discussants agreed the PCE-induced
13 neurotox represented the most robust endpoint, two reviewers, as explained in
14 more detail below, thought the agency needed to better explain why they chose
15 CNS neurotoxicity as a critical health effect rather than kidney injury. And the
16 issue of kidney injury with PCE is going to be discussed a lot today.

17 The EPA IRIS assessment published in 2012 identified
18 visual deficits, especially diminished color discrimination (audio gap). Visual
19 impairment has been described in both occupational and residential settings. In
20 one particularly convincing study, the color visual impairment was noted in dry
21 cleaning workers exposed to PCE for an average of 8.8 years. The same
22 population of workers, when examined after an additional two years of PCE
23 exposure, demonstrated even more impairment.

1 Other studies linked PCE exposure with decreased
2 cognitive skills, mainly impaired visual spatial memory, vigilance, and
3 information processing skills. On the other hand, more recent studies conducted
4 after the IRIS review have failed to link PCE exposure to increased incidents of
5 neurodegenerative diseases, mainly Parkinson's and ALS.

6 One discussant thought the description of PCE-induced
7 visual spatial deficits in Section 3.2.3.1.2 was misleading. The text there leads
8 the reader to believe that repeated unstated magnitude, duration and frequency
9 exposure to PCE causes colorblindness, or even more, perhaps more serious
10 problems as summarized in Table 1 of Schreiber et al.

11 So the recommendations -- and I'm sure we'll hear some
12 more from the participants -- the text in the Draft Risk Evaluation should be
13 clarified to explain the extent of PCE-related deficits in color discrimination. An
14 EPA re-review of the color vision and visual pattern data should examine which
15 test -- for example, the Lanthony's Desaturated 15-Hue Test -- were
16 administered to find the magnitude and frequency of these changes and explain
17 the severity of the deficit.

18 The discussant also recommended that the text should
19 explain that while repeated PCE exposure can elicit changes in color vision, this
20 is a phenomenon also seen with other volatile solvents. Now, I personally don't,
21 in that this should be mentioned that these changes are not unique to PCE. I'm
22 not convinced the discussion of other chemicals that cause a response similar to
23 PCE is necessary for the Draft Risk Evaluation and would be only useful if it

1 could be shown that they shared a common mechanism. But I'm sure that we'll
2 be hearing from some other discussants on that point.

3 As noted above, the evidence for PCE-induced
4 neurodegenerative disease was not convincing. And along these lines, one of the
5 discussants noted the deficiencies of two of the studies into the
6 neurodegenerative diseases and, as we heard, questioned their inclusion into the
7 Draft Risk Evaluation.

8 Since the evidence for neurodegenerative disease was
9 summarized by the agency as ambiguous or conflicting and thus not considered a
10 major health hazard in the DRE, it is not clear that detailed description of the
11 study deficiencies is warranted. Hence, the criticism of these papers will be
12 confined to written comments unless the discussants think otherwise.

13 So, aside from neurotoxicity induced by adult exposure,
14 several recent studies have examined the ability of fetal or early childhood
15 exposure to PCE to induce neurotoxicity in children or young adults. The
16 endpoints included likelihood of risky behavior, math scores, bipolar disorder,
17 schizophrenia, and autism spectral disorders. These studies have generated a
18 complicated pattern of effects which most of the discussants thought were
19 similar between negative and equivocal.

20 It would've been useful if the agency had summarized the
21 studies as such instead of just describing them individually and leaving it up to
22 us to distill the results. Two of the discussants described the deficiencies in
23 mostly negative results of the studies by Aschengrau, Getz, Stingone concerning
24 the ability of PCE to induce developmental neurotox in humans.

1 Once again, since developmental neurotox was not
2 described in the DRE as a major health hazard, issues with the specific
3 developmental neurotox studies will be confined to the written comments unless
4 the discussants think otherwise. Bottom line, the connection between PCE
5 exposure and developmental neurotox is not as compelling as the robust and
6 reproduceable neurotox effects resulting from adult PCE exposure.

7 And recommendations -- given the sparse evidence, the
8 agency should consider revising the first paragraph of Section 3.2.3.1.2 on
9 neurotox to more precisely summarize the developmental neurotox studies. The
10 agency should also consider whether the studies by Stingone et al in 2016 and
11 several case control studies that describe nonsignificant CNS effects are worth
12 being included or should be considered off-topic.

13 Now I'm just going to talk a little bit about animal studies
14 for neurotox. They provide mostly support evidence for the effects seen in
15 humans and studies in mice, rats, and gerbils which develop clinical signs of
16 neurophysiological changes in brain alterations following PCE exposure.
17 However, one discussant noted that a study in rats the agency barely mentioned
18 is that of Oshiro of 2008. They described this as a high-quality study in rats with
19 inhalation exposure tested for months for visual signal detection.

20 Dose respond effects were found at multiple measures,
21 including outcomes such as PCE-induced increase in false positive response rate.
22 And I'm going to ask the discussant whether they want to recommend that the
23 agency actually includes this in the DRE. In other words, is there a
24 recommendation associated with this comment?

1 The agency identified the endpoint of impaired visual
2 function carried forward for dose response analysis to represent the neurotox
3 hazard domain. This seemed appropriate. PODs were derived from two
4 medium-quality human inhalation studies with equivalent cumulative uncertainty
5 factors of 100. One study described a human equivalency at concentration of 2.2
6 parts per million and the other one 8.3 and has explained in the DRE the agency
7 used a midpoint number of 5.2 parts per million as the POD.

8 Recommendations -- neither the IRIS 2012 or the ATSDR
9 study of 2019 reports discuss persistent effects of PCE after exposure has ended.
10 So one discussant thought that this topic should at least be mentioned if effects
11 are irreversible that make the effects more serious. Another discussant said, for
12 the acute human study of Altmann 1990, human equivalency concentrations
13 were developed for both occupational and consumer exposure durations.

14 For the chronic PODs, the PBPK model provided human
15 equivalents to the concentration outputs for PODs from animal studies adjusted
16 to a 24-hour continuous exposure which were compared to 24-hour TWA
17 exposure values during risk estimation. A chronic human neurotoxicity POD
18 was derived both based on continuous exposure and occupational exposure.

19 The Altmann et al data are appropriate for derivation of
20 acute HECs, but a citation in the charge question should also cite the key studies
21 for the chronic POD determination. After that, I think that's all I have for the
22 neurotox part of this hazard identification section and I'm sure we've got people
23 who would like to chime in at this point.

1 **DR. KENNETH PORTIER:** Kathleen, this is Ken
2 Portier. I get some feedback on your presentation, and I think maybe that your
3 phone jack is not fully in and/or your papers are touching the jack. So, just kind
4 of be aware of that.

5 **DR. KATHLEEN GILBERT:** Okay. Sorry.

6 **DR. KENNETH PORTIER:** No, that's fine. At this
7 point, we'll open it up to any of the associates or anyone else on the committee
8 who wants to comment on the neurotox, any issues with the neurotox that Dr.
9 Gilbert brought up. Dr. Vorhees, is now a good time for you to jump in?

10 **DR. CHARLES VORHEES:** Yeah. So I wanted to go
11 back to this study by Bove which is really a carcinogenicity study, but they do
12 talk about it in the neurotox section in terms of ALS and multiple sclerosis
13 diagnoses among these large cohorts. And the DRE actually says that there's an
14 increase in ALS between the control group at Camp Pendleton versus the
15 experimental group at Camp LeJeune. But in fact, I think they've got it
16 backwards.

17 Because, see, there were 27 ALS cases in Camp Pendleton
18 and only 21 in Camp LeJeune, so it's not an increase. There was actually a
19 decrease. I don't know whether it was significant with 27 versus 21 cases, but I
20 think they need to double check their description of that. And as far as MS is
21 concerned, they're talking about 10 cases at Camp Pendleton, the control, and 12
22 cases at Camp LeJeune. That's clearly not going to be a significant effect.

23 They cite a study by Goldman in 2012 which examined 99
24 World War II veteran twins that are discordant for Parkinson's disease. The

1 problem with the way they cite it is it makes it sound like there was an increase
2 in Parkinson's disease, and actually, the increase they found was for TCE
3 exposure of p less than .03. But for PCE, the association was 0.053. They're
4 right borderline, so that doesn't seem like very strong evidence.

5 Then those studies of the Cape Cod by Aschengrau and
6 Getz have problems. Those studies are not as strong as one might think, even
7 though they do find associations. The strongest association is with later drug
8 abuse after prenatal and childhood exposure. But most of the other outcomes
9 that are described in the DRE really don't turn out to be significant. They
10 mention head injuries. Well, the study shows that there was no significant
11 difference in head injuries.

12 And I've written out a detailed description of that study
13 and what the DRE says versus what the study says in terms of these effects, and
14 there are a number of issues around the strength of the findings in those studies
15 which I don't think are very strong evidence for some of the effects that the DRE
16 lists.

17 Some of the animal studies, as I mentioned, are fairly
18 good. As far as the Oshiro study is concerned, they mention it. They don't say
19 much about it, but I do think that's a study they might want to talk more about
20 because the evidence there is quite strong. It's a very well designed, well
21 executed study, very rigorously analyzed the data. So, I think they should put
22 more attention on that study. I think it would help their case even though the
23 doses are somewhat higher, but they show very clear neurotoxicity.

1 And then Kate has already mentioned some of the
2 problems with the neurodevelopmental studies by Aschengrau so I won't go over
3 those again except to say that, as far as the association with schizophrenia is
4 concerned, they're talking about three cases of schizophrenia in the exposed
5 group versus the unexposed group. And I really question whether that is of any
6 significance. They do mention PTSD also, but as I read the paper, the increase
7 in PTSD is also not significant.

8 So, again, I think there's a tendency, as Dr. Grant
9 mentions, of what he called indiscriminate citation of outcome measures,
10 whether they were significant or not. And I think they could improve the
11 readability of the report considerably by focusing on those effects which are
12 significant and dropping out the listing of a lot of nonsignificant effects. Thank
13 you.

14 **DR. KENNETH PORTIER:** Thank you, Dr. Vorhees.
15 Dr. Johnson and then Dr. Hossain. Dr. Johnson?

16 **DR. MARK JOHNSON:** Yeah, thank you, Chip. I
17 appreciate that. My comments dovetail with Dr. Vorhees' as well because, in a
18 lot of cases, particularly that case when discussing Camp LeJeune, they talk
19 about a nonsignificant increase. I mean, we use statistics to help us determine
20 what's real and what's not. It's just a tool. Sometimes there's trends.
21 Sometimes our sample sizes are small and we have to look beyond statistics, but
22 in many cases, it's helpful to me that if we talk about what's significant and
23 what's not, we leave that term associated with biological significance.

1 So, it's either different or not based on statistics, and if we
2 see a trend, we can then discuss it in more detail. But if it's not statistically
3 significant, it's not different. And I found a lot of cases in the document where
4 they talk about a non-statistically significant increase or decrease. It's really not.
5 Unless there's a trend there or something else that you want to give greater
6 explanation to, I would keep it simple and just say it's different or it's not
7 different.

8 And in the case of Altmann, I thought it was a great study
9 to use. I'm on board with it. I agree that those differences in action potentials
10 are a hazardous effect. But I'd like to see it tied to a clinical association with
11 disease if that's possible. I don't know; maybe some of my colleagues do. I
12 think this is a test that's done often, and maybe certain action potentials or delays
13 in those potentials can be tied to a disease state. If that can be done, I think it
14 would be a much stronger document. Thank you.

15 **DR. KENNETH PORTIER:** Mark, this is Ken Portier.
16 I want to second what you said. I was kind of bothered by some of the
17 terminology like non-significant increase. You know? And I kept thinking, how
18 do I really want to say it? And I liked what you said, and you might want to add
19 this to the general comments.

20 You know, if it's not statistically significant, it shouldn't
21 be a significant increase. If it is significant, then you need to talk about
22 biological effect and whether it's important. I like the way Dr. Johnson
23 mentioned that. Dr. Gilbert, did you want to comment on that before I go to Dr.
24 Hossain?

1 **DR. KATHLEEN GILBERT:** I just wanted to chime in
2 on Dr. Johnson's point. When I was looking at HEVs, which I was not familiar
3 with, I found that they are used in the diagnoses of multiple sclerosis. So, they
4 do apparently have some clinical benefit. And I take the point of --

5 **DR. KENNETH PORTIER:** Thank you. Dr. Hossain?
6 Oh.

7 **DR. KATHLEEN GILBERT:** No, go ahead.

8 **DR. KENNETH PORTIER:** I was just going to move
9 onto Dr. Hossain, but we'll come back to you, Kathleen, at the end. You can
10 wrap up.

11 **DR. MUHAMMAD HOSSAIN:** Okay. I have
12 additional comments regarding the neurodegenerative diseases that are missing
13 in the report. For example, there is actual association between Perchloroethylene
14 exposure and Alzheimer's disease. There is one single case study reported that
15 serum levels of Perchloroethylene was 15 times higher in a man who worked at
16 the dry cleaner for over 30 years.

17 And ultimately, this man was diagnosed with probable
18 Alzheimer's disease. But this piece of data are missing in the report. I think
19 EPA should include this data for better understanding of the outcome of the
20 some of the risk.

21 And then another thing is that also relative with the
22 neurotoxic, there's one -- a retrospective cohort study determined the long-term
23 health effects of early-life exposure to Perchloroethylene-contaminated drinking

1 water. They found that prenatal and early childhood exposure increases the risk
2 of epilepsy about 1.15 fold when compared with unexposed participants.

3 But the sample size was really smaller. They used, I think
4 -- compared, the data was only 7 unexposed and exposed participants. I think
5 this data would be a useful tool and so it should be included into the DRE.

6 Thank you.

7 **DR. KENNETH PORTIER:** Thank you, Dr. Hossain.

8 Dr. Lash?

9 **DR. LAWRENCE LASH:** Hi, yeah. I just wanted to
10 briefly reinforce a statement about the significance. I think this was the only
11 section I found, and this was always one of my pet peeves. There were
12 statements about nonsignificant elevation or borderline significant or
13 nonsignificant increased RRs.

14 So I just wanted to support the statements that were made
15 about that that these need to be properly stated. And as you said, even when
16 there are significance detected, you need to consider the biological. So that was
17 it.

18 **DR. KENNETH PORTIER:** Thank you. Oh, Dr.

19 Kaufman.

20 **DR. ALAN KAUFMAN:** Sorry. It took me a second to
21 get off mute. Yeah, I was going to say count me in that camp as well. If you
22 don't have statistical significance, you really don't have anything to talk about.
23 And once you've got it, that by itself is not enough. You need a plausible
24 biological mechanism to go along with it.

1 **DR. KENNETH PORTIER:** Thank you. In my
2 readings last week on trying to understand how others do weight of evidence, I
3 came across a study out of the Netherlands where what they first do is look at
4 how many research studies have looked at this outcome for this chemical, and
5 they've kind of said, what traction were significant? So there's kind of a
6 reproducibility fraction that comes out of that. And then they go on to discuss
7 the significant results and what those tell us.

8 That kind of two-part approach I kind of like because it
9 first talks about the reproducibility of the results. Though, if it's only one study
10 out of ten, our confidence in this discussion, I think, goes down for most of us.
11 Right? So somebody mentioned 2 studies out of 300. That doesn't engender a
12 lot of confidence on my part that there's a lot here to be looked at.

13 Dr. Hossain, your hand's still up, and Dr. Kaufman, your
14 hand's still up. Additional comments? Dr. Barone, I see your hand. I want to
15 go back to Dr. Gilbert real quickly to see if there's anything she wanted to add,
16 and then we'll ask you to kind of comment on that. Dr. Gilbert?

17 **DR. KATHLEEN GILBERT:** Well, I got the point that
18 was reiterated by several people that they should concentrate more on the
19 significant studies and not even mention, or at least downplay, the nonsignificant
20 studies. I'll be sure to put that into the recommendation. And I also just wanted
21 to ask Dr. Hossain if he would write a little brief description of that study he was
22 talking about and send that to me. Thanks. That's all I have.

23 **DR. KENNETH PORTIER:** You're welcome. Dr.
24 Barone, you wanted to comment or ask a clarifying question (audio gap)?

1 **DR. STAN BARONE:** Yes, Dr. Portier. I wanted to
2 provide two clarifications on two topics. One was the issue of diagnostic
3 prediction of disease. The sensory-evoked potentials and sensory-evoked
4 potential batteries are diagnostic tools used for human assessment. And
5 electrophysiological dysfunction is an adverse effect. Electrophysiological
6 dysfunction behavior, neurochemical imbalances, are all adverse effects as we
7 have outlined in our neurotox risk assessment guidelines that can occur in the
8 absence of overt pathology.

9 So, I wanted to emphasize that point and the other point of
10 the visual-evoked potential testing is it does look at the potentials that occur from
11 the receptor in the eye, up through the midbrain, to the cortex. So, you can
12 actually see changes in the visual-evoked patterns across the pathway. And we
13 also have evidence for deficits in the retina. Again, those were referred to earlier
14 as color-vision deficits. Those color-vision deficits are not red-green color
15 blindness which is the most common genetic type of color deficit; it's blue-
16 yellow and it's very unique. And it's very unique to solvent exposure, in fact.

17 The other issue, which I think the committee spent a lot of
18 time on and I think we need to think about, is the issue of citing negative studies.
19 And again, our risk characterization guidelines in our risk evaluation will require
20 us to discuss the positive and the negative in a balanced way. I think the
21 committee's recommendations on how to do this more effectively will be quite
22 helpful and to put things in the appropriate context.

23 I hope that clarifies why we have so much discussion of
24 the negative studies and, again, we could put the study summaries -- we tried to

1 put more of the study summaries in the appendixes and have less of that clutter
2 in the -- I think some people refer to it in the body of the document, in the
3 narrative. But definitely, your suggestions, recommendations will be helpful to
4 us.

5 **DR. KENNETH PORTIER:** Dr. Vorhees?

6 **DR. CHARLES VORHEES:** Yeah. In response to what
7 Dr. Barone just said, one of the things I would like to suggest is that if they want
8 to include balance of the positive and the negative data around neurotoxicity, that
9 they organize those paragraphs with where they put the emphasis on the
10 significant effects and then cluster the nonsignificant effects. And then, at the
11 end of each of those paragraphs, they need a concluding sentence which
12 basically states what the agency is taking out of those studies.

13 So, if they cite multiple studies or one study in a
14 paragraph, what is it that the agency is putting its emphasis on out of all those
15 endpoints that got measured? I think that would -- least for me, that would've
16 made those neurotox sections much easier to follow if I knew what the agency
17 was extracting from each paragraph. Thank you.

18 **DR. STAN BARONE:** Thank you, Dr. Vorhees. That's
19 actionable.

20 **DR. KENNETH PORTIER:** I was going to say the
21 same thing, a very practical suggestion to improve the document. Dr. Willhite?

22 **DR. CALVIN WILLHITE:** Yes sir. The Safer
23 Chemicals, Healthy Families submission states, "Human studies of short-term
24 exposure also document an association between PCE and serious" -- they

1 emphasize -- "serious vision impairments in both occupational and residential
2 settings." Now, the problem with the dossier as written is that it leads to this
3 conclusion on the part of the readers: serious vision impairments. Now that
4 could go all the way from what we see with methanol exposure to what we see
5 with aging.

6 We do know, from studies here in Marin County,
7 California that the school bus that you see, the yellow when you're age seven, is
8 actually slightly different than the school bus yellow when you're 70. And the
9 actionable item here is to go back to the actual color vision tests that were
10 administered and determine the seriousness, or perhaps lack thereof, in color
11 vision decrements. Are these such that it's truly you can't tell the difference at a
12 traffic stop the yellow from the green? Or is it just simply a subtle effect,
13 nevertheless adverse, similar to that associated with aging? Thank you.

14 **DR. KENNETH PORTIER:** Dr. Johnson?

15 **DR. MARK JOHNSON:** Yeah. I just want to get back
16 to the comment made by Dr. Barone. Yeah, I absolutely agree with everything
17 he said. Basically, when you take it down, it comes back to the comment that
18 was made earlier. The difference between statistical significance and biological
19 impact. I'm not going to say biological significance because I don't want to be
20 misinterpreted.

21 But I'm sure, and I'm fairly positive sharing everything
22 everyone has said so far about differences in these action potentials, is you can
23 maybe be able to tie these differences to a disease state. It would just make a

1 stronger argument. The way it reads when I read it is that there's just a statistical
2 difference. I guess you want to show that there's more than that.

3 Kind of along the lines of what Dr. Willhite was saying, if
4 you can show that this difference in action potential is tied to a significant
5 difference in the way colors are perceived, that would let a lot more strength for
6 that argument selection of that endpoint. Thank you.

7 **DR. KENNETH PORTIER:** Thank you. I'm going to
8 move back to Dr. Gilbert to any comments on this, and let's move forward.

9 **DR. KATHLEEN GILBERT:** I just wanted to say that I
10 completely agree with Dr. Vorhees about the need for concluding statements in a
11 lot of the sections or paragraphs. It would've made it much easier to digest the
12 information. And that's been a problem with several of these DRE. It certainly
13 is in this one, especially in certain sections. So, I will definitely put that in too.

14 **MS. RUTHANN RUDEL:** This is Ruthann. Can I add
15 one thing on statistical significance either now or later?

16 **DR. KENNETH PORTIER:** Now's a good point,
17 Ruthann.

18 **MS. RUTHANN RUDEL:** Okay. I agree with the need
19 to try to sort through the many studies and figure out what's real, and it's a very
20 demanding task actually. But I don't think that the decision or idea of just
21 discounting anything that's nonsignificant is current, like best practice, I guess.

22 There was a big nature article in 2019 about this topic, and
23 I'm just going to quote one part which said, in 2016, the American Statistical
24 Association released a statement in the American Statistician warning against

1 misuse of statistical significance and p-values. The issue included many
2 commentaries. This month, a special issue in the same general attempts to push
3 these reforms further. It presents more than 40 papers on statistical inference in
4 the 21st century, a world beyond p less than 0.05.

5 The editors introduced the collection with a caution: don't
6 say statistically significant. Another article with dozens of signatories also calls
7 on authors and general editors to disavow those terms. We agree and call for the
8 entire concept of statistical significance to be abandoned.

9 So I just wanted to put that out there because hearing so
10 many of the folks on the panel saying that it should be sort of a bright line, that's
11 really in dramatic contrast, I guess, to that. And I just actually will tell a quick
12 anecdote. Even in rodent studies, I've seen examples of nonsignificant results
13 that were dismissed. And then, in retrospect, once the biology was better
14 understood, it turned out they were treatment related.

15 So, a 1990s multi-gen rat study of dibutyl phthalates had a
16 couple odd reproductive anomalies in the male offspring but too few because it
17 wasn't significant and they were dismissed. And after, I don't know, another
18 decade or so of work and changing the designs to reflect the biology and better
19 understand what was happening, they went back, actually, and reinterpreted that
20 study as positive.

21 And similarly, of course, like counting studies, I
22 understand the wish to do it. But it really doesn't work to get to the truth
23 because, if you have one very good study, that's worth a lot more than ten that
24 were not sensitive. So that's my comment.

1 **DR. KENNETH PORTIER:** Dr. Cory-Slechta?

2 **DR. DEBORAH CORY-SLECHTA:** Yeah. I wanted to

3 come back to this issue that was raised about the severity of deficits in color
4 vision and essentially reinterpret what was said. Is it just something that would
5 be a part of normal aging? Well, what you're actually saying is, is that just
6 accelerated aging? Which, to me, is an adverse effect, especially when we're
7 talking about exposures that are not voluntary. It's one thing when you're taking
8 therapeutics, but not for an involuntary exposure.

9 So, to say, gee, it's just like normal aging when you're
10 talking about something happening early in life, can hardly be considered
11 something that we should dismiss. Certainly, if you went to your doctor and
12 they told you that, I'm not sure you'd be very happy. Thank you.

13 **DR. KENNETH PORTIER:** Dr. Vorhees?

14 **DR. CHARLES VORHEES:** Yes. I wanted to comment

15 on this whole problem of both the statistical inference, which I'm sure, Ken, you
16 would have a lot to say about. You know, ideally in these studies, we would
17 have more than just tests of statistical significance. We'd also have effect sizes.
18 And if we had effect sizes data in these studies, we'd be a lot better informed
19 about how meaningful a particular effect is.

20 But unfortunately, calculating effect sizes is not something
21 that's very common, even in contemporary literature, let alone in older studies.
22 So we have to go by what's most likely to be meaningful. And I think looking
23 for statistical significance is sort of the first pathway of making a decision about
24 whether to use data from a study to indicate an adverse effect versus not. Many

1 of these nonsignificant effects are really trivial. So, I think you can look at the
2 data and see why they're not significant. Now that's one point.

3 And I'd also like to reinforce something that I think Dr.
4 Cory-Slechta is indicating which is, when we bring people into a laboratory and
5 do a specific test like a visual-evoked potential test, we can often pick up effects
6 that are more subtle than that person might realize in their day to day life. But
7 that doesn't mean it's not significant, because all these effects lie along a
8 continuum. And the question is always, well, when does it reach the threshold
9 that it becomes a detectable impairment?

10 But if somebody has a deficit, even if they don't currently
11 indicate it, if it's found in a group of people and is statistically significant, then it
12 indicates the probability that if there's more exposure, it's going to become
13 worse. So, all these effects lie along a continuum. And I think, when you find it
14 in a controlled setting, yeah, it's more sensitive than in an uncontrolled setting.
15 But it's still important and I think it implies that they're headed towards a more
16 severe impairment if the exposure continues. Thank you.

17 **DR. KENNETH PORTIER:** Thank you. Dr. Daniels?

18 **DR. MICHAEL DANIELS:** Yes. I can't help myself. I
19 need to comment on the statistical significance stuff a little bit. I think it's a little
20 bit dangerous to think about just kind of statistical significance or not as some
21 sort of initial cut to whether we're going to consider a study or not. The 0.05
22 error rate upon a 1 out of 20, it's kind of been the significant effect cutoff
23 forever. But I mean, there's some arbitrariness to it and it's just saying, well, if
24 there's no effect, we'll get it wrong, like, 1 out of 20 times.

1 Similarly, like when we're looking at studies that are kind
2 of smaller and there's kind of no statistical significance, there could potentially
3 be large effects in those studies, so it would be helpful to see confidence
4 intervals like we see for some of these studies as well. And it could be that
5 there's just a little bit too much variability so the sample size wasn't sufficient.
6 But it's not like the not significant ones are not evidence that there's no effect.
7 It's just there wasn't enough evidence that this effect that we saw wasn't due to
8 chance.

9 So, I mean, when possible, I think -- and a lot of journals
10 are doing this more now, is to, when it's available in the literature -- maybe for
11 some of the older literature it's not -- just give -- an effect size would be great,
12 but as was noted, it's often not there and you can't even figure it out from what's
13 in the paper. But at least reporting the estimate and a confidence interval and
14 one can see if the confidence interval -- for example, if it's a risk ratio -- is
15 slightly covering one.

16 Yet it wouldn't be significant, but if that point estimate is
17 quite large, I think you'd kind of view it differently than if that confidence
18 interval wasn't covering one and the point estimate was, like, just unimportantly
19 from a biological perspective kind of different from one. So I just wanted to
20 comment that we probably want to be careful with what we recommend in terms
21 of the studies to be including or not and the significance cutoff and that sort of
22 thing. Thanks.

23 **DR. KENNETH PORTIER:** Okay. Thank you. Dr.
24 Willhite, and then I think we're going to go back to Dr. Gilbert because we have

1 kidney toxicity, liver toxicity, repo developmental toxicity, and immunotoxicity
2 left to go in 5.1. So just a warning. Dr. Willhite? Dr. Willhite, your phone may
3 be muted.

4 **DR. CALVIN WILLHITE:** Okay. Now I'm back?

5 **DR. KENNETH PORTIER:** Yes.

6 **DR. CALVIN WILLHITE:** The most robust and
7 concise discussion of the visual contrast sensitivity color vision that I've come
8 across is the Schreiber paper, *Environmental Health Perspectives, Volume 110,*
9 *July 2002.* And in that analysis there, they conclude on Page 662, "although the
10 visual contrast sensitivity deficits are subclinical in that, alone, they are not
11 diagnostic of illness and are not known to indicate a progressive disease process,
12 they do represent a long-lasting adverse alteration in neurobehavioral function."
13 What the document needs to do as an actionable item is to define the severity of
14 those deficits. Thank you.

15 **DR. KENNETH PORTIER:** Thank you. Back to Dr.
16 Gilbert. Let's move on. Oh, Dr. Barone, did you want to add a comment here?

17 **DR. STAN BARONE:** Just a clarification, visual
18 contrast sensitivity is not the same thing as a color vision deficit or the test for
19 color vision. They're two separate things and actually get at different receptors,
20 the rods versus the cones in the retina. So, we will do a better job at making
21 those clarifications and indications of adversity.

22 **DR. KENNETH PORTIER:** Thank you. Dr. Daniels,
23 you can put your hand down. Dr. Gilbert, let's move on.

1 **DR. KATHLEEN GILBERT:** Okay. So we're going to
2 consider chronic liver toxicity together with chronic kidney toxicity. I've been
3 told that sometimes you hear feedback on my presentation, so tell me if you do
4 and I'll try and fix it. As far as chronic liver toxicity, there's conflicting
5 evidence of PCE-induced liver toxicity across several occupational studies of dry
6 cleaning workers. On the other hand, liver toxicity has been reported in multiple
7 animal studies examining PCE exposure by oral or inhalation routes.

8 One of the most consistent findings is that it increased
9 liver waste. Taken together, the EPA concluded that the weight of evidence was
10 sufficient to carry forward both kidney and liver toxicity for dose response
11 analysis. Two high-quality animal studies with total uncertainty factors of 30
12 were used to define the PODs for the liver and kidney toxicity and this seemed
13 appropriate. So, as far as the kidney toxicity, the DRE seems to indicate that the
14 effects of PCE on kidney toxicity are less well documented compared to
15 neurotoxicity.

16 Epidemiological studies in dry cleaning workers showed
17 increases in some but not all signs of kidney toxicity, including increases in
18 urinary RBP and glutamine synthetase, but no increases in acetyl glucuronidase
19 or alanine aminopeptidase. Other studies have found that PCE exposure does not
20 lead to chronic renal disease. Mixed evidence including both positive and
21 negative findings of kidney toxicity reported in animal studies.

22 However, more than one discussant thinks the PCE-
23 induced kidney toxicity did not receive the attention it deserves. This issue will
24 come up again in Question 5.5 when we discuss cancer hazard identifications.

1 Discussants described the studies showing the mutagenicity of nephrotoxic PCE
2 metabolites. They also reference Table 3-10 on Page 313 of the DRE and asked
3 if kidney nuclear enlargement in proximal tubules for chronic exposure
4 consistency gives lower ATD values than the various CNS or neurotoxicity
5 endpoints. Why is neurotoxicity chosen for POD calculations and risk
6 estimates?

7 In all the risk estimates provided in the table in Section 4,
8 kidney histology consistently provides the lowest MOE values for chronic
9 exposures that are usually at least two-fold lower than CNS effects. In Section
10 5.3, detailed risk determinations by conditions of use where there are
11 unreasonable risk of injury identified, the driver benchmark for chronic exposure
12 is neurotoxicity. As noted, kidney toxicity consistently has lower benchmark
13 MOE values and lower MOE values for both high-end and central tendency.

14 Another discussant similarly thought the renal toxicity
15 section was underdeveloped. They mentioned that recent studies, Moody and
16 Price, do show shedding of renal epithelial cells increased urinary albumin
17 brush-border antigen serum anti-glomerular basement membrane antibodies and
18 alkaline phosphatase.

19 So the recommendations were that EPA needs to explain
20 why CNS neurotoxicity was chosen as a critical health effect when the kidney
21 effect consistently provides lower HED values. The associates on this section
22 also provided a number of editorial recommendations which I will put in the
23 written response. So I'm sure that some of the folks are going to want to talk
24 about the kidney toxicity. I'm going to let them do that.

1 **DR. KENNETH PORTIER:** So raise your hand if you
2 want to chime in on this. Dr. Bruckner?

3 **DR. JAMES BRUCKNER:** Hi. I was one of the ones
4 who had concerns about just the adequacy of the coverage of the basic science
5 for both liver and kidney. For example, in the discussion of human evidence for
6 kidney injury, there were just two references. One was just the IRIS document
7 and one was the study by Mutti which was the one that was actually utilized.

8 The problem was in the short paragraph when they
9 mention the findings and that one human study that was cited, it wasn't clear that
10 that particular author or researchers were actually ones who did that particular
11 study. There wasn't anything about the limitations of the study. There wasn't
12 any information about other supporting studies, particularly in occupationally
13 exposed people.

14 So, my concern was just the adequacy and the depth and
15 breadth of the coverage of studies in human subjects. I found the same thing was
16 true in the liver. I think it was stated that there was limited evidence of liver
17 injury. There was one review study that was cited but no other information
18 about any other particularly occupational exposure studies.

19 I would've also like seeing some discussion about the
20 relative sensitivity of humans versus rats, and particularly rats, for which we
21 have the most animal data. So I would like to know, as I look at when it's
22 proposed to use both the rat and a human study as the point of departure, there's
23 no information about the relative susceptibility of those or how you can

1 extrapolate from one to another or what the basis might be for an interspecies
2 extrapolation.

3 So it was just both the liver and kidney which I know a
4 little bit more about. Those discussions and the information and the references
5 were just really underdeveloped. I would like to see more attention focused on
6 that. Thank you.

7 **DR. KENNETH PORTIER:** So, Dr. Bruckner, in your
8 comments, can you add a little bit on what you'd like to see as a kind of -- build
9 out that discussion? I mean, just to give them an anchor on where they should be
10 going.

11 **DR. JAMES BRUCKNER:** I did. And actually, I've
12 sent that to our lead in this area. I think she'll have that information. I can send
13 that again. I developed two paragraphs, one for liver and one for kidney.

14 **DR. KENNETH PORTIER:** No, we'll look. But thank
15 you. If you sent it to Dr. Gilbert, she's got it and she's incorporated it. It's good.

16 **DR. JAMES BRUCKNER:** All right. Thank you. That
17 was it.

18 **DR. KENNETH PORTIER:** Dr. Lash?

19 **DR. LAWRENCE LASH:** Yes, hi. I think Dr. Gilbert
20 did a great job of summarizing the main comments, and mine on kidney in
21 particular. I guess I just want to emphasize, the thing that I was struck by is
22 when you look through the tables, there are a couple of tables in Section 3, such
23 as 3-8, that lists human equivalent concentrations and uncertainty factors. The
24 kidney chronic noncancer was the lowest.

1 Then what really struck me -- and this, I guess, goes more
2 towards some of the later questions in Charge Question 6, the series of questions.
3 But in the tables in Section 4, there's table after table after table on all the
4 different occupational exposure scenarios. And they list risk estimates for
5 noncancer for each one, and consistently, kidney is lower, as Dr. Gilbert said, by
6 a factor of two or more, sometimes even closer to ten-fold for kidney.

7 So, I don't see why -- and then there's also misstatements
8 with regard to -- it's not just male rats that some of these adverse kidney effects
9 were observed. Granted, there are some studies where they didn't observe
10 effects, but there's a large number where adverse effects were observed in both
11 male and female rats and male and female mice. That's always been an issue
12 with regard to kidney toxicity that the male rat has some unique susceptibilities.
13 And I don't think that that can be easily dispensed with here.

14 My other work, I'm not sure we've talked about yet
15 because this section in Section 3.2 also talks about metabolism. And I know that
16 metabolism and some of these mechanistic issues are not as much the purview of
17 TSCA as they are other assessment activities that the EPA undertakes. But I
18 thought this section, while there was some portions that were nicely concise and
19 all, but there were several misstatements and I noted those as Dr. Gilbert
20 mentioned. There's a lot of specific comments.

21 But there was one that really struck me. There was a
22 comment that stated that one percent of PCE undergoes glutathione conjugation
23 which, first of all, I don't think there's any evidence for that. In fact, that
24 statement didn't even have a citation. And that issue's been discussed at length

1 in other reviews that the way of quantifying flux through the different pathways
2 that you can't just go by urinary metabolites because of the unstable metabolites
3 that are not detectable because they decompose or bind to the macromolecules
4 and so on.

5 So I think those, to me, were the two key points relevant
6 to leading cancer out but just talking about chronic noncancer effects and
7 metabolism. So that was what I wanted to emphasize. That's it.

8 **DR. KENNETH PORTIER:** Thank you. Dr. Bruckner,
9 I see your hand's still up. I don't know if you have an additional comment or
10 you just forgot to put it down.

11 **DR. JAMES BRUCKNER:** I forgot to put it down and it
12 will go down now.

13 **DR. KENNETH PORTIER:** Thank you. Any
14 additional comments? Dr. Gilbert, we're kind of due to take a short break. And
15 I didn't know if you're going to go on to repo and developmental next, whether
16 we can take a break now. What do you suggest?

17 **DR. KATHLEEN GILBERT:** There's a fair amount on
18 the reproductive and developmental tox. We might want to take a break first.

19 **DR. KENNETH PORTIER:** Okay. Why don't we do
20 that? I have 11:20 Eastern Time. Why don't we take a 10-minute break until
21 11:30? Give us a chance to stand up and move around. So we'll reconvene in
22 10 minutes. Thank you.

23
24 **[BREAK]**

1
2 **DR. KENNETH PORTIER:** Thank you, everyone. It
3 was a short break, but I have 11:30. So, Dr. Gilbert, please continue.

4 **DR. KATHLEEN GILBERT:** Okay. We're going to
5 talk about reproductive and developmental toxicity. Assessing the effects of
6 PCE on reproductive and developmental toxicity in Section 3.2.3.1.5 was
7 difficult due to the fact that the material was presented in a somewhat
8 disorganized fashion and did not demonstrate the hard work of distilling the
9 information.

10 In the brief section describing the evidence for human
11 reproductive toxicity, the DRE noted that multiple endpoints were evaluated in
12 the EPA IRIS assessment but did not describe the outcomes of those evaluations.
13 And then, with no apparent rationale, they go on to a short paragraph that
14 discusses a single human study that noted no effect of PCE on sperm. And then
15 they discuss an apparently problematic Danish case-control study that noted
16 some association between PCE and time-to-pregnancy. A few animal studies
17 described also found little reproductive toxicity aside from some equivocal
18 results on sperm abnormalities. One was left with the conclusion that PCE-
19 induced reproductive toxicity is no big deal, even though it was carried through
20 for dose response analysis.

21 However, in the weight of evidence section, 3.2.4.1.5, the
22 agency states that the EPA IRIS assessment reported strong epidemiological
23 evidence of adverse pregnancy outcomes including spontaneous abortion in
24 women exposed to PCE. They conclude that evidence of both male and female

1 reproductive effects in animals and association between exposure and female
2 reproductive effects in humans along with indications of developmental effects
3 in both study types. Both reproductive and developmental tox following PCE
4 exposure are supported by the weight of evidence. So it doesn't really
5 correspond with what's in the hazard identification section.

6 The reproductive endpoint used for POD derivation in
7 Table 3-8 was reduced sperm quality from a mouse study. It was not clear why a
8 minor effect in mice compared to adverse pregnancy outcomes including
9 spontaneous abortion in women was used for POD derivation. This also
10 highlighted another problem: what constitutes reproductive versus
11 developmental toxicity? Sometimes the two were lumped together in the DRE
12 and sometimes they were considered independently.

13 It also highlighted the problem with having a weight of
14 evidence summary pages and pages away from the hazard identification section.
15 In this case, the weight of evidence summary was much more detailed and yet
16 concise and generally useful as compared to the hazard identification section. It
17 is not clear why this duplicative and confusing structure is used in the DRE.

18 So the recommendation for reproductive toxicity, the
19 Section 3.2.3.1.5, reproductive developmental toxicity needs to be rewritten with
20 more attention to paragraph structure and organization and in such a way that
21 supports the conclusions described in the weight of evidence section. The two
22 sections need to be complementary but not duplicative. And the EPA needs to
23 clearly define what constitutes reproductive versus developmental toxicity.

1 And in the sections where they're talking about clearly
2 defined human developmental as opposed to reproductive toxicity, the hazard
3 identification section on Page 268 consists of five lines stating that evidence
4 suggests that PCE exposure is associated with spontaneous abortion. It is also
5 noted that drinking water studies have suggested associations between PCE
6 exposure and pre-term birth, low birthweight, oral cleft defects, eye and ear
7 anomalies, once again referencing the EPA IRIS assessment rather than
8 individual studies. All in all, it was a curiously underdeveloped assessment of a
9 potentially big deal of human health hazard.

10 So recommendations -- the hazard identification of
11 developmental toxicity was too superficial to allow an accurate assessment of
12 this very important endpoint. It is recommended this section needs to be
13 rewritten to better reflect the strength of evidence for this hazard.

14 And then I also want to make a point that Aschengrau and
15 her colleagues, which were referenced for their neurotoxicity studies, have also
16 published a series of papers in the last few years looking at the reproductive and
17 developmental effects of PCE-contaminated drinking water in the Cape Cod
18 area. These papers were not referenced in the DRE even though they were listed
19 as on-topic in the bibliography supplemental file.

20 Some of the results from the Aschengrau developmental
21 studies were not significant. For example, early life exposure to PCE did not
22 increase the incidence of adult onset reproductive disorders. However, some of
23 the results were significant and potentially important. They found that maternal
24 PCE exposure in the drinking water at concentrations greater than 40

1 micrograms per liter increased the odds of having a child with certain birth
2 defects, such as spina bifida, cleft lip, and others. They also noted a PCE dose
3 dependent increase in stillbirths stemming from placental dysfunction.

4 The Aschengrau studies were in agreement with Ruckart
5 and Kyyronen studies that similarly related public drinking water levels of PCE
6 with oral cleft defects, spontaneous abortion, and congenital malformation. The
7 DRE also notes that the EPA IRIS assessment using data from multiple human
8 studies indicate an increased risk of spontaneous abortion. In addition, drinking
9 water studies have suggested association between PCE exposure and pre-term
10 birth, low birthweight, cleft defects as referenced in the IRIS assessment.

11 The description of animal studies of developmental PCE
12 toxicity again quoted the IRIS assessment which noted multiple negative impacts
13 upon implantation while including implantation losses, increased malformations,
14 decreased fetal weight, decreased postnatal survival, and increased incident of
15 skeletal retardations in rats and rabbits.

16 So the recommendations -- a rewrite of the human
17 reproductive developmental toxicity hazard identification should include the
18 Aschengrau studies or at least an explanation for their exclusion. The rewrite
19 should also make evident the substantial weight of evidence from the human
20 epidemiological and animal studies linking PCE exposure to developmental
21 toxicity.

22 With all the evidence linking PCE exposure to birth
23 defects in humans, it is unclear why developmental neurotoxicity, decreased fetal
24 weight, and skeletal effects in animal studies were the endpoints used to

1 calculate PODs for developmental toxicity. The Nelson study that generated the
2 neurotoxicity endpoint -- there were three studies that were used to develop the
3 PODs for developmental tox.

4 One of them was the Nelson study that was 40 years old
5 and rated as low quality by the EPA. The study concluded that there were
6 generally few behavioral or neurochemical differences observed in the offspring
7 of rats exposed to 900 parts per million of PCE, either days 7 through 13 or 20
8 through 24. This study identified an HEC of 29 parts per million. The agency
9 explained that although the study only scored a low in data quality, it was
10 considered for dose response analysis because it's the only identifying study with
11 adequate dose response information relating to functional and molecular
12 indicators of developmental neurotox.

13 The other two studies which were used to develop the
14 endpoints of increased F2 pup weight and decreased fetal weight were conducted
15 and rasped by the Halogenated Solvents Industry Alliance. That's the Tinston
16 and Carney papers. One was a multigenerational study, which was 247 pages, in
17 which animals were exposed to PCE at concentrations of 100, 300, or 1000 ppm
18 during preparing lactation and during pregnancy.

19 They saw effects -- reduced pup survival, a decrease in
20 litter size and pup weight in the F2 generation at 1000 ppm with a NOAEL for
21 reproductive effects at 300 ppm. The Carney studies show detrimental
22 developmental effects at 600 ppm, consisted of reduced gravid, uterus, placental,
23 and fetal weights and decreased ossification of central thoracic vertebrae.

1 The EPA used the two studies to derive human
2 equivalency concentrations of 18 ppm and 16 ppm for use in the POD derivation.
3 It is difficult to reconcile these PCE exposures with those in the Aschengrau
4 studies. This is complicated, of course, by the fact that the oral PCE
5 concentrations in the epidemiological studies have to be compared to the
6 inhalation exposure levels in the animal studies.

7 However, admittedly unsophisticated calculations by this
8 reviewer suggested that developmental toxicity in the animal studies required
9 concentrations in the hundreds of micrograms per kilogram per day level while
10 the toxicity in the human studies was seen at one to two micrograms per
11 kilogram per day level.

12 Recommendations -- the agency needs to better justify
13 using three mouse studies instead of human epidemiological studies to calculate
14 the POD. It also needs to reconcile the apparent discrepancy in the
15 concentrations of PCE needed to generate developmental toxicity in rodents
16 versus humans. The agency also needs to explain why endpoints of sperm
17 quality and skeletal effects were used instead of birth defects.

18 The agency sometimes states that poor quality studies
19 were used to derive PODs because they examine multiple concentrations. If that
20 rationale is used, the agency at least needs to acknowledge the potential
21 discrepancy with single dose better quality epidemiological studies. And that's it
22 that I have for the reproductive and developmental toxicity.

23 **DR. KENNETH PORTIER:** Thank you, Dr. Gilbert.

24 Anyone on the committee or any of the associates want to add to those

1 comments? Just raise your hand and I'll find you. I'm not seeing any hands
2 raised, so I think, Dr. Gilbert, you did a pretty good job of summarizing your
3 own and anybody else's comments. Dr. Apte?

4 **DR. UDAYAN APTE:** I just wanted to mention that
5 there are some new studies that are published most likely after the draft was
6 ready so they would not have been considered. But maybe in the revision, they
7 should be in there from the same group that is published extensively on
8 reproductive toxicity with the first author -- Aschengrau, I guess. So there are a
9 couple of those studies, and I'll mention them in my -- I'll add it in comments.

10 **DR. KENNETH PORTIER:** Thank you. Anyone else?
11 Okay. Maybe I'll turn to EPA. Any clarifying questions on the repo and
12 developmental toxicity noncancer endpoints?

13 **DR. STANLEY BARONE:** Not at this time, Dr. Portier.

14 **DR. KENNETH PORTIER:** Thank you. At least you
15 can't say we're not being complete on these reviews. Dr. Gilbert, anything else
16 on Question 5.1? Is there a -- we doing the cancer endpoint?

17 **DR. KATHLEEN GILBERT:** Got immunotox.

18 **DR. KENNETH PORTIER:** Immunotox and blood
19 toxicity, yes.

20 **DR. KATHLEEN GILBERT:** Can't forget immunotox.

21 **DR. KENNETH PORTIER:** Please proceed.

22 **DR. KATHLEEN GILBERT:** Okay.

23 **DR. KENNETH PORTIER:** No, can't forget
24 immunotox.

1 **DR. KATHLEEN GILBERT:** This is the last section. It
2 was difficult to assess the immunological effects of PCE exposure based on the
3 information provided in Section 3.2.3.1.6. The agency starts off by stating that
4 the association between PCE exposure and changes in multiple immune markers
5 have been indicated in dry cleaning workers and in children in Germany but does
6 not provide specifics or references. They did mention studies apparently
7 showing no association between PCE exposure and serum cytokines or IgE
8 levels in young children but only reference the EPA IRIS assessment rather than
9 the specific studies.

10 After tracking down the individual studies, this conclusion
11 appeared to be correct. The two animal studies quoted in the DRE section on
12 immunotox, Seo et al. 2012 and Boverhof 2013, were said by the EPA to provide
13 conflicting results. Although both studies use somewhat unsophisticated and
14 nonspecific methodology, they examine quite different aspects of the immune
15 system and their results are not necessarily incompatible.

16 Boverhof showed a decrease in anti-SHEEP red blood
17 cell, plaque-forming cells for spleen in rats exposed to PCE via inhalation at
18 1000 parts per million, while the Seo paper showed that mice exposed to PCE in
19 drinking water at concentrations ranging from 0.01 to 1 milligram per kilogram
20 had a dose dependent increase in the passive cutaneous anaphylaxis test for Type
21 1 hypersensitivity. Inflating these two responses underscores, as has been
22 previously mentioned, that the EPA needs to improve its assessment of
23 immunotoxicity.

1 More problematic was the EPA's dismissal as off-topic
2 the study by Emara et al. 2010 which correlated blood levels of
3 tetrachloroethylene in dry cleaning workers with increased levels of IgE and
4 increased blood levels of several lymphocytes in serum IL-4. This study was
5 described in detail in the EPA IRIS assessment and was described in that
6 document as "strongest study examining immunologic and hematological effects
7 of PCE exposure in terms of experimental design." It's not apparent why this
8 important paper was omitted from the DRE.

9 The agency also states that there is limited or negative
10 data connecting PCE exposure to asthma or autoimmune diseases in humans.
11 However, the EPA did not include -- not listed as on-topic or off-topic in the
12 bibliography -- the animal study by Wang et al in 2017 which uses a mouse
13 model to show the drinking water exposure to PCE for 18 weeks accelerated the
14 generation of antinuclear and antiscleroderma as well as other markers of
15 inflammation. In view of the deficiencies described up here, it is not clear that
16 the EPA's inclusion that the weight of evidence does not support immunotoxicity
17 as a hazard domain is warranted.

18 The recommendation -- the EPA needs to rewrite the
19 immunotox section to take into account the issues and omissions described about
20 and to alter or at least better justify the conclusion that PCE-induced
21 immunotoxicity is inconclusive and did not warrant dose response analysis. And
22 that's all I have for the immunotox.

23 **DR. KENNETH PORTIER:** Does anyone on the
24 committee want to add their comments? Dr. Apte?

1 **DR. UDAYAN APTE:** Yeah. I just wanted to add one
2 thing which is the complicated relationship the immune system has with other
3 organs. Immunotoxicity generally looks at -- the assays generally look at the
4 immune system itself, but there are many diseases and conditions where immune
5 system's deeply involved. And one particular disease that is relevant here is
6 non-alcoholic fatty liver disease, which has been discussed at a limited length in
7 the report. But because PERC is fat soluble, it becomes relevant to think about
8 obesity in that field.

9 These diseases are significantly affected by immune
10 system whether -- the immune system is significantly involved in this process.
11 So when we look at these things, I don't think it's a good idea to just look at
12 them in isolation. So, the agency might want to, going forward, think about
13 these endpoints in conjunction with the relevant diseases that might be associated
14 with these chemicals.

15 **DR. KENNETH PORTIER:** Thank you. Anyone else?
16 I don't see any hands up. Dr. Gilbert, is there anything else on this question?

17 **DR. KATHLEEN GILBERT:** No, I am actually done
18 with Question 5.1.

19 **DR. KENNETH PORTIER:** Oh, we were only -- what?
20 An hour over? That's okay. I knew it was going to be a difficult question. EPA,
21 is there any clarifying questions at this time before we move on? Not hearing
22 any.

23 **DR. STAN BARONE:** No, not at this time.

1 **DR. KENNETH PORTIER:** Okie-doke. Let's move
2 onto Question 5.2. Dr. Mohamadu?

3 **DR. YVETTE SELBY-MOHAMADU:** Hi.

4 **DR. KENNETH PORTIER:** I noticed that Dr. Lee has
5 joined us, so I don't know who's going to read here. You fight it out.

6 **DR. YVETTE SELBY-MOHAMADU:** I'll go ahead
7 and read. I'm already unmuted. This is Yvette Selby-Mohamadu. So I will read
8 Question 5.2.

9

10 **CHARGE QUESTION 5 (5.2)**

11

12 **DR. YVETTE SELBY-MOHAMADU:** The acute
13 human study, Altmann et al, HECs were developed for both occupational and
14 exposure durations. For chronic PODs, the PBPK model provided HEC outputs
15 for PODs from animal studies adjusted to 24-hour continuous exposure which
16 were compared to the 24-hour TWA exposure values during risk estimation. The
17 chronic human neurotoxicity POD was derived based on continuous exposure
18 and occupational exposure.

19 Question 5.2: Please comment on EPA's approach for
20 POD derivation, including selection of uncertainty factors and assignment
21 benchmark MOEs for each endpoint. Please also include consideration of the
22 methods and assumptions used for deriving the Human Equivalent
23 Concentrations for each exposure scenario and receptor type. And this is about
24 Section 3.2.5.3.

1 **DR. KENNETH PORTIER:** Thank you. Dr. Bruckner
2 has the lead and he has also a large group of associates who've helped him with
3 it. Dr. Bruckner?

4 **DR. JAMES BRUCKNER:** Were we able to come up
5 with the slides that I prepared and Tamue received just this morning? The
6 PowerPoints?

7 **MS. TAMUE GIBSON:** They're ready. Yes, we're
8 ready. It's up.

9 **DR. KENNETH PORTIER:** You should be seeing them
10 now.

11 **DR. JAMES BRUCKNER:** Okay. Okay, good. This
12 was just prepared. Actually, I think I misinterpreted Tamue's directive last night
13 in preparing slides. I thought that those were to be used today. So, these are not
14 complete and they're not the best. I think we could use them just to begin
15 discussion from.

16 This first point is that, I think, most people or most
17 respondents or the associates thought that the approach of EPA's was really
18 appropriate. You know? And quite well done with just a few conditions or
19 detractions, so we can cover some of those. I guess the first question that's one
20 of mine, really, is the use of karyomegaly, or nuclear enlargement, as a
21 nephrotoxic endpoint. I guess my problem with this was, I guess, one was the
22 biological significance.

23 This particular case, I think that EPA had the choice of
24 using this animal study by the Japan institute as their toxic endpoint or they

1 could've used the study by Mutti, which was a human study in which at least 20
2 different measures of kidney injury were used in an occupational exposure study.
3 So I guess my question here is the selection of the study that was actually used at
4 the end for the point of departure and for the risk assessment.

5 I guess, in this particular case, my interpretation was that
6 EPA chose the animal study over the human study because, one, they judged that
7 the animal study was of higher quality. And also, the fact that there was a
8 NOAEL meant that they didn't have to use an uncertainty factor to go from the
9 LOAEL to a NOAEL. So, my interpretation was that EPA saw there was less
10 uncertainty in using the animal study.

11 My problem with this was that I guess I would replace
12 entire rodents on using human data in a fairly sensitive study. And also, I like
13 the biological significances. In the human study, we're actually looking at
14 markers of glomerular and proximal tubular damage as opposed to increase in
15 the size of the nucleus. So I'm not sure what significance. I'd like some input
16 from other people on the committee.

17 I'm not sure whether nuclear enlargement is really a
18 toxicologically significant endpoint in terms of toxicity, whereas the human
19 study actually used measures of enzymes in urine. And as I said, actually 20
20 different enzymes were measured in 50 different workers.

21 So, maybe we could stop there and get some comments
22 from the committee or other committee members. I just had a question about
23 which study in the end -- the human study or the animal study -- was the most

1 appropriate to use in risk assessment. I'll stop for just a minute and see if we
2 have any other comments.

3 **DR. KENNETH PORTIER:** Sure. Any of the
4 associates or anybody on the committee want to comment on this? Dr. Barton.

5 **DR. CHARLES BARTON:** Yes. I couldn't find a place
6 to add this, so I think this might be a good place. I just wanted to reiterate that,
7 like with carbon tet, there's a more than 10 times chance for human variability in
8 terms of bioactivation in particular with Cytochrome P450 2E1. I suggest that an
9 uncertainty factor greater than 10 is needed, and I think that should be
10 considered because of the great range of the 2E1 found in humans. Thank you.

11 **DR. KENNETH PORTIER:** Thank you. Dr. Lin?

12 **DR. ZHOUMENG LIN:** Hi. I just want to add an
13 additional comment on the first bullet point. EPA's approach to derive the
14 chronic PODs is appropriate. However, the approach of deriving human
15 equivalent dose for each exposure scenario in the receptor type is really not
16 clearly described in this DRE document, specifically when it is mentioned that
17 all chronic PODs were derived as 24-hour human equivalent concentration under
18 the result based on PBPK output and then inside the U.S. EPA 2012 document.

19 However, I went back to this document in order to find the
20 section that supported the statement. But this document is more than a thousand
21 pages and I couldn't find the specific section that described how the PBPK
22 model results were generated in order to support this statement. So, still, I asked
23 this question on Tuesday during the technical presentation discussion.

1 But I still think that it is important to clearly state there
2 how the results from animal study were adjusted and then how the human PBPK
3 model were simulated in order to get an equivalent dose. Specifically, for each
4 exposure scenarios that were used in the PBPK model in both animals and
5 humans should be clearly described.

6 It's just the report to the previous document that is more
7 than a thousand pages, it's really difficult to find there. And then I don't have a
8 very clear idea how they were calculated. So, if it has to report to the previous
9 document, at least it should specify which section of the previous document that
10 has specifically described this answer. Thank you.

11 **DR. KENNETH PORTIER:** Anyone else want to
12 comment? So, Dr. Bruckner, I'm not seeing anybody commenting specifically
13 on this statement. My question to you is, did the Mutti et al. 1992 paper lead to a
14 lower POD than the animal study?

15 **DR. JAMES BRUCKNER:** Just one second. Let me
16 check that in the document.

17 **DR. KENNETH PORTIER:** And I'm hoping we will
18 come back to the PBPK model because, in addition to Dr. Lin's comment, I have
19 someone on the model as well.

20 **DR. JAMES BRUCKNER:** Actually, it was not very
21 different from either the Mutti and the other. One of the numbers was a little bit
22 larger; one of them was a little bit smaller. But no real significant difference.
23 What I was sort of hoping to do was get a response from Larry Lash on what he
24 thought of the biological or toxicological significance of karyomegaly. In my

1 mind, cytotoxicity is a more biologically significant effect than karyomegaly. I
2 wondered if Larry would care to comment on that.

3 **DR. LAWRENCE LASH:** Hi. This is Larry. Yeah, I
4 mean, I think there are a lot better markers that have been used than
5 karyomegaly. I mean, yeah, I don't know that that's really that -- well, certainly
6 mechanistically, I don't think it aligns that well with other responses and with
7 dose responses. So, I've mostly looked at other things. So yeah, I don't know. I
8 didn't really have too many thoughts on that. Maybe while I'm on, I just
9 comment on your statement, the little paragraph above that about the interspecies
10 uncertainty factor.

11 I was trying to think of which paper you were referring to
12 there. It might be a 2005 paper or it might even be a 2001 paper, but I looked in
13 here. I couldn't find a 2006 paper. But I think that's an interesting -- yeah, the
14 uncertainty factors is an interesting point. And I think three is probably
15 reasonable. I think there's still certainly uncertainties. But yeah, I didn't have
16 too much particularly to say about the karyomegaly. That's it.

17 **DR. KENNETH PORTIER:** Yeah, Dr. Bruckner can
18 (audio gap) --

19 **DR. JAMES BRUCKNER:** Okay. Just one other
20 comment, I have just a real problem with just routine use of an uncertainty
21 factor, whether it's interspecies, intraspecies, just as a matter of course that you
22 applied that. Regardless of the information, the scientific information, I think
23 that's where I'm coming from there. Also, if you look at the comment on the

1 uncertainty factor in the Mutti study of being too large, I guess I was struck
2 when I looked at this particular study.

3 You can see that they measured actually -- I was
4 impressed -- 20 different enzymes and indices of glomerular and proximal
5 tubular damage. I was just impressed by how many pretty sensitive measures of
6 tubular damage that were measured. I had a problem again with using just
7 routine measurement of a ten-fold safety factor in light of this particular study.
8 So I just wanted to make that comment when we were talking about uncertainty
9 factors.

10 **DR. LAWRENCE LASH:** Hi. This is Larry again.
11 Yeah, so, thinking more about the uncertainty factors, I mean, certainly if it had
12 been a ten, I think there would've been a concern. But there is still lots of
13 uncertainties using rodent data, the human data for the kidney as a target organ.
14 There are issues like you mentioned. As I said, I think it's either a 2005 or a
15 2001 paper actually that we compared rodent, rat, and human primary
16 subcultures, and there was a significantly lower susceptibility in the human cells.
17 And that was for DCVC.

18 Presumably, I always caution -- and I've said this in
19 several places -- that extrapolating from TCE to PERC can be dangerous
20 because, yes, they share some common metabolites or they have similar
21 metabolites. But for example, when you're dealing with the glutathione
22 conjugation pathway, the reactive thiols that are generated from DCVC versus
23 TCVC, trichlorovinyl cysteine, the TCVC metabolites are much more reactive
24 and so there's differences there.

1 Then you have just overall differences in
2 pharmacokinetics between PERC and TCE, so that even though they may
3 generate the same metabolites, their proportions and rates of generation are very
4 different. And it's very different across species. There's still lots of
5 uncertainties, I think. So, I mean, I'm comfortable with the three. But as I said,
6 if there had been a ten, I think that -- because there's more information available.
7 So that was all I wanted to add.

8 **DR. KENNETH PORTIER:** Thank you. Dr. Daniels?

9 **DR. MICHAEL DANIELS:** Yeah. So I'm not sure if
10 this is the right time to bring up some issues with the analysis of a PBPK model
11 or not. What are your thoughts, Dr. Portier or Dr. Bruckner?

12 **DR. JAMES BRUCKNER:** I was just thinking we're
13 going to cover PBPK in the next charge question and your comments, I think,
14 would best fit in that part.

15 **DR. MICHAEL DANIELS:** Okay. No worries.
16 Perfect. Thanks.

17 **DR. KENNETH PORTIER:** Yeah. So, Dr. Bruckner,
18 continue. Other comments under this question?

19 **DR. JAMES BRUCKNER:** No, I think that's about it
20 for now, addressing the studies that were used for the POD and then assessing
21 some safety factors or uncertainty factors. We might go ahead and go to the next
22 slide then on liver.

23 **DR. KENNETH PORTIER:** I wanted to make a
24 comment about the uncertainty factor of three. I mean, you know, it's standard

1 practice when utilizing a PBPK model to develop to the cross-species
2 extrapolation that when the model is a PK model, you're going to drop three of
3 the ten uncertainty. But if you don't have a dynamic model, you still have that
4 uncertainty factor of three that they apply.

5 I'm not clear, and I'm hoping when we get to the PBPK
6 model discussion that we talk about how adequate the PK model is and why that
7 PB component, the dynamic component, may or may not be important here. So
8 you're ready to move on to Question 5.3 you said? Or the next slide?

9 **DR. JAMES BRUCKNER:** We have one more slide on
10 5.2, to do with liver.

11 **DR. KENNETH PORTIER:** Oh, okay. Good. Proceed.

12 **DR. JAMES BRUCKNER:** We're looking at neuro
13 now, so we need the one on liver. There we go. Okay. If you take a look at the
14 first point, this is really the same question that I raised with kidney. Again, I
15 have a problem just with -- I guess one is with looking at the EPA judged that the
16 Japanese study was of high quality and that the NTP study -- it didn't really say
17 what the quality of that was.

18 And then the other question is the biological -- or I should
19 say toxicological significance of -- I'm not sure I can pronounce it -- angiectasis,
20 which I take it to be abnormal dilation of blood vessels. So, again, I still have
21 the same question is, what is the significance? If someone can help me with this,
22 that's one that I had to look up. I looked at a lot of pathology slides. It's not one
23 that I ever consider as far as toxicologic effect. So this study, the Japanese

1 study, was used in favor or instead of the NTP study which they saw more
2 degeneration and necrosis of liver cells.

3 So, I guess I just have a problem with selecting a study
4 which gives you a lower number when the biological significance of that is, in
5 my mind still, really quite uncertain. So I guess I'd like if anyone has any
6 comments on that particular point.

7 **DR. KENNETH PORTIER:** Dr. Apte?

8 **DR. UDAYAN APTE:** So I could just briefly comment
9 on angiectasis. It's a really rare finding in there that you just mentioned. The
10 significance is not really well known, but the overall physiological change has to
11 do with the change in portal hyperpolar pressure of the blood and may be leading
12 to portal hypertension in the animal. So that's strictly coming from a pathology,
13 physiology standpoint. That's the significance of it.

14 Liver necrosis and vacuolar degeneration are a lot more
15 significant, I think, when it comes to a clear-cut endpoint and their association
16 with both noncancer and cancer endpoints. Again, angiectasis is associated with,
17 as you probably know very well, changes in the endothelial cell biology in the
18 liver. And it's just not a very well-studied phenotype at this point.

19 So, whether that leads to changes in portal hypertension
20 and cirrhosis is a question. Does it besiege that? Or does it make a difference in
21 terms of total liver function? Because it will change how blood interacts with
22 the parasites.

1 But as you said, currently, its significances is not known
2 and it's not a very common finding. So the weight of evidence and how much
3 you consider back in risk assessment is something that needs to be discussed.

4 **DR. KENNETH PORTIER:** Dr. Lash?

5 **DR. LAWRENCE LASH:** Yeah. Well, I just wanted to
6 comment, and this is kind of true for the kidney as a target site and the liver as
7 well, and I think Dr. Bruckner mentioned about the biological significance of
8 certain observations is important. So I think there's two kind of deficiencies in
9 the risk evaluation that kind of permeates many sections, particularly the human
10 health assessment, is that the issues of physiological are relevant but also of
11 human relevance when you're extrapolating from animals to humans.

12 And I think this is an example here. I mean, this comes up
13 more with liver cancer, I think, and we'll discuss that later. But kidney certainly
14 comes up a lot, the issue of relevance to humans. So, this makes me think of that
15 too. That's all.

16 **DR. KENNETH PORTIER:** This is Ken Portier. One
17 of the questions I had is whether this angiectasis is reversable or is it a step
18 toward? And, Dr. Apte, you kind of said it's unknown, but could you comment
19 on that? Do we know to that extent whether this is a short-term reversible
20 condition, or -- yes?

21 **DR. UDAYAN APTE:** It's generally associated with
22 other pathologies including neoplasm. So it would be a part of a significant
23 change in the liver histopathology. We cannot consider it an isolation. It
24 probably is an initial step in something that's going to go wrong over the period.

1 And I don't think anybody really knows whether it is
2 directly reversible if the insult is taken away. Because it has just not been that
3 well studied, it's an observations made generally in association with liver
4 cancers and neoplasms in the liver in general.

5 **DR. KENNETH PORTIER:** So what I'm hearing is that
6 the -- oh, Dr. Bruckner, I wanted to say -- I think what I'm -- yeah. Go ahead.

7 **DR. JAMES BRUCKNER:** Oh, I was going to ask if
8 that changed, the increased blood flow could be angiogenesis associated with
9 cancer or precancerous change.

10 **DR. UDAYAN APTE:** Yes, yes. That could be
11 construed as a precancerous lesion. Now, in the liver field, we use lots of these
12 terms, as dysplasia and regenerative nodule formation and things like that. So
13 it's one of those terms used by pathologists. But angiectasis this is not only the
14 liver, right? It's a common pathology term known for all blood vessels.

15 Its significance in the liver is that it is generally
16 considered as one of the earlier signs of liver dysfunction because that would
17 change how the blood flows in the liver. And liver function significantly
18 depends on the way blood flows and the partial pressure of the blood in the liver.
19 It will affect two things.

20 One, it will affect how a parasite sees the blood, at what
21 speed and how they can interact with the blood, exchange of nutrients, taking up
22 nutrients, things like that. That's one thing at a molecular level.

23 The other thing is change in the liver blood flow will
24 actually affect (inaudible) pressure of the blood, which is a significant problem

1 especially in diseases like non-alcoholic fatty liver disease in a process of all
2 sorts. So this is, again, one of the changes in a sequel of events that will lead to
3 epidemiology.

4 **DR. KENNETH PORTIER:** This is Ken Portier. One
5 of the things I noticed in the Draft Risk Evaluation discussion of the liver, Page
6 302 and 303, is they assign an uncertainty factor of 30 to the JISA 93 study
7 results when they did a -- based on a NOAEL. And in a LOAEL from the NTP
8 study, they assign an uncertainty factor of 300.

9 So, Dr. Bruckner, it sounds like there was more
10 uncertainty associated with the NTP study, at least in the minds of the risk
11 evaluators here.

12 **DR. JAMES BRUCKNER:** Dr. Portier, I was just
13 thinking that EPA should be urged, I think, to discuss what is known about the
14 biological significance and whether this is something that -- or just to describe a
15 little bit more about what is known and what its implication might be to health.

16 **DR. UDAYAN APTE:** I can look into it and provide
17 more description about pathophysiology of angiectasis for that purpose if
18 needed.

19 **DR. KENNETH PORTIER:** Dr. Lash, your hand is still
20 up.

21 **DR. LAWRENCE LASH:** Yes, yes. I just had a
22 question with regard to this angiectasis. I was looking up a couple things and it
23 noted, like Dr. Apte said, I think, that it's often associated with neoplasms. But

1 it also makes a mention in something I found, I think on an NTP site, that it's
2 also an incidental finding associated in aging mice.

3 So, I'm wondering if it also can be one of those things,
4 like we also talk about some of the rat studies that certain responses and
5 processes seem to be endemic to certain strains as they age. So here too, I think,
6 I wonder if that could be an issue to the biological relevance of this response.
7 That's all.

8 **DR. KENNETH PORTIER:** The big question in my
9 mind is whether this is a co-factor or a precursor. And I've heard Dr. Apte kind
10 of say it's a precursor and then Dr. Lash kind of saying, well, it's associated with
11 -- which means it occurs at the same time.

12 But does the cancer produce this? Or is this a precursor of
13 a cancer and all the other noncancer effects? I don't think that's clear, and I
14 think Dr. Bruckner is right in asking for more discussion and justification on that
15 in the Draft Risk Evaluation. Any additional comments? Dr. Bruckner, anything
16 else on Question 5.2?

17 **DR. JAMES BRUCKNER:** I would just say that I didn't
18 have any problems forwarded to me on reproductive or immunological or any
19 other endpoints. That's all I was going to say.

20 **DR. KENNETH PORTIER:** Yeah, okay. I was going
21 to say Dr. Pennell's got his hand up.

22 **DR. MICHAEL PENNELL:** Yeah. We're finishing up
23 5.2. I wanted to make sure that I got my comment in, some of which weren't
24 provided in these slides. So one general comment I had is that it looked like --

1 well, not just looked like. Uniformly NOAELs of the NOAEL/LOAEL approach
2 was used for determining the POD as opposed to a benchmark dose, and there
3 was a short explanation for this at the end of 3.6.2 saying that the data for the
4 selected endpoints were unable to be BMD modeled.

5 And you know, I looked at the papers and I agreed that
6 this was the case in a lot of the instances, because there's situations where there
7 really wasn't much of an identifiable dose response or there's just, like, one or
8 two nonzero doses. But in some cases, I did notice there are situations where
9 dose response modeling may have been possible. I didn't go and attempt to do it
10 myself, but it looked like there was enough doses that you could have fit some
11 models, such as the Japan institute data, the Buben and O'Flaherty paper, and the
12 Tinston paper.

13 So, I would appreciate a better discussion of why each
14 dataset was considered inadequate for dose response modeling. Because on the
15 surface, it just looks like -- and I'm sure this wasn't the case, but it looked like it
16 was just sort of a uniform decision that was made. We're just not going to do
17 any dose response modeling. And when the case it could've been first selected
18 endpoints, maybe you could've done it. And you know, as noted in the
19 document, there are a lot of advantages of doing dose response modeling as
20 opposed to using the NOAEL and LOAEL.

21 Some other points I wanted to bring up -- I was a little
22 confused in the Mutti study how they ended up at the dose for the LOAEL.
23 Because looking at that paper, it looked like it was a two-group study,
24 exposed/unexposed. So was a summary measure used there. If so, I would like

1 to know a little bit better description of how that dose was derived. Another
2 point I have is that, in the Buben study -- this is again for liver endpoint -- the
3 EPA reports that a LOAEL was available when, in fact, there was a NOAEL for
4 PERC at 20 ppm. So, I'm wondering if they could be mistakenly referring to the
5 TCE results which only had a LOAEL.

6 Moving to the reproductive and developmental studies, the
7 EPA reports a single POD for decreased fetal and placental weight and skeletal
8 effects for the Carney et al study, which appears to be inconsistent with the data
9 reported in the paper. There was a significant effect on fetal and placental
10 weight at 250 ppm, but no significant skeletal effects were reported up to the
11 maximum dose in this study.

12 And then I also have some comments about the cancer
13 analysis. I don't know where it would be best to make those comments, if I
14 should make them now or save them for later. I wasn't specifically assigned to
15 any of the cancer charge questions. I don't know. Dr. Portier?

16 **DR. KENNETH PORTIER:** Well, I think we're going
17 to take up cancer in 5.5. So, Dr. Pennell, why won't you hold it until then? I
18 think that'd be the best place to fit it in.

19 **DR. MICHAEL PENNELL:** Okay. Sounds good.

20 **DR. KENNETH PORTIER:** Was that done then? Dr.
21 Pennell, you're done?

22 **DR. MICHAEL PENNELL:** Yes. Those are all my
23 comments then.

24 **DR. KENNETH PORTIER:** Thank you. Dr. Vorhees?

1 **DR. CHARLES VORHEES:** Yes. I wanted to go back
2 just for a second to the Altmann paper, because several people have made the
3 point that the Altmann paper doesn't have a control group. But I looked at that
4 paper again and I just want to say that that's a before and after design. So, each
5 of the two groups, the 10 parts per million and the 50 parts per million, what they
6 did is they have a baseline of no exposure. There are two separate groups. So
7 they took the baseline of evoked potentials and then they compared them after
8 they got the exposure for four days.

9 So, yeah, there's no control group in the traditional sense.
10 What they're doing is comparing the evoked potentials after the exposure to PCE
11 versus before. And yeah, there's no cross-group comparison. It's a before and
12 after. But it seems to me that's still a legitimate design, although it would've
13 been nice if they had then withdrawn the PCE and done one more phase and
14 shown that the values were returned back to baseline. They didn't do that,
15 unfortunately, but it seems like it's a legitimate design or at least it is as far as
16 I'm concerned. Thank you.

17 **DR. KENNETH PORTIER:** Any additional comments?
18 Dr. Pennell, your hand's still up.

19 **DR. MICHAEL PENNELL:** Yeah. Actually, I have a
20 comment about what Dr. Vorhees just said. I was one of the individuals that had
21 that concern. You know, honestly, I don't think it's a great study design, a pre-
22 post design. It doesn't include a vehicle control to make sure that if you were to
23 go through the same sort of exposure scenario minus the PERC that you

1 wouldn't get any sort of change in the neurological outcomes from comparable
2 to maybe the small doses.

3 But with that said -- and I actually also submitted this
4 when I submitted my response to this question -- in this scenario, I doubt that
5 even if you had that vehicle control that would make much a difference in your
6 decision. But again, I want to emphasize that I didn't think this was the best
7 designed study.

8 **DR. KENNETH PORTIER:** Thank you. Any
9 additional comments? Dr. Bruckner, is this the end of Charge Question 5.2?

10 **DR. JAMES BRUCKNER:** Yes. I just wanted to
11 mention that Dr. Pennell's comments are correct about some of the LOAELs and
12 NOAELs, I just didn't include those on the slide. I think we're done here then,
13 or I am.

14 **DR. KENNETH PORTIER:** Okay. I'll turn to EPA.
15 Any clarifying questions, comments?

16 **DR. STAN BARONE:** Just one clarifying comment.
17 Human variability and evoked potentials is quite well known and using the pre
18 and post design lowers the variability and the overall endpoint outcome quite
19 considerably so that you're using the same individual as their own control in
20 these studies. So, it's widely accepted in this field.

21 **DR. KENNETH PORTIER:** Dr. Pennell, your hand's
22 up.

23 **DR. MICHAEL PENNELL:** Yeah. So I would counter
24 that. I mean, I understand the pre-post does have the aspect that you are cracking

1 for the baseline of individuals. But again, if you don't have a zero dose control
2 group, you can't parse out an effective dose from an effective time or the fact of
3 just going through the same sort of experience minus the active agent.

4 **DR. KENNETH PORTIER:** Yeah. The effective agent
5 from the effect of intervention is the thing. And I like Dr. Vorhees's point about
6 if they had done a follow-up after the treatment to show a return to baseline, I
7 think that would've helped me a lot. Okay. Why don't we move onto Question
8 5.3 and see if we can get through 5.3 before lunch? Actually, let's go ahead and
9 just read 5.3 and 5.4 into the record.

10
11 **CHARGE QUESTION 5 (5.3)**
12

13 **DR. YVETTE SELBY-MOHAMADU:** Okay. Hi, this
14 is Yvette Selby again. Question 5.3: Please comment on EPA's application of
15 the PBPK model to the dose-response analysis for all endpoints and the selection
16 of dose metrics when considering the sensitivity, uncertainty, and variability of
17 the data. And this is Sections 3.2.2.2 and 3.2.5.3.

18 And then Question 5.4: EPA derived dermal HEDs by
19 extrapolating from both oral and inhalation PODs when available. Please
20 comment on the transparency and clarity of EPA's methodology for deriving
21 dermal PODs and the selection of particular values for risk estimation. This is
22 Section 3.2.5.4.1.

23 **DR. KENNETH PORTIER:** Thank you. Dr. Bruckner,
24 do you have slides for this one as well?

1 **DR. JAMES BRUCKNER:** I do. So we can take a look
2 at the first one of those. Okay. What I did here, since my area is toxicokinetics,
3 I couldn't help but want more information. So, what I've done here, before we
4 talk about the modeling, I just took a look at the information that was presented.
5 And as you can see there, in the first point, second line, I think that the
6 description here was really way too brief. It really needs to be expanded
7 considerably and not just to cite the EPA IRIS document.

8 I know you can't reproduce all the information that's
9 there, but I would urge you to go and at least pick out, particularly in the areas of
10 absorption and distribution and metabolism, some of the key references that
11 support what's being done particularly in the modeling. Just for example, there
12 was an assumption of 100 percent absorption if inhaled Perchloroethylene, which
13 I'm not sure why it's necessary to assume 100 percent absorption when there are
14 great publications, some from my web, which show, depending upon the time of
15 exposure and the concentration, about a 60 percent absorption of the inhaled
16 vapor depending on some factors. But it's really well worked out.

17 When it comes to actual data that's used for validation of
18 the models, there's a number of publications where PERC was administered
19 orally by inhalation, intraarterial injection. A lot of good data of which a few
20 cited references might be cited. I would've liked to have seen a diagram
21 showing the oxidative and the glutathione conjugation pathways. I think that
22 you'll find that in most any publication, whether it's an ATSDR document or a
23 tox profile.

1 So I'd like to see a diagram -- and when we're talking, I
2 guess I'm just having a problem with a lack of information showing what we
3 know about specific metabolites of PERC and their association or link to
4 particular adverse effects. I would've liked to have seen that more developed.
5 And then, since we're talking about using both animal studies and human
6 studies, down at that next bottom point, I'd like to see a little bit more
7 information on the relevance of animals, particularly in terms of kinetics to
8 humans.

9 For example, there was one study that -- sorry I can't point
10 to this. We're next to the bottom point. We're talking about addressing the
11 apparent contradiction. I saw a contradiction saying that, as I read it, any outside
12 PCE metabolism is more rapid. You produce more metabolites in humans than
13 in mice or in rats. But the metabolites have a longer half-life.

14 And that raised the question in my mind, does that mean
15 that one species difference cancels out the other? Of course, it depends upon the
16 metabolite. So that's where I would like to see more of what we know about
17 linking specific metabolites with specific adverse effects. I didn't see any
18 information in this section on that. I guess the last point I really made already
19 previously, so I'll stop for just a minute and see if anyone has any comments
20 before we go to modeling.

21 **DR. KENNETH PORTIER:** Anyone else want to add
22 comments? While you're putting your hands up, Jim, I was thinking about this
23 this morning. In the ADME section, I agree it needs a little bit more. And I
24 think this is in a place where the DREs should set up for some discussion on task

1 later on. What are the ADME differences among adults versus infants or the
2 elderly or ADME issues that might be related to genetic defects or whatever that
3 might affect the metabolic pathways?

4 I mean, I think there's information out there that could be
5 put here that would set us up for a little bit more effective discussion on paths
6 later on. We talked about this on the exposure side, but we haven't really talked
7 about potentially exposed susceptible subpopulations on the hazard side. But in
8 the ADME part was where I would start that conversation. Anyone else want to
9 add some comments in?

10 **DR. JAMES BRUCKNER:** I think that's a great idea. I
11 was going to say I think that this would be the place to do it and talk about
12 differences in kinetics and metabolism.

13 **DR. KENNETH PORTIER:** All right. Exactly, and
14 how that occurs. I was reading some discussion this morning about inhalation
15 differences between infants, adults, and the elderly. You know? They're quite
16 different, but maybe we should mention that here. Dr. Apte?

17 **DR. UDAYAN APTE:** Yeah. This is Udayan Apte. I
18 just wanted to comment on one study that has come again after this report was
19 probably put together. And I've mentioned that in my written comment this is
20 from Dr. Chiu's group in Texas A&M on PBPK modeling impact of non-
21 alcoholic fatty liver disease on the PBPK model work.

22 And I think that is a very interesting study and should be
23 considered going forward, mainly because it combines the PESS issue and
24 susceptible populations and the fact that people with increased fat content are

1 going to retain this chemical longer and will have a different ADME and
2 possibly biological effects. So, this paper is essential to be considered, I think.

3 **DR. KENNETH PORTIER:** Thank you. Anyone else?
4 Dr. Lash.

5 **DR. LAWRENCE LASH:** Yes. I just want to comment
6 about some of the statements that sort of get propagated over time are -- you
7 know, this thing about PCE metabolism in this third paragraph, that it's faster in
8 rats than humans. I mean, I think there's some data to support that, but it really
9 derives from -- there was an old paper, I think back in the '60s maybe, that
10 showed that Perchloroethylene was a very poor substrate for -- you know, its
11 half-life in humans was not much longer in general.

12 And there have been a couple of studies showing that, as
13 compared to trichloroethylene, it's a porous substrate for CYP2E1. But the
14 problem is there's not a lot of data on Perchloroethylene. And a lot of the
15 comments are made either based on just a small number of old studies or it's just
16 kind of a thing that's been propagated along through time. So I'm not sure how
17 accurate that is; that's why I just wanted to add.

18 **DR. KENNETH PORTIER:** Anyone else? Who else is
19 listed on here? Dr. Hossain, Dr. Daniels, Dr. Pennell, Dr. Vorhees, anyone want
20 to comment on these four issues? Dr. Bruckner, you want to move on?

21 **DR. CHARLES VORHEES:** This is Dr. Vorhees. I put
22 my hand up.

23 **DR. KENNETH PORTIER:** Oh, oh. I'm sorry. I
24 missed that. Go ahead.

1 **DR. CHARLES VORHEES:** So part of this is to discuss
2 the issue of uncertainty. I don't know whether this is the right place to make a
3 comment on that. But just as a practical matter in the way the uncertainty factors
4 are laid out on Page 302, the agency did a really nice job of laying them out -- 1,
5 2, 3, 4 -- for the neurotoxicity. And then, when they moved onto kidney and
6 liver and reproductive and developmental, they don't lay out the uncertainty
7 factors in a nice, clear-cut way. And in fact, under some of them, it's a little
8 confusing what the uncertainty factors are that they're referring to for whether
9 it's an interspecies or intraspecies, et cetera.

10 So, I just thought if they would lay out the uncertainty
11 factors for kidney and liver and developmental and reproductive the way they've
12 laid them out for neurotoxicity, it would be much easier to understand what the
13 uncertainty factors are that they were applying and why. Thank you.

14 **DR. KENNETH PORTIER:** Excellent point. I had
15 noticed the same thing; I just didn't make a note of it. Dr. Hossain?

16 **DR. MUHAMMAD HOSSAIN:** I have additional
17 comments regarding the uncertainties on conducting the route-to-route
18 extrapolations for PBPK model. So however, the PBPK models are used
19 (inaudible) but they increase uncertainty on conducting route-to-route
20 extrapolations. For example, data from the inhalation exposures and oral
21 exposures are not equivalent. So, I think there is more discussion needed on this
22 uncertainty in PBPK model, particularly route-to-route extrapolations from oral
23 to inhalation exposure.

1 And another thing, since occupational users are exposed to
2 PCE 8 or 12 hours a day, it would not be reasonable to run the PBPK model
3 based on the human concentration column, yet 8 or 12 hours after exposure to
4 PCE per risk estimation rather than 24 hours adjustment --

5 **DR. KENNETH PORTIER:** Hello? Dr. Hossain?

6 **DR. MUHAMMAD HOSSAIN:** Yes.

7 **DR. KENNETH PORTIER:** Is anyone here? Yeah.
8 Are you done? We kind of lost you there. I wasn't quite sure if you were done.

9 **DR. MUHAMMAD HOSSAIN:** Okay. I'm done.

10 **DR. KENNETH PORTIER:** Yeah. Thank you. Dr.
11 Vorhees? Oh, hand went down. Okay. Let's see. So we've had comments
12 from Dr. Apte, we've had comments from Dr. Hossain, Dr. Vorhees. Any of the
13 other associates? Dr. Daniels? Maybe I should ask Dr. Bruckner if this is the
14 last slide or we have another slide that you want to go through.

15 **DR. JAMES BRUCKNER:** This is the last slide on
16 kinetics. We have another slide now on PBPK.

17 **DR. KENNETH PORTIER:** Why don't we move to
18 PBPK? Because I know Dr. Daniels and Dr. Pennell and Dr. Hossain and Dr.
19 Apte all want to probably comment on the PBPK modeling.

20 **DR. JAMES BRUCKNER:** Okay. If we begin at the
21 top, what I would like to see is -- again, you read the first sentence. I'd like to
22 see a discussion here expanding considerably. There's really very little
23 information given here. Actually, these are the same recommendations we made
24 for the trichloroethylene risk assessment, although in the PCE, there was actually

1 more information given. I'd like to see, just for the general reader, a description
2 of what a model is and how it can be used to reduce uncertainty in risk
3 assessments. And I think it would be a good idea just to describe or give an
4 illustration of the basic model structure that Chiu and Ginsberg developed.

5 That's, of course, the model that's being used in the risk
6 assessment and the only one I think that needs to be addressed here since most of
7 the models have evolved into that one. And then just an explanation, again for
8 the reader, of actually how the models were used, sort of a step by step on how
9 they were used in the route-to-route and interspecies extrapolations to determine
10 the human equivalent concentrations. You know, it's very simple but it may not
11 be apparent.

12 In this document, we've simply talked about models were
13 used to derive these, but just the simple steps in how you actually determine in
14 route-to-route how you would begin with an inhalation or an oral exposure. You
15 determine by the model what the concentration might be in the target tissue with
16 inhalation, and then you go to your human model and determine what inhalation
17 exposure would be required to produce that tissue concentration. So just a real
18 simple explanation of how that modeling was utilized in the risk assessment.

19 If you look under the third from the bottom, I'm
20 concerned that there was very little information as far as the scientific
21 justification particularly. We're picking particular dose metrics. And those in
22 the tables that, particularly for the chronic human equivalent concentrations or
23 human points of departure, the dose metric wasn't even presented in the table, so
24 it's not clear actually what was used in that calculation. So, I'd like to see both

1 the dose metrics presented and some discussion or justification for why
2 particular dose metrics were chosen. That wasn't clear.

3 The last two statements, I'm going to let Dr. Pennell and
4 others and Dr. Lin who made these statements actually explain in detail what
5 their real concerns were about the model analysis and about how those results are
6 limited. So I'll defer to those people.

7 **DR. KENNETH PORTIER:** Thank you. And once I go
8 through this list, I wanted to make the point that Figure 3 in Chiu and Ginsberg
9 is a great picture of the basic model structure. And I think that figure should be
10 reproduced in the DRE. Table A-1 in the Chiu and Ginsberg is the list of all the
11 input parameters. It's a very clear, full table. It's long, so it probably would be
12 in the appendix. But I think that's another -- you know, your second item here,
13 very easy to handle by just extracting those things from the paper.

14 Maybe I'll just go down the list of associates to see if they
15 want to add any comments to this. I see Dr. Daniels' hand, but let me first as Dr.
16 Apte if he wanted to add anything on PBPK models.

17 **DR. UDAYAN APTE:** No. Not anything else other than
18 the paper I mentioned in the previous comment.

19 **DR. KENNETH PORTIER:** Good. Dr. Daniels?

20 **DR. MICHAEL DANIELS:** Okay, thanks. Yes, I had
21 some kind of major issues and I'm sure Dr. Pennell did as well, in particular on
22 the PBPK modeling and not the model itself but the way they used to kind of fit
23 it in quotes. So I went back to that original Chiu and Ginsberg paper and went
24 through that carefully and their supplementary materials and all that stuff. And

1 after reading through it, the first thing I thought of is, how on God's green earth
2 did this thing ever get published? Because the analysis is just a mess.

3 So they're using something called Markov chain Monte
4 Carlo. Just think about it as a way to kind of get point estimates and to kind of
5 characterize uncertainty about all these quantities that are going to be of interest
6 in terms of finding PODs and that sort of stuff. And basically, it doesn't work
7 like it's supposed to, so it doesn't kind of converge if we want to use that sort of
8 terminology. And there's multiple reasons why it might not converge.

9 There's a bunch of different possible estimates that kind of
10 fit the data sufficiently well. It could be that the model is so complicated, even
11 with some of the prior information they bring in, there's identifiability issues.
12 So, it doesn't know where it's kind of going in terms of doing the estimates. Or
13 an issue that happens with this way of fitting it in terms of the algorithm isn't
14 working particularly efficiently, sometimes called mixing. So it could be any of
15 those three things.

16 There's very different implications of all those three
17 things, and they kind of say, well, it could be one of the former two that I
18 mentioned. But they don't really kind of explore what it is at all. And they have
19 this basically model-fitting procedure that didn't converge. And then they're just
20 drawing all the conclusions in the result section which is what's informing the
21 EPA document from that.

22 So, I think there's multiple issues here. One is I don't
23 think, if you're going to be scientifically principled at all, you can use anything
24 that's in that paper in terms of the results. The model itself, yeah. Fine. But the

1 results? I don't think there's any scientific principles to doing it because it's
2 incredibly ad hoc.

3 There's two different things they can do. They could've
4 done a more careful full evasion analysis which they mentioned in the
5 discussion, but then they said, well, that's probably too complicated and I don't
6 think it's going to change anything. Well, that's not true most likely. The other
7 thing is, in terms of how they're doing it, one advantage of using a full evasion
8 analysis of these PBPK models is to kind of get uncertainty right. And because
9 this thing isn't converging appropriately, they can't really get uncertainty at all.

10 So, they do all these ad hoc checks as predictions from the
11 model which didn't converge and how well it matches up with the data. So I
12 think, on some level, I know this paper was published. But module of the paper
13 being published, I don't think it would be a good idea to use any of the
14 conclusions and the results from that paper in any sort of science-based risk
15 evaluation. And I have more details in the writeup that I sent to Dr. Bruckner.
16 Thanks.

17 **DR. KENNETH PORTIER:** Thank you, Dr. Daniels.
18 Dr. Hossain, did you want to add anything to this?

19 **DR. MUHAMMAD HOSSAIN:** No additional
20 comments.

21 **DR. KENNETH PORTIER:** Thank you. Dr. Lin?

22 **DR. ZHOUMENG LIN:** Yes. I have quite a lot of
23 comments on this model. First of all, I have reviewed the paper by Chiu and

1 Ginsberg 2011. In addition, I request the model coder from Tamue and I looked
2 through the model coder.

3 My first comment is about overall documentation of the
4 DRE document and the risk paper. The documentation in the DRE document
5 regarding this PBPK model is too concise. It's just very brief, not enough
6 details. On the other hand, the paper by Chiu and Ginsberg 2011, I would say
7 that among all PBPK papers that I have read, the description is -- I'll say I
8 would divide it to two parts.

9 In terms of justification of the model, why we model this
10 pathway and why we use these model structure, why we use those metrics. The
11 model structure is properly justified. And regarding your diagram of the ADME
12 process, actually, this paper has a very nice diagram.

13 And in addition, regarding the calibration and the
14 evaluation, I would say the model is rigorously calibrated by the available
15 technology at that time, early 2010. At that time, the software was most
16 commonly used, you know, to do the PBPK modeling.

17 So, inclusion of data for calibration and evaluation are
18 reached and are properly described. They basically have data for calibration, and
19 then they have independent dataset for evaluation. And the evaluation criteria is
20 to say data predicted versus observed data. The difference is most of the time is
21 reading two folds the difference, which was acceptable. According to WHO
22 PBPK modeling guidelines, there was some data they are (inaudible), but no
23 majority, so this is fine. This is in terms of calibration and evaluation.

1 However, Dr. Daniels just now raised another point about
2 Bayesian analysis. This part, I agree that the description is not so detailed. It
3 would be very difficult to report these results. But overall, the quality of this
4 model in the paper is pretty nice. There is some limitation, as Dr. Daniels said,
5 that overall is good.

6 Now my second question is about reproducibility of the
7 results. And the availability of that final complete model codes for future
8 reference. So, first of all, in the DRE document, they refer to Chiu and Ginsberg
9 2011b regarding the PBPK model code. But this reference is not listed in the
10 DRE document. This reference is missing. I had to request from Tamue to
11 obtain this code. So, this should be added.

12 Second, the model was developed using a legacy software
13 program called XLX, ACXLX (phonetic). This software was a commonly used
14 software at that time, but unfortunately, this software was discontinued by the
15 company in 2015. So, now, very few people have license to run this model. For
16 me, I used to develop a model using this software, but now I no longer have this
17 software. So it will be difficult for people to use it to report use of the result
18 unless they have the legacy software.

19 And then, regarding the model coder, first of all, your
20 paper is pretty good at providing some key equation and there is some
21 descriptions. This is fine from publication purpose, even though I would hope
22 that they post the entire code equation, you know, supplementary. Because key
23 equation, the actual code are somewhat different and it will take time to write a
24 whole code.

1 And then, when I look in the model coder, I feel that this
2 is not -- the final code is not completed because many of the parameters have the
3 value of one or zero. That means this is not the final model code. It was the
4 final parameter values, even though the final parameter values did state in Table
5 A-1, as Dr. Portier said. But if anyone gets this final model, try to run it, it's
6 impossible to get the result described in the paper because the parameter value is
7 1.0 under 0.1.

8 So, I suspect that based on my experience, this is why I
9 suspect that this is just the model structure. And then you also may have many
10 (inaudible) files to run each scenario. Each exposure scenario has at least
11 scenario-specific parameters. It may not have a lot of (inaudible) files, but these
12 (inaudible) files are not available.

13 For this model, you typically include a main model code,
14 and there are lots of other supporting files, data files. And then, together, it
15 becomes a workstation. When I send models to people, when I review models
16 that's viewed using this software, typically they stay in the entire workspace and
17 then with some instructions so that I can reproduce the result.

18 But anyway, for this, with the available information
19 provided by the agency, by this document, I'm not about to report just the result.
20 So I suggest that, if possible, agency convert the model to a contemporary
21 software program such as Berkeley Madonna and add language and then provide
22 some documentation regarding how to reproduce the result. It'd be important for
23 the future application perspective.

1 Now my next comment is about the selection of four dose
2 metric. The selection of this four dose metric is properly justified in the paper by
3 Chiu and Ginsberg 2011. This is fine. However, unfortunately, in the DRE
4 document, this dose metric is inconsistent in different places. Like I found at
5 least three places mention about this four dose metrics, and the four dose metrics
6 are different. For example, in Section 3.2.2.2, they list the four dose metrics.

7 And one of the dose metrics is AUC of PCE in blood, and
8 another of the dose metrics is the rate of kidney GSH conjugation. This is one
9 place. However, in the section of 3.2.5.3.2 in the appendix E, Benchmark Dose
10 Response Analysis, the dose metrics become PCE AUC liver dose metrics.

11 So previously it says PCE AUC in blood, but now they
12 actually analyze the data of PCE AUC liver. So I'm confused. Exactly which
13 dataset are used to do that dose response analysis?

14 In addition, in a paper by Chiu and Ginsberg 2011, it is
15 clearly mentioned that PCE produced in the liver and excreted directly to urine is
16 not included since it does not reach target organs or (inaudible). In this regard,
17 how can the agency use the way of GSH conjugation as a key dose metric? This
18 is contradictory to what is described in the paper.

19 So, anyway, my point is that the paper is fine but the DRE
20 document, several places regarding the dose metrics description is inconsistent,
21 causing difficult time to understand it. And this one comment.

22 Okay. Another comment is I mentioned before regarding
23 (inaudible) test to -- regarding how PBPK estimation is actually performed. I
24 suggest the agency to describe how the PBPK model in human simulation was

1 performed. What's the duration? Is it two years exposure? Or if it is lifetime
2 exposure, is it from adult to 70 years old or from adult to 80 years old, or from
3 birth to death?

4 Because the dose metric is every study AUC. That means
5 it depends on the AUC and the length. Because we will end up with total AUC
6 divided by the duration. So, it's important to know the duration used in the
7 PBPK estimation. So I would request the agency provide some description about
8 how the scenario was simulated.

9 Okay. My last two comments are minor. In Line 6477 to
10 Line 6479, I think that is not correct. The sentence is wrong. The sentence
11 should be changed to, the model predicts decreasing oxidative metabolism from
12 mice to rats to humans, meaning that humans are predicted to receive a smaller
13 internal dose to metabolize and a large internal dose of (inaudible) for the same
14 applied dose compared to rodents, after accounting for body weight. The
15 sentence should be fixed.

16 And last minor comment is Line 7979. It is mentioned
17 that DMCF ppm is derived from a PBPK model, but it doesn't specifically
18 clarify what this factor means, how it is from. Is it inhalation, dose metric,
19 conversion factor from what to what? Conversion from what to what is not very
20 clear to me. That's all for my comments about the PBPK model. Thank you.

21 **DR. KENNETH PORTIER:** That's a lot. Thank you.
22 Dr. Pennell, do you want to add any comments?

23 **DR. MICHAEL PENNELL:** Yeah. So I agree with a
24 lot of the comments Dr. Daniels made. I'm not a PBPK modeler. I mean, I've

1 had to review this stuff in the past, another model by Dr. Chiu for TCE. And my
2 impression of it is there is a lot of identifiability problems, and in these Bayesian
3 analyses, in order to get things converged, you do have to specify very
4 informative priors.

5 So, with that said, it concerns me that they didn't do any
6 sensitivity analyses or full Bayesian analysis to give an adequate analysis of the
7 uncertainty of their estimates because of those issues.

8 As I've maybe kind of alluded to, in TCE, it seemed like
9 they did a pretty good job with that. And I don't know what it is, you know, that
10 these data, if it's more limited, that wouldn't have made that possible, I don't
11 know. But if they're not going to do those analyses, there needs to be a bit more
12 discussion of why they weren't done because I think they could've added very
13 important information to the assessment.

14 **DR. KENNETH PORTIER:** Is that it, Dr. Pennell?

15 **DR. MICHAEL PENNELL:** Yes.

16 **DR. KENNETH PORTIER:** Thank you. Let's see.

17 Who else? Dr. Vorhees.

18 **DR. CHARLES VORHEES:** I don't have anything to
19 add.

20 **DR. KENNETH PORTIER:** Good. This is Ken Portier.
21 I have something to add to the comments by Dr. Lin, Dr. Daniels, and Dr.
22 Pennell. I actually got quite interested in this PBPK model and I also
23 downloaded a copy of the code. And not having access to the application

1 software that the model was run on, I actually proceeded to convert this to OR
2 (phonetic).

3 And I have a version of the model that actually is running
4 in OR, or mostly running in OR. So, I can at least kind of verify the fact that this
5 model is able to be converted and able to be run.

6 On some of the issues that came up, on the Bayesian
7 analysis, most of it is assuming a log uniform prior, which to my way of thinking
8 is pretty non-informative rather than the informative priors that Dr. Pennell was
9 kind of mentioning. And in a lot of cases, those parameters set to one are
10 parameters that were a certain weight to body weight. And then the Bayesian
11 analysis is basically changing that one value to be around a mean of one and a
12 variance of one on this log uniform prior distribution. So they're not actually
13 varying the parameters, they're varying a ratio to the background value.

14 My biggest problem with being able to run this and
15 reproduce the results is that there's no scenario data in the code. It doesn't tell us
16 -- for example, if the model were used for analysis for a specific endpoint -- what
17 the inputs are. We're have the physiological parameters on the model defined.
18 But what we don't have are things like, you know, for a specific scenario, what
19 was the concentration coming in? What were the molecular weights of the
20 animals, whether it was an IV dose or an inhalation dose or a drinking dose?

21 Those kind of things are not in the model and they're not
22 clearly in the paper, and they're not in the code files. So actually reproducing
23 the results and showing whether the PBPK model was used properly is very
24 difficult here.

1 I agree that the Chiu paper kind of focuses on variability.
2 I'm not sure they focus on uncertainty. And they talk about doing a sensitivity
3 analysis, but I think their concept of sensitivity analysis was more the calibration
4 analysis that Dr. Lin was talking about, rather than a true sensitivity to the
5 critical endpoints.

6 So there's a lot that could've been done with this model to
7 really improve our confidence and its use here, but I don't think it has been done.
8 And I suspect it's not going to be done before this DRE is rolled out before the
9 end of the year. So, I'm not quite sure what the take home message in all of this
10 is.

11 I think that the easiest thing is whether the non-Bayesian
12 model, the standard PBPK model, could be parameterized, rolled out in
13 something like OR with the scenario models, so that those of us who at least
14 have an understanding of the model and an understanding of the code could have
15 reproduced and come back and basically say, yeah, at least all the parts fit.
16 Everything flows correctly. All the equations in the model are properly coded.
17 That kind of analysis could've been done here.

18 So I kind of add my results, my conclusion of serious
19 reservations to the prior conclusions on this. But I'm not sure, Dr. Bruckner,
20 what the take home message is going to be on this. And with that, I'll end my
21 conclusion.

22 So I'm going to continue to play with the model, simply
23 because I'm interested in actually understanding how it's working. And it's not
24 clear to me that everything isn't there somewhere between the paper and the

1 code. It's just taking hours to find it and put it in place. Dr. Bruckner, I'm going
2 to turn it back over to you for some final comments.

3 **DR. JAMES BRUCKNER:** Okay. I'd like, on this last
4 issue, to propose we have a subcommittee. Let's call it of yourself and at least
5 three other individuals to see if we can't craft something that we conclude as a
6 recommendation. I'll try to write that up once we get consensus.

7 But if we could perhaps draw on each person's expertise --
8 some of the statistics are beyond my area of expertise. So, I'd like to see if we
9 can't continue with this to come up with something that everyone can sign off
10 on, that is that subgroup, that's reasonable.

11 **DR. KENNETH PORTIER:** I think, for the committee
12 minutes, what's reasonable is to come up with a list of what these serious
13 reservations are and kind of describe them. Again, I'm not confident as to what
14 the next step is because the next step is a major analysis. The next step is to take
15 this model and rework this -- I guess it's a 10-year-old study now, and kind of
16 rework it, re-describe it. The model's used in a lot of scenarios here, so it's
17 months of work to actually make this fit back into this structure here.

18 We can certainly make the recommendation that EPA do
19 that work and provide some guidance on what a minimally acceptable rework
20 might look like. And maybe that'll be a good goal of this subgroup with Dr.
21 Daniels, Dr. Pennell, Dr. Lin, and I.

22 **DR. JAMES BRUCKNER:** Okay. I think that sounds
23 reasonable.

1 **DR. KENNETH PORTIER:** Yeah. And Dr. Daniels,
2 your hand's up?

3 **DR. MICHAEL DANIELS:** Yeah, I just wanted to just
4 kind of reiterate that the analysis they did, in terms of the model setting, is just
5 not correct and the thing didn't converge. It's like you have some software and
6 you fit some model and it crashes every time, so you don't worry that it crashed.
7 You just take, like, the last primary value before it crashed and say, well, that's
8 my primary estimate. And even having the code and having it wrong, the last
9 thing you'd want to do is reproduce the results that they have because the thing
10 just doesn't work.

11 My guess is the model's so complicated and with all these
12 identifiability issues, to really get it to converge properly, you'd have to kind of
13 write very specialized code to do it. Yeah. So, again, just to emphasize that I
14 would not be comfortable at all with any sort of conclusions in the DRE being
15 based on the conclusions from when they fit that PBPK model.

16 **DR. KENNETH PORTIER:** Yeah. Mike, I was just
17 counting how many variables have hyperparameters assigned to it in the model
18 and it's probably over priority. So this could be 20, 50-dimensional in a
19 Bayesian context and I'm not surprised it didn't converge. You know? I'm not
20 sure any code could handle that.

21 **DR. MICHAEL DANIELS:** Right. Yeah, yeah. I was
22 just going to say I'm not surprised at all that it didn't converge, because it's an
23 extremely complicated model. But it's just -- I don't know. I just find it

1 partially shocking in that it didn't converge and then they just used that for the
2 analysis and the conclusions.

3 That's the thing that's kind of -- yeah, because it's going
4 to be a very complicated model with all the parameters and probably limited data
5 to actually get something like that to converge. But it doesn't mean you should
6 have it not converge and then use everything they fill out.

7 **DR. KENNETH PORTIER:** But in the deterministic
8 sense, if we leave out the Bayesian approach, assuming just the systems of
9 differential equations with the baseline parameters that they assigned, it's
10 solvable. You come up with a solution. And in fact, I think as Dr. Lin
11 mentioned, when they did that, they get pretty good comparisons back to the
12 original data. So, when they do a scenario based on a study and compare the
13 model-predicted results to what they got in the study, they can get a pretty good
14 fit within a two-fold or three-fold fit.

15 Where convergence crashes is when you take it to that
16 next level and you start assigning hyperparameters and trying to really get at a
17 global uncertainty on the model. So what I was trying to recommend is that, in
18 the short-term, they do more of a, fit the deterministic model, discuss the fit, and
19 then maybe do some limited sensitivity and forget trying to look at global model
20 uncertainty. Dr. Daniels? Did you want to --

21 **DR. MICHAEL DANIELS:** Yeah. I mean, to kind of
22 do the proper fully Bayesian thing, it's like, that's not going to happen in the
23 next however many months, if it can even happen at all. So, what you're

1 suggesting is probably the only realistic kind of way forward probably at this
2 point. But yeah. Thanks.

3 **DR. KENNETH PORTIER:** Dr. Pennell, you want to
4 jump in?

5 **DR. MICHAEL PENNELL:** Yeah. I like that idea too.
6 My comment earlier about needing to set informative priors is -- and not
7 necessarily that all of their priors they set in this analysis were informative, but
8 in order to get things to converge, they probably have to set it so informative that
9 they might as well just do what you recommend where they do these
10 deterministic analyses and then do pretty thorough sensitivity analyses on inputs.
11 That'd probably be a lot easier for them to do than try and tweak this model
12 further. So I like that.

13 **DR. KENNETH PORTIER:** Yeah. Dr. Lin?

14 **DR. ZHOUMENG LIN:** Hi. I would like to make a
15 comment on what Dr. Daniel and Dr. Pennell just mentioned. So, first of all,
16 sensitivity and analysis, I think, in the paper, they have already done that. They
17 did a local sensitivity analysis. And this is a very traditional approach that is
18 typically used in the field of PBPK modeling. So sensitivity has been done.

19 The other thing is regarding the application of Bayesian
20 analysis in this PBPK model. In our lab we recently incorporated Bayesian-
21 based mockup (inaudible) submission to PBPK models, so I understand that they
22 could have done better by including the convergence chain plots to show that it
23 is actually converged. And they also can mention the diagnostic criteria about a
24 convergence.

1 But the thing is, 10 years ago when people developed the
2 PBPK models. Most models don't even have multicolor simulation, let alone to
3 include Bayesian analysis. Some PBPK models, they just simulate the ADME
4 process of everything, individual. And then it is good to do for application in
5 risk assessment.

6 Now, the thing is, PBPK models have a lot of advantages
7 today, it's why agency now are using it for risk assessment. But there is also
8 some limitation. One limitation is it is complex, has a lot of parameters, require
9 extensive dataset to verify it. In many cases there are some parameters that we
10 just don't have experiment data.

11 So in order to do Bayesian analysis, we won't be able to
12 include all our known parameters into the Bayesian analysis because we just
13 don't have enough data to run the entire Bayesian analysis to convert the model.
14 So, sometimes people have to select the specific subset of the unknown
15 parameter to run Bayesian analysis.

16 And then the rationale of selecting a subset of parameters
17 is typically we do a local sensitivity analysis to identify the highly sensitive
18 parameters that really require our attention to incorporate into the Bayesian
19 analysis, so I think this is what they have done.

20 So, overall, I think I agree with Dr. Daniels and Dr.
21 Pennell that from the statistical perspective, if they had data, they could have
22 done better. But from my point of view, my background is more toxicology. So,
23 from my point of view, I see in this model they also have done their best at the
24 time with the technology that were available at the time.

1 So the model, for me, is good, the documentation because,
2 you know, Bayesian analysis could have done better. For example, in my recent
3 paper I tried to provide all the source data, the source code into the GitHub and
4 then provide a tutorial for how to reproduce the data.

5 So documentation was -- it could be done better, but
6 overall it's not perfect, but the quality is really good among the published PBPK
7 models they have read. So I just want to make a balance between these
8 viewpoints. Thank you.

9 **DR. KENNETH PORTIER:** This is Ken Portier. I
10 wanted to add another point to his. This model doesn't just output area under the
11 curve. So, there are other potential dose metrics that the model will provide so
12 that the conversation on appropriate dose metric that whatever this Bullet 4 on
13 this Charge Question 5.3 response, it's not limited by the PBPK model. It
14 should be more of a discussion about what is the appropriate dose metric.

15 And I know a lot of it is AUC stuff, but when we get to
16 the cancer discussion, I hope we kind of come back to that discussion of
17 appropriate dose metric. I think that's kind of -- oh, I know what I wanted to
18 say, too, is that I'm not quite sure how the Bayesian analysis was done with the
19 individual scenarios that were run.

20 I mean, I just can't see them running that for every one of
21 the hundreds of -- I was looking at all these charts at the end of the supplement to
22 the Chiu and Ginsberg paper. But it sounds like they actually did that or
23 attempted to do that in each of these. That was a lot of work that got done here.

1 And you're right, it's ten years ago. But it was a lot of work ten years ago as
2 well.

3 Dr. Bruckner, anything else on 5.3? Or panel? Oh, Dr.
4 Daniels, I see your hand's still up.

5 **DR. MICHAEL DANIELS:** Yeah. I just put it back up.
6 I just wanted to say one more thing. I think everybody's probably starving at
7 this point, including myself. But just to emphasize that -- just kind of harking it
8 back to what Dr. Lin had mentioned. Yeah, I agree that a simpler model
9 probably should have been ultimately set but they didn't do that. And they have
10 plots in the document that show it didn't converge.

11 And then related back to your comment, Dr. Portier, one
12 of the criteria they used to pick the best dose metrics is this plot that basically
13 says, well, this one converged the best so that's the best dose metric, and that
14 doesn't really seem like a particularly principled way to be using as a part of the
15 criteria to actually pick the dose metric.

16 Because basically, they run a bunch of chains and if they
17 kind of come together, that'd be good, which kind of suggests it's kind of, yeah,
18 that seems like it might be converging. And if they don't, it's not. So even how
19 they're picking the dose metric, they're doing it based on kind of pretty weird
20 things in terms of model converging and stuff.

21 And one final thing and then I'll just shut up basically.
22 Okay, so this table was in 2011. There was kind of very good MCMC stuff that
23 was being done kind of even from the mid-2000s, and it kind of slowly gets into
24 different areas including probably the PBPK area as well. But I don't think

1 that's kind of much of a justification of, okay, so yeah it was complicated. It was
2 2011, so we should give them a pass. And I'll officially shut up now.

3 **DR. KENNETH PORTIER:** Dr. Bruckner.

4 **DR. JAMES BRUCKNER:** You have my blessing to go
5 to lunch.

6 **DR. KENNETH PORTIER:** That's what I wanted to
7 hear. I have just at 1:30 Eastern Time. I would like to reconvene at 2:15, give us
8 a 45-minute lunch break. And we'll continue with Question 5.4 at that time.
9 Thank you.

10
11 **[BREAK]**

12
13 **DR. KENNETH PORTIER:** Hopefully everyone has
14 returned. I have 12:15. I'd like to continue the discussion. The panel has
15 completed its comments on Question 5.3, but I did not ask EPA if they had
16 additional comments or questions on the discussion, especially around the PBPK
17 model. Discussion that we had in the last hour.

18 **DR. YVETTE SELBY-MOHAMADU:** At this time,
19 EPA does not have any comments or questions.

20 **DR. KENNETH PORTIER:** Thank you. Dr. Bruckner,
21 your hand's up. I don't know if you just forgot to put it down or you've got a
22 final comment you want to make on 5.3.

23 **DR. JAMES BRUCKNER:** I forgot again.

1 **DR. KENNETH PORTIER:** Okay. Good. I think, at
2 this point, I estimate that we're about an hour behind our published agenda, just
3 a warning for those listening in. But my goal is still to get through what we
4 proposed to get through today.

5 We may run a little bit long, and we may run a little bit
6 short. But that's the nature of these kinds of meetings. We do what we do. I'm
7 not going to cut conversations short if I feel like the conversations are being
8 productive. So, speaking of that, let's move on to Question 5.4 about dermal
9 HEDs, extrapolations --

10 **MS. TAMUE GIBSON:** Excuse me, Dr. Portier?

11 **DR. KENNETH PORTIER:** Yeah?

12 **MS. TAMUE GIBSON:** Would we like to do the roll
13 call at this time?

14 **DR. KENNETH PORTIER:** Oh, that's right.

15 **MS. TAMUE GIBSON:** Yes.

16 **DR. KENNETH PORTIER:** The roll call, yes. Thank
17 you for reminding me. See, I'm running along here.

18 **MS. TAMUE GIBSON:** Yes.

19 **DR. KENNETH PORTIER:** Dr. Anderson?

20 **DR. HENRY ANDERSON:** Present.

21 **DR. KENNETH PORTIER:** Dr. Barton? Dr. Barton?
22 Dr. Bennett?

23 **DR. STEVEN BENNETT:** I'm here.

24 **DR. KENNETH PORTIER:** Dr. Blystone?

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DR. SHERI BLYSTONE: I'm here.

DR. KENNETH PORTIER: Dr. Bruckner?

DR. JAMES BRUCKNER: Here.

DR. KENNETH PORTIER: Dr. Cory-Slechta?

DR. DEBORAH CORY-SLECHTA: I'm here.

DR. KENNETH PORTIER: Dr. Davies?

DR. HOLLY DAVIES: Here.

DR. KENNETH PORTIER: Dr. Doucette?

DR. WILLIAM DOUCETTE: Present.

DR. KENNETH PORTIER: Dr. Gilbert?

DR. KATHLEEN GILBERT: I'm here.

DR. KENNETH PORTIER: Dr. Johnson?

DR. MARK JOHNSON: Online. I'm here.

DR. KENNETH PORTIER: Thank you. Dr. Kaufman?

DR. ALAN KAUFMAN: Here with bells on.

DR. KENNETH PORTIER: Dr. Kissel? Dr.

Rowlands?

DR. CRAIG ROWLANDS: I'm here.

DR. KENNETH PORTIER: Ruthann Rudel?

MS. RUTHANN RUDEL: Yep, I'm here.

DR. KENNETH PORTIER: Dr. Schlenk?

DR. DANIEL SCHLENK: Here.

DR. KENNETH PORTIER: Dr. Apte?

DR. UDAYAN APTE: I'm here.

1 **DR. KENNETH PORTIER:** Dr. Cobb?

2 **DR. GEORGE COBB:** I'm here.

3 **DR. KENNETH PORTIER:** Dr. Daniels?

4 **DR. MICHAEL DANIELS:** Here.

5 **DR. KENNETH PORTIER:** Dr. Grant?

6 **DR. STEPHEN GRANT:** Here I am.

7 **DR. KENNETH PORTIER:** Dr. Hossain?

8 **DR. MUHAMMAD HOSSAIN:** I'm here.

9 **DR. KENNETH PORTIER:** Dr. Lin?

10 **DR. ZHOUMENG LIN:** Hi, I'm here.

11 **DR. KENNETH PORTIER:** Dr. Meliker?

12 **DR. JAYMIE MELIKER:** Yes, I'm here.

13 **DR. KENNETH PORTIER:** Thank you. Dr. Roby?

14 **DR. KATHERINE ROBY:** Yes, I'm here.

15 **DR. KENNETH PORTIER:** Dr. Vorhees?

16 **DR. CHARLES VORHEES:** I'm here. Can you hear

17 me?

18 **DR. KENNETH PORTIER:** Yes.

19 **DR. CHARLES VORHEES:** All right.

20 **DR. KENNETH PORTIER:** Dr. Willhite?

21 **DR. CALVIN WILLHITE:** Here.

22 **DR. KENNETH PORTIER:** Dr. Pennell?

23 **DR. MICHAEL PENNELL:** Here.

24 **DR. KENNETH PORTIER:** Let's see. Dr. Barton?

1 **DR. CHARLES BARTON:** I'm here. I had talked to
2 you with my mute button earlier.

3 **DR. KENNETH PORTIER:** Okay. Good.
4 Everybody's here and present. So let's proceed with --

5 **DR. LAWRENCE LASH:** Oh, and Larry Lash is here.

6 **DR. KENNETH PORTIER:** Oh, how did I miss Dr.
7 Lash?

8 **DR. LAWRENCE LASH:** I don't know.

9 **DR. KENNETH PORTIER:** I don't remember. I
10 thought I heard you say here.

11 **DR. JOHN KISSEL:** John Kissel.

12 **DR. LAWRENCE LASH:** Yeah, no.

13 **DR. KENNETH PORTIER:** Oh, John. That's right.
14 Kissel.

15 **DR. JOHN KISSEL:** Yeah, I'm on also.

16 **DR. LAWRENCE LASH:** Okay.

17 **DR. KENNETH PORTIER:** Got it. Okay. I knew
18 everybody was here. Thank you for chiming in if I missed you. Dr. Lash, that's
19 twice I've missed you. I'm going to have to put you in bold on here. Okay.
20 Move to Question 5.4. Again, a fairly large discussion group led by Dr. Johnson.
21 Dr. Johnson?

22

23 **CHARGE QUESTION 5 (5.4)**

24

1 **DR. MARK JOHNSON:** Okay. I'm going to
2 summarize the comments I got so far from the team. So basically I think, based
3 on the comments I got, everyone thought that the approach that the EPA used to
4 extrapolate dermal PODs from inhalation PODs was reasonable and transparent.
5 In fact, some even did the math, got the same numbers. That's always good.
6 But there also was a fairly large agreement that the EPA's methodology for
7 deriving dermal PODs from extrapolation from oral PODs wasn't clear.

8 And I think what they did is they pretty much normalized
9 everything to the oral dose, but it just wasn't clear to others who reviewed it.
10 The selection of particular values for risk estimation is mentioned and selected
11 for neural POD values. But the justification for selection of these particular
12 values are not specifically provided. And in that sense, that's all I have. So, I'd
13 like to turn it over to the individual reviewers if they would like to add to that.

14 **DR. KENNETH PORTIER:** Sure. Let me run down the
15 list. Dr. Bruckner, anything to add? Dr. Cory-Slechta?

16 **DR. DEBORAH CORY-SLECHTA:** Sorry. No, I think
17 that kind of summarized my thoughts about it.

18 **DR. KENNETH PORTIER:** Thank you. Let's see. Dr.
19 Meliker?

20 **DR. JAYMIE MELIKER:** Sorry, just taking a little
21 while to get off mute. No, I really didn't have anything else to add either.

22 **DR. KENNETH PORTIER:** Okay. Dr. Pennell?

23 **DR. MICHAEL PENNELL:** I just have one more thing
24 to add, and the rest of the comments very well summarized what I thought. The

1 EPA states that the most robust values were selected for use in risk estimation.
2 Okay? According to 310, when both oral and inhalation drive values were
3 available, the smallest POD was usually chosen which makes sense from a
4 precautionary principle standpoint but is not overly conservative because they're
5 all within a factor of two. But the only exception to this practice I saw was for
6 the -- do we just want to save this? Because this is about cancer.

7 **DR. KENNETH PORTIER:** Well, you can say it here
8 and then say it again in cancer.

9 **DR. MICHAEL PENNELL:** Okay.

10 **DR. KENNETH PORTIER:** Yeah. You can say it here
11 and then say it again in cancer.

12 **DR. MICHAEL PENNELL:** Okay, okay. All right.
13 Yeah. It's hard to parse some of these out because it's overlapped so much. So
14 the only exception to this practice I noticed was for the cancer dermal POD. The
15 hepatocellular tumor POD derived from oral exposure, that was used even
16 though it was twice the value of the inhalation drive POD. And that's perhaps
17 where that robust criterion comes into play, but it wasn't clear to me what makes
18 the value more robust, and so some clarification is needed. And I guess I'll say
19 that again later.

20 **DR. KENNETH PORTIER:** Thank you. Dr. Vorhees,
21 anything?

22 **DR. CHARLES VORHEES:** I didn't have anything to
23 add on this one.

1 **DR. KENNETH PORTIER:** Dr. Willhite? You're not
2 muted in Webex. Your phone might be muted, Calvin.

3 **DR. CALVIN WILLHITE:** I'm finger challenged here.
4 I don't have anything on this, but I'll wait until 5.5.

5 **DR. KENNETH PORTIER:** Okay. Good. And I know
6 Dr. Kissel's got his hand up. John?

7 **DR. JOHN KISSEL:** Yeah. So I had asked a clarifying
8 question on Tuesday because I was confused about the dermal carcinogenic
9 slope factor generated from inhalation data. And I ultimately decided that I think
10 what EPA did is consistent with what they've done before, but they've labeled it
11 differently and that's unnecessarily confusing. In our previous experiences, EPA
12 has converted inhalation dose to an equivalent dermal dose by correcting for
13 both inhalation rate and body weight and an assumed incomplete efficiency of
14 absorption via the lungs.

15 I think that's what they did here also, but they just didn't
16 say it that way. So, in this oral to dermal, at least for the -- actually, I searched
17 the whole document and oral to dermal only appears in tables. It doesn't appear
18 in text anywhere. So I think it's a misnomer, and this is my problem. If you
19 look at Table 3-10 -- and it's actually at the bottom of it where the cancer stuff
20 is, so that's on Page 315 of the DRE -- there are eight columns in the table. The
21 fourth one is labeled inhalation to dermal HED, and the fourth one is oral to
22 dermal HED.

23 And what they really are is the first one -- the fourth one is
24 inhalation to dermal without correction for incomplete inhalation absorption.

1 And the other one is with the correction, and it has nothing to do with oral
2 whatsoever because the study was actually an inhalation study to my
3 understanding. It's just basically, you divide by 70 percent which is the assumed
4 inhalation efficiency and you get a larger number. And the difference -- it's two
5 times because there's rounding and not because the factor was actually 0.5. So,
6 maybe EPA can clarify that.

7 But my recommendation would be that EPA have some
8 kind of a continuity consultant who would read each of these documents and just
9 check to see that the presentation is consistent from document to document
10 because, while the overall methodology is actually the same here as for carbon
11 tetrachloride, the labeling is quite different and that's just unnecessarily
12 confusing.

13 **DR. KENNETH PORTIER:** Thank you. Let's see. Oh,
14 Dr. Jacobs, you wanted to jump in with a clarifying statement?

15 **DR. KEITH JACOBS:** Yes. Can you hear me? Just
16 want to check if I'm clear today.

17 **DR. KENNETH PORTIER:** Yes. Yep.

18 **DR. KEITH JACOBS:** Great. Yeah, I just wanted to
19 clarify on those extrapolations. Honestly, I'm not too familiar with carbon
20 tetrachloride, but this is consistent with what was done for the 1-BP assessment.
21 Those are not misnomers really with how they're labeled. So we have a PBPK
22 model, which we won't go into the issues with it, but through the PBPK model,
23 you can take an animal study, whether it was oral or inhalation, and then get that

1 internal dose and then output a human equivalent HED as an oral HED, or you
2 can output the equivalent inhalation HEC.

3 So, really, maybe they need a just slight update in
4 labeling. The inhalation to dermal HED means you're taking the inhalation POD
5 from the animal study and converting it to an HED using the exposure factors
6 that are in the second column of body weight and breathing rate. You're taking
7 the HEC, really, and then turning it into a dermal HED.

8 For oral to dermal, you're taking the oral HED, which is
9 provided by the PBPK model, and really, you're just using that directly with no
10 adjustment as the dermal HED because the absorption adjustment, which Dr.
11 Kissel was referring to, is done on the exposure side as was discussed yesterday.
12 Different methods, but still the point is that the produced absorption via dermal
13 is accounted for on the exposure assessments.

14 So, on the POD side, you can just take the oral POD. And
15 of course, there's a lot of assumptions in there. But you're essentially just taking
16 the oral HED output of the PBPK model and using it directly as the dermal HED,
17 while for inhalation, you're actually converting the units, basically, by saying
18 what's the breathing rate, what's the body weight we get from milligrams per
19 meter cubed into milligrams per kilogram. It's an internal dose either way.

20 **DR. KENNETH PORTIER:** Dr. Kissel, did you want to
21 comment?

22 **DR. JOHN KISSEL:** Well, I would have to go back and
23 run the numbers again. But it looked to me that the stated assumption is it's 100
24 percent available, while the dermal dosing is -- in the exposure, the absorption

1 fraction's built into that equation. So, you're getting an absorbed dose number.
2 The absorbed dose is 100 percent absorbed, which is just kind of toxicology. For
3 oral, the text says that the oral is 100 percent dose, so the dermal and the oral
4 ought to be the same thing. So I'm a little confused. But the insertion of the
5 PBPK modeling into it is the factor that I hadn't considered.

6 I do, however, consider this to be inconsistent with the
7 stated methodology in the carbon tet DRE that we went through because, in the
8 carbon tet model, in what is the third column, there would be three factors which
9 would be the 20 cubic meters a day, the 80 kilogram body weight, and an
10 assumed efficiency, which for carbon tet, if I remember correctly, was 0.63
11 instead of 0.7, but the same idea.

12 So this is slightly different, and maybe it's because this is
13 derived from the PBPK modeling and not from just a direct computation. But
14 anyway, the fact that the phrase "oral to dermal" doesn't appear anywhere in the
15 document except in this table and in Table 4-67 suggests that explanation that the
16 methodology is inadequate.

17 **DR. KEITH JACOBS:** Thank you. I agree. We can
18 definitely add further clarification of, I think, especially where that HED oral to
19 dermal came from and explain that it is really representing the PBPK oral HED.
20 Like I said, I can't speak to comparing department's HED. Maybe they had
21 different absorption assumptions, but I don't want to get into that. But your
22 point is taken about clarity. Thank you.

23 **DR. KENNETH PORTIER:** Thank you for that
24 clarification, Dr. Jacobs. Dr. Rowlands?

1 **DR. CRAIG ROWLANDS:** I have nothing to add.

2 **DR. ZHOUMENG LIN:** Hello?

3 **DR. KENNETH PORTIER:** I'm sorry. Dr. Lin. Dr.
4 Lin, yes, go ahead.

5 **DR. ZHOUMENG LIN:** Oh, yes. I was initially
6 assigned as an associate discussant for this question so I also reviewed this
7 question. So I tried to reproduce the result by doing a calculation based on the
8 equation presented in this document. For the inhalation HED, the equation on
9 how to convert inhalation POD to dermal POD for non-cancer and cancer
10 effects, the equations are presented and explained.

11 So, I was able to calculate a number, get the same result
12 presented in the table. But it took me some time because only the equation is
13 presented and then all the others are just some explanation, but I was able to get
14 the same values.

15 For oral HED to dermal HED, there is only one sentence
16 saying the oral HEDs was used directly for dermal exposure, and then there is no
17 additional description. So I wasn't able to find where the oral HED happened
18 and how it was converted to dermal exposure.

19 So my recommendation is to present an example. There
20 are many studies, many dermal HED, so maybe just show one example how the
21 inhalation POD was converted to a dermal HED, and another example for oral
22 HED to dermal HED. Show an example and it will be clear. Otherwise, it will
23 be difficult to try to reproduce the results. That's my recommendation. Thank
24 you.

1 **DR. KENNETH PORTIER:** Thank you. Any
2 additional comments? Dr. Johnson, did you catch all of that? Any final
3 comments?

4 **DR. MARK JOHNSON:** Yes sir, I did my best.

5 **DR. KENNETH PORTIER:** Good. Any clarifications
6 or comments from EPA?

7 **DR. YVETTE SELBY-MOHAMADU:** We have no
8 additional comments.

9 **DR. KENNETH PORTIER:** Thank you. I'd like to
10 move onto Question 5.5. Let's go ahead and -- 5.5 and 5.6, we'll go ahead and
11 read those into the docket.

12

13 **CHARGE QUESTION 5 (5.5)**

14

15 **DR. YVETTE SELBY-MOHAMADU:** Okay. This is
16 Yvette Selby-Mohamadu again. EPA concluded that the reasonably available
17 evidence supports a complex mode of action for tumorigenesis with
18 contributions both from genotoxicity and non-genotoxic MOAs including
19 cytotoxicity in PPAR activation. EPA concluded that while these non-genotoxic
20 mechanisms likely play a role in tumorigenesis, a causal link for necessity cannot
21 be established and they are unlikely to be sufficient for induction or progression
22 of tumorigenesis on their own.

23 EPA's Guidelines for Carcinogen Risk Assessment
24 support a default linear extrapolation approach when the MOA information is

1 supportive of linearity or the MOA is not understood. Evidence of genotoxicity
2 supports the use of a low-dose linear assumption while other mechanisms are not
3 well enough supported to suggest a potential threshold approach. Next slide
4 please.

5 For Question 5.5: Please comment on whether the cancer
6 hazard assessment has adequately described and supported the MOA conclusions
7 and the selection of a low-dose linear model and discuss any potential alternative
8 approaches. This is Section 3.2.3.2.4.

9 And then Question 5.6: Please comment on any other
10 aspects of the human hazard assessment that have not been discussed, including
11 the data quality evaluation and the characterization of assumptions and
12 uncertainties in Section 3.2. Thank you.

13 **DR. KENNETH PORTIER:** Thank you. So Dr. Gilbert
14 and half of the panel have been assigned to this question on cancer hazard
15 assessment. Dr. Gilbert, why don't you lead off the conversation?

16 **DR. KATHLEEN GILBERT:** Okay. So, as in 5.1, I got
17 a lot of comments from the associates and I will try and summarize them. First,
18 I'll start with general comments and then segue into the description of the MOA.
19 The agency is to be commended in identifying many new publications
20 potentially impacting on the carcinogenicity of PCE. These were described in
21 Table 3-3. The discussion of this data, however, is decidedly lacking, consisting
22 largely of a laundry list of references and the table with information that doesn't
23 go beyond what could be gleaned from the title or abstract.

1 Also, with considering with what we mentioned earlier
2 that while the newer epidemiological studies were subjected to a systematic
3 review of relevance and quality in accordance with the TSCA systematic review
4 principles, none of the previous IRIS and ATSDR epidemiological studies were
5 evaluated under the TSCA systematic review principles. There, by assessing the
6 quality of relevance of only some studies but not all the studies, considered it in
7 the risk evaluation for cancer. A significant source of bias has been introduced
8 that may prevent an objective weight of evidence conclusion to be reached.

9 Other discussants also had concerns regarding the data
10 presentation and the weight of evidence. As it stands, the DRE did not really
11 present the evidential link between PCE exposure and human cancer in a
12 comprehensible or convincing way. We were told that the EPA IRIS assessment
13 “concluded” that there was a pattern of evidence associating PCE exposure with
14 several types of cancer -- specifically bladder cancer, Non-Hodgkin’s lymphoma,
15 and multiple myeloma -- and that more limited data supported a suggestive
16 effect, were available for cancers of other sites including kidney, lung, and liver.

17 However, no specific studies were referenced in the text.
18 EPA provides Table 3-3 with a summary of the epidemiological studies.
19 However, no attempt was made to integrate the new results with the old results.
20 So recommendations -- the agency should evaluate the quality and relevance of
21 key studies and of course the TSCA systematic review principles that the agency
22 relies on for understanding of the relevant epidemiological evidence considered
23 in its weight of evidence evaluation of cancer.

1 The agency should distill the old and new epidemiological
2 studies and the old and new animal studies into an understandable and
3 convincing bottom line. One of the reviewers also noted that several criteria
4 need to be included in evaluation of the epidemiological studies. And these
5 criteria will be described in detail in my written comments. So I'll segue into the
6 mode of action.

7 In the MOA section, 3.2.3.2.4, it was not clear why we are
8 considering the MOA for the specific cancers listed: liver, kidney, and blood.
9 Was it because these cancers were found in animals even if they are not found as
10 often in humans exposed to PCE? One member noted that the evidence for liver
11 cancer in rodents -- i.e., rats and mice -- is clear, but there is a concern with using
12 this endpoint for the cancer hazard assessment because what human data are
13 available are generally negative or, at best, equivocal.

14 So the recommendations -- the agency needs to explain the
15 choice of cancers used to determine the MOA. One discussant also noted that
16 the evidence for the MOA needs to take into account the role of PCE
17 metabolism. Metabolism of PCE in the liver appears to primarily involve
18 oxidative metabolism with a smaller role for glutathione conjugation. In the
19 section on the liver MOA, it's stated that previous research focused on
20 metabolite TCA. This is consistent with previous metabolism in PBPK
21 modeling sections which discusses conversions to TCA.

22 However, the only mention of TCA in the genotoxicity
23 section states, "Testing of the oxidative metabolite TCA is ambiguous because
24 interpretation of TCA in vitro results is complicated by pH changes induced by

1 the compound.” The discussant also goes on to say that, if TCA is an important -
2 - if not critical -- metabolite, why are we simply referenced to another document
3 for discussion of its effects without even a summary or conclusion based on the
4 other evaluation?

5 So the recommendation here was the role of TCA in liver
6 genotoxicity needs to be clarified in a manner that ensures continuity between
7 sections. Now, the MOA for liver cancer in the weight of evidence conclusion,
8 the agency stated that the most noble findings were increases in the incidence of
9 liver tumors in mice exposed to PCE by inhalation or ingestion.

10 So, with regard to liver cancer, the EPA considered four
11 MOA: genotoxicity, cytotoxicity, epigenetic alterations, and PPAR activation.
12 The supportive evidence for most of these MOA was minimal and/or
13 circumstantial. For example, the evidence for an epigenetic MOA seemed to be
14 that hypomethylation of proto-oncogenes occurs in the mouse liver after
15 exposure to some PCE metabolites.

16 As one member pointed out, almost all genetic pathways
17 in cancer involve signal transduction mechanisms effecting regulation of
18 downstream genes. This gene regulation is almost always accompanied by
19 changes in DNA methylation for histone modification and so on. So, unless it
20 can be shown that an agent is directly causing changes in one of these processes,
21 they should be considered biomarkers of a genetic effect.

22 So, in terms of the genotoxic MOA which is one that's
23 received the most emphasis, it appears to stem primarily from general or
24 systemic results rather than liver results. For example, Everatt described

1 increased frequencies of micronuclei in DNA damage in lymphocytes from dry
2 cleaner workers that correlated with levels of PCE and personal breathing zone
3 samples. The support for this result and other epidemiological studies was
4 equivocal. The studies of PCE-induced genotoxicity, including DNA damage,
5 mutagenicity of chromosomal aberrations in animals yielded marginal, negative,
6 or inconclusive results making it difficult to draw a conclusion one way or the
7 other.

8 In addition, one member pointed out that none of the in
9 vitro genotoxicity assays considered have been evaluated for quality following
10 the evaluation criteria for in vitro studies under the TSCA systematic review
11 principles and guidance. In terms of liver-specific genotoxicity, the results
12 seemed confined to showing that some of the PCE metabolites detected in liver
13 shows some indication of mutagenetic activity in vitro.

14 All in all, there did not seem to be a strong association
15 between PCE exposure and genotoxicity in the liver or other tissues. Indeed, one
16 discussant argued that there was more evidence of the significant contribution of
17 a genotoxic MOA in PCE-induced renal but not hepatic tumorigenesis. And
18 we'll be talking about that more.

19 So recommendation -- if the EPA wants to persist with the
20 consideration of a genotoxic MOA for PCE, it should provide a table with all the
21 positive and negative genotoxicity studies that have been inducted on PERC and
22 its metabolites. This should include study design, relevance, results, and should
23 compare this dose response to PCE, TCA, and TCA-induced genotoxicity with
24 the PBPK model.

1 Okay. For the toxic MOA, the evidence with this in liver
2 cancer was relatively thin and circumstantial but included several studies
3 showing that different types of hepatotoxicity, including increased liver weight and
4 increased serum alanine aminotransferase can be found in mice and rats exposed
5 to PCE.

6 One member pointed out that the DRE discussed
7 cytotoxicity and genotoxicity as distinct and unrelated processes. When aging
8 associated with both processes it is important to see evidence that the
9 cytotoxicity is not simply apoptosis-induced by excess genotoxicity. Other
10 members, though, were more impressed with the evidence for hepatotoxicity-
11 induced regenerative proliferation as a mechanism of liver cancer.

12 The agency also discussed the PPAR activation MOA for
13 liver cancer, as the transcription factor of PPAR activation upregulates many
14 genes associated with multiple pathways and is thought to promote
15 tumorigenesis perturbing cell proliferation and apoptosis. One discussant
16 thought there was significant data supporting a plausible MOA for PCE and its
17 metabolized induction of mouse liver tumors due to activation of PPAR.

18 However, they also note that the EPA IRIS assessment
19 described the lack of concordance of peroxisome proliferation, one of the signs
20 of PPAR activation in occurrence of liver tumors across species; and concluded
21 that PPAR activation does not play a significant role in liver carcinogenicity.

22 Another discussant pointed out that PPAR activation is not
23 a mechanism that usually translates to humans. Specifically, peroxisome
24 proliferation seems to be a predominant MOA for liver cancer in rodents, but the

1 scientific consensus is that the human liver does not respond to peroxisome
2 proliferation in the same manner as a rodent liver.

3 In summary, the EPA stated that PCE seems to reduce
4 liver tumors in mice through multiple MOA including all the four we just
5 discussed. This conclusion seemed to be based more on the fact that these
6 mechanisms can occur in the liver of PCE-induced individuals, rather than that
7 they'd actually been linked to carcinogenicity. Based on the standard default
8 that when there's evidence of genotoxicity, or when the MOA is not understood,
9 the evaluation concludes that a linear extrapolation approach is appropriate. This
10 seemed correct.

11 Oh, and another member pointed out mechanistic study
12 observations, absent a description of where and how they fit into a causal
13 pathway conceptual model from exposure to adverse outcomes, does not
14 provide, one, the ability to assess the relevance of the observations, two, the
15 biological plausibility considerations of a weight of evidence conclusion.

16 Recommendations -- it seems fair to state that, although
17 the four mechanisms may play a role, there is very little direct evidence that they
18 do and that the MOA for liver cancer is basically unknown. It is recommended
19 that the EPA either acknowledge this or provide a better justification for their
20 conclusion that these mechanisms may be involved in PCE-induced liver cancer.
21 Towards that end, the agency should evaluate the quality and relevance of these
22 studies in accordance with the TSCA systematic review principles.

23 The agency should include a biological plausibility causal
24 pathway models for each of the proposed MOA adverse outcome pathways,

1 listing the molecular initiating event and key events leading to an adverse
2 outcome (inaudible). More details on this point will be included in the written
3 comments.

4 **DR. KENNETH PORTIER:** Kathleen, one minute. Is
5 anybody else getting feedback?

6 **DR. ALAN KAUFMAN:** Yes, a little static on the line
7 from time to time.

8 **DR. GEORGE COBB:** Yes, I'm getting it.

9 **DR. KENNETH PORTIER:** Okay.

10 **DR. DEBORAH CORY-SLECHTA:** Yes.

11 **DR. KENNETH PORTIER:** Yeah. And Kathleen keeps
12 getting lighter and lighter when that happens. I just wanted to ask the Battelle
13 people to see if they can look into that and boost the signal a little bit. Please
14 continue Kathleen. Sorry.

15 **DR. KATHLEEN GILBERT:** That's okay. Does it
16 sound okay now?

17 **MS. TAMUE GIBSON:** Yes.

18 **DR. KATHLEEN GILBERT:** Okay. So I'm -- not that
19 much more to go. I'm talking about the kidney cancer MOA. The weight of
20 evidence conclusion states that aside from the liver tumor induction, additional
21 findings potentially related to treatment included increases in renal tubular
22 adenomas and adenocarcinomas in male rats exposed by inhalation. Three
23 different discussants disagreed with this relative comparison and stated that the

1 evidence supporting renal cancer instead of liver cancer being the primary cancer
2 outcome for PCE.

3 This is accompanied by numerous references which
4 they've provided. So I'm going to let them present their case and ask them if
5 they have any specific recommendations. At this time, I'm going to turn it over
6 to them. And they know who they are.

7 **DR. KENNETH PORTIER:** I was going to go down the
8 long list here and see who wants to add. And I've added to the list of associate
9 commenters Dr. Willhite because I know he's got something he wanted to say.
10 Dr. Apte? Dr. Barton? Now I'm worried. Can anybody hear me?

11 **DR. DEBORAH CORY-SLECHTA:** Yes.

12 **DR. KATHLEEN GILBERT:** We hear you.

13 **DR. MARK JOHNSON:** Yes.

14 **DR. KENNETH PORTIER:** Okay. Just wondered. I
15 will keep going down the list. Dr. Bruckner?

16 **DR. JAMES BRUCKNER:** I guess my basic position
17 was that the overall weight of scientific evidence doesn't support the genotox
18 and mode of action for our liver toxicity. I think the evidence there is mixed at
19 best and not very conclusive. I think it is very certain for our genotoxic mode of
20 action for renal carcinogenesis. And just on first glance and look at the
21 epidemiology studies, it's clear that kidney cancer and urinary tract cancer is
22 much more frequently seen than liver cancer or other types of cancer.

23 So just looking at the mechanism of action, it's clear that
24 we have a genotoxic mode of action that's been well worked out for kidney.

1 And as I said for liver, it's very dubious in my mind. So that's my basic
2 thinking.

3 **DR. KENNETH PORTIER:** Thank you. Dr. Cory-
4 Slechta?

5 **DR. DEBORAH CORY-SLECHTA:** I don't have
6 anything to add.

7 **DR. KENNETH PORTIER:** Dr. Daniels?

8 **DR. MICHAEL DANIELS:** I have nothing to add.

9 **DR. KENNETH PORTIER:** Dr. Grant, we haven't
10 heard from you recently.

11 **DR. STEPHEN GRANT:** I spoke up a little this
12 morning. I sent extensive notes which have been pretty well put forward. There
13 are a couple of things that I wanted to add were I think we are overemphasizing
14 the liver tumors. That's a really big issue. A lot of data from the animal model,
15 but the animal model involves mechanisms which don't translate well to human.
16 So, they would be more dubious to begin with.

17 One of the types of data that hasn't been considered
18 however, and I'll give you a little background -- I work on breast cancer, but I
19 work on mutagenicity in breast cancer. And every once in a while, less so
20 nowadays but in the old days a lot, an endocrinologist would challenge me and
21 say mutation isn't involved in breast cancer.

22 Well, one of the things that you can do is you can look at
23 the endpoint, which is the tumors that developed, do they have aberrant
24 karyotypes? That's an indication of genotoxicity. Do they have activated

1 oncogenes and inactivated tumor suppressor genes due to point mutations?
2 Those are indications of genotoxicity. And even if we can't see a direct
3 mechanism, then there must be an indirect mechanism. We can start talking
4 about the effects of hyperproliferation, but it still means there's a genotoxic
5 mechanism at the bottom.

6 But I really wouldn't want to defend the mechanism in
7 liver cancer because I think, again, it's well established in kidney. There is some
8 issue of assuming that a mechanism that has been well established in one tissue
9 type or cell type doesn't translate to others. It may not be that it is a stronger
10 association with kidney tumor; it may be that it's easier to prove that in the
11 kidney tumor. That's just one thing I'd like to say.

12 The other thing is I asked in the TCE evaluation for a table
13 of genotoxic endpoints, and I got my wish -- be careful what you ask for -- in
14 this one, and it still wasn't satisfying because, again, it's just a bunch of results.
15 One of the things that has to happen is there needs to be some interpretation of
16 those results. And yes, I know that can be an interpretation of bias, but not if
17 you explain why.

18 For example, not all genotoxic biomarkers are of equal
19 importance. Chromosome aberrations and micronuclei have been shown in large
20 European studies to be prospectively predictive of cancer incidence. So I would
21 say that indications that PCE causes those endpoints -- and yes, that was in the
22 lymphocytes -- is a much more important endpoint than things that don't have
23 that amount of evidence. There are some other ones that have retrospective
24 analyses, but they're not as strong as prospective analyses.

1 And I would mention, for example, that in the same
2 studies that show chromosome aberrations in micronuclei, there was no
3 association with sister chromatids exchange. This is one of those cases where
4 you see, if we simply look at the endpoints as all being relevant and all being
5 equally relevant, then we're going to see negative results that are not as
6 important as some other ones. That was one of the ways I would organize the
7 data, by the evidence that the endpoint has been more or less directly associated
8 with cancer. Okay. You know what? I think I'll leave anything else in case it
9 has to come up later. Thanks.

10 **DR. KENNETH PORTIER:** Thank you. Dr. Johnson?

11 **DR. MARK JOHNSON:** Yeah, I just have a couple
12 clarifying questions. On Page 292, Line 7473 through 7484, it presents overall
13 conclusions on cancer. And if you just read that paragraph, it talks about the
14 cancer animal data results, the complex metabolic profile. There was just some
15 data gaps that concludes the animal data represented for humans. From the
16 preceding sentences, the conclusion doesn't match. So, I would ask you to go
17 back and take a look at that and see if you can clarify that a little bit better.

18 And then, on Page 298, Table 3-4, for clarity, it would
19 help a lot if you could show which results are statistically different from
20 controls. Either you do it with the asterisk or some kind of superscript. That
21 would also help in transparency. And that's all I have.

22 **DR. KENNETH PORTIER:** Okay, okay. Thank you.

23 Let's see, who's next on my list? Where am I? Apte, Bruckner, Cory-Slechta,
24 Daniels, Grant, Johnson, Lash. Dr. Lash.

1 **DR. LAWRENCE LASH:** Yep, I'm here. Let me see.

2 Let me find my notes. So I think, actually, Dr. Gilbert summarized most of the
3 points pretty well. I think the issue is, the liver cancer -- I just don't think there's
4 any consensus that it has relevance for humans. I mean, the data are good for
5 mice in particular and the relevance for humans is just not there. I think there's
6 been a lot of studies on peroxisome proliferation and the role that it plays, and
7 there's just nothing in humans that -- I mean, it's sort of like the [alpha]-2[mu]
8 thing for male rat kidney. It's just not relevant, so this reliance on the mouse
9 kidney is kind of baffling to me.

10 Further, with regard of the comment made about the MOA
11 for kidney, the whole problem with PCE as compared to TCE is that a lot of
12 assumptions are made. I mentioned this earlier. A lot of assumptions are made
13 based on the similarities between the two, and I think there's some good
14 genotoxicity study data that are mostly in vitro but showing that the reactive
15 metabolites are mutagenic and that they're actually better mutagens than the
16 DCVC derived metabolites, the ones from the glutathione conjugation pathway
17 of TCE. So I think there's better, but we just don't have a lot of the data for
18 kidney otherwise besides those type of tests.

19 So I think the liver cancer and I also had made a comment,
20 I think -- let me find it -- yeah. So the issue also specifically for human data is
21 that I cited from -- you know, the 2014 IARC Monographs is on
22 Perchloroethylene. It's Volume 106 as cited. And in my comments that I sent to
23 Dr. Gilbert, I noted, in late 2012, that what IARC always does is, prior to
24 publication of the monograph, they publish a short summary in LANSAs.

1 So there was one published in December of 2012, and I
2 guess, just to paraphrase a couple of points that were noted, one is it talked
3 about, in particular, the epidemiology studies show positive associations between
4 PERC exposure with several cancers including bladder, esophagus, kidney,
5 cervix, and non-Hodgkin lymphoma. But they noted the only one that showed a
6 consistent pattern across studies was bladder cancer, but they also noted that --
7 and this was a particular Nordic study that had sort of the best data and that
8 corrected for other confounded factors. But they noted, you know, a relatively
9 small sample size and a modest dose response.

10 So I know, in terms of for TSCA, I guess, for using this
11 for point of departure calculations and all, that may be problematic. But I was
12 just really struck by the kind of complete absence of consideration of bladder
13 cancer. And the reliance on the mouse liver, I think, is just not appropriate based
14 on so many mechanistic sets of studies. I think my other points were pretty
15 much made. So yeah, that's what I have to add. That's it.

16 **DR. KENNETH PORTIER:** Thank you, Dr. Lash. Dr.
17 Roby?

18 **DR. KATHERINE ROBY:** Yeah, I don't really have
19 anything different to add. I think everything has been summarized really nicely.
20 I would just kind of reiterate that I agree with everyone that the emphasis on the
21 liver seems a little bit perplexing given the data really just doesn't quite support,
22 I think, that level of emphasis. But I would also like to add that Dr. Lash's last
23 comment about bladder cancer, I agree. I think that that was largely overlooked

1 but it seems like there's a strong impact there. I'm not sure why that has been
2 overlooked. And that's all I have.

3 **DR. KENNETH PORTIER:** Thank you. I know that
4 Dr. Willhite early on got interested in the cancer issue and especially the kidney
5 cancer stuff, and I think he's worked up a pretty extensive set of comments. Dr.
6 Willhite, is this a good time to jump in? Dr. Willhite, you're muted in Webex.

7 **DR. CALVIN WILLHITE:** Okay, now I'm there, eh?

8 **DR. KENNETH PORTIER:** Yep.

9 **DR. CALVIN WILLHITE:** Okay. I'm going to be far
10 more blunt than my colleagues on this particular review committee. I believe,
11 and I have a write-up that I will finalize, that we are talking about not only the
12 wrong target organ, but we're talking about the wrong species. So, here, the
13 EPA asked us whether the most scientifically robust critical health effect for
14 PCE have been identified.

15 And then, "EPA used PODs in cancer slope factors,
16 human equivalent concentration, inhalation unit risk, and dermal slope factor for
17 evaluating non-cancer and cancer risks respectively for chronic exposure to
18 Perchloroethylene." Derivation of EPA's Perchloroethylene cancer potency
19 factors were reviewed by the National Research Council ten years ago.
20 Essentially, the current document just repeats those same results.

21 The problem here -- I'll jump to the recommendation and
22 then I'll go back to the data -- the current document with regard to PCE
23 carcinogenicity is badly dated primarily due to its reliance on the animal
24 bioassay data and the IRIS discussion of PCE carcinogenic potency in animals.

1 That is mouse liver and rat leukemia. Overall, EPA currently considers PCE is
2 likely to be carcinogenic in humans.

3 Now, the TSCA dossier does not include a weight of
4 evidence presentation on PCE carcinogenicity in humans. And there is no TSCA
5 conclusion on level of confidence in the current descriptor. The current
6 descriptor is that PCE is likely to be carcinogenic to humans. The overall weight
7 of evidence from renal biochemical mode of carcinogenicity, the genotoxicity of
8 PERC metabolites present in the proximal tubule, the animal chronic
9 carcinogenicity data, structure activity relationships with TCE, and the
10 observations that dry cleaning workers who repeatedly inhaled high PCE
11 concentrations over many years are at substantially elevated risk for kidney and
12 quite likely bladder cancer.

13 Just a second here. Points to the conclusion that PCE
14 should be classified by EPA as carcinogenic to humans. At a minimum, a formal
15 reanalysis of EPA's cancer descriptor and cancer potency factors should be
16 completed prior to final public release of the Draft Risk Assessment. EPA's
17 staff in this meeting told us that they "reviewed the IRIS document" and that was
18 the end of it. So what they did is they adopted this old IRIS value that's based
19 on animal data.

20 But what we have now -- and we can look at EPA's
21 current cancer guidelines. The current guidelines state: carcinogenic to humans,
22 this descriptor indicates strong evidence of human carcinogenicity. It covers
23 different combinations of evidence. This descriptor is appropriate when there is
24 convincing epidemiologic evidence of a causal association between human

1 exposure and cancer. When we look at the data, there is no single sentinel study
2 that unequivocally describes a causal relation between occupational PCE
3 exposure and human urinary tract cancer. But the preponderance of evidence
4 taken together is strong and it cannot be dismissed outright.

5 Being just an amateur epidemiologist here, I see that there
6 are at least 13 epidemiologic reports of increased cancer of the human urinary
7 tract among dry cleaning workers exposed to PCE without concurrent exposures
8 to other known or suspected human kidney or bladder carcinogens. There are at
9 least two, Mundt (phonetic) from 2003 and McLaughlin (phonetic) and Block
10 (phonetic) from 1997, who conclude there was either no or there was inadequate
11 causal evidence for kidney or bladder cancer associated with high-dose PCE
12 exposure.

13 But look at the dates of those -- 2003 and 1997. If we go
14 over and if we look at Vlaanderen et al. 2014, our metanalysis demonstrates an
15 increased risk for bladder cancer in dry cleaners reported in both cohort and case
16 control studies and some evidence for an exposure response relationship. One of
17 the more convincing here is the retrospective analysis conducted by the National
18 Cancer Institute of 1,217 cases of kidney cancer. And they found there was a
19 statistically significant association between PCE exposure and increased risk.
20 Perdue concluded high exposure to Perchloroethylene was associated with
21 kidney cancer.

22 And that's consistent with Callahan, 2019 who found
23 elevated hazard ratios for bladder and kidney cancers among 5,369 dry cleaners
24 in St. Louis. Therefore, we have a mode of action. We have the evidence in

1 humans, the epidemiologic evidence, and we need not turn to the animal data
2 with all the confounding problems of the [alpha]-2[mu] in the male rates --
3 there's going to be some debate about that -- and certainly, the mouse liver
4 which gives us a signal of biological unwanted activity, certainly, but that's all
5 we can really use that for.

6 Therefore, it's recommended that EPA go back and update
7 and fix the cancer potency value and its basis in the old IRIS that they've just
8 taken wholeheartedly here without really going into depth on it. We need to look
9 at the human data. That's the species that's of interest. The only thing that we'll
10 have as a problem, of course -- we won't have extrapolation between species.
11 But it's the high to low dose.

12 And that's where the linear part of this calls into question
13 even though we have a genotoxic mode of action. Because we see the kidney
14 cancer and bladder cancer risk elevated, but those are at orders of magnitude
15 exposures much higher than the consumer using a spot cleaner on his carpet or
16 his shirt. So that's essentially what I found and I will get the written review to
17 the lead.

18 But probably one of the most interesting -- and these
19 studies -- Wolfgang Dekant and that group have done excellent work. And
20 they've done controlled Perchloroethylene inhalation studies in human
21 volunteers and in rats. These are papers that were published in 1998 and 1999.
22 Controlled PCE studies in human volunteers and rats at 10, 20, or 40 ppm for six
23 hours demonstrated the exposure dependent generation of genotoxic metabolites

1 and DNA adducts as a consequent, and they found that in the urine of both
2 species, both humans and rats.

3 I don't know -- we have a very clear line of reasoning we
4 can follow. We can see it in the 13 epidemiologic studies. And that, to me, is a
5 pretty solid argument how to go about doing the cancer risk assessment and
6 classification for PCE. Thank you, Mr. Chair.

7 **DR. KENNETH PORTIER:** Thank you, Dr. Willhite.
8 And I know I've seen the preliminary draft of your report. You have a lot of
9 references of all these publications, so just make sure you keep all of that in
10 when you send it to the lead. Dr. Pennell?

11 **DR. MICHAEL PENNELL:** Yes, I had a comment I
12 mentioned in 5.2 on the (inaudible) in cancer data. And you said we'd postpone
13 it until 5.5, so I'm saying it now. So, in the dose response modeling, they used
14 the multistage dose response model. (inaudible). This is sort of a default
15 mechanistic model for the carcinogens (inaudible) that have been used.
16 (Inaudible).

17 **DR. ALAN KAUFMAN:** Can we hear Dr. Pennell?

18 **DR. KENNETH PORTIER:** Yeah, I can't hear him. I
19 thought it was my earphones.

20 **DR. DEBORAH CORY-SLECHTA:** I can't hear him.
21 I'm having a lot of trouble.

22 **MS. RUTHANN RUDEL:** Yeah, I can hardly hear him.

23 **DR. ALAN KAUFMAN:** Yeah, I'm having trouble
24 hearing.

1 **DR. MICHAEL PENNELL:** Can you guys hear me?

2 **DR. KATHERINE ROBY:** No. Can we start over?

3 **DR. KENNETH PORTIER:** Well, you sound like
4 you're in a faraway room, Mike.

5 **DR. MICHAEL PENNELL:** All right. I had to switch
6 to my cell phone because --

7 **DR. KENNETH PORTIER:** I think you may have to
8 use the communicate button and disconnect it and reconnect. And we'll wait for
9 you.

10 **DR. MICHAEL PENNELL:** Can you --

11 **DR. KATHERINE ROBY:** There we go.

12 **DR. KENNETH PORTIER:** Oh, now we can hear you.

13 **DR. MICHAEL PENNELL:** Yeah, I can switch to my
14 computer for a moment just to make this comment, even though I know I'm not
15 supposed to. Yeah, I think it's an issue with using my cell phone.

16 **DR. KENNETH PORTIER:** Yeah, that's good. We can
17 hear you.

18 **DR. MICHAEL PENNELL:** Yeah.

19 **DR. KENNETH PORTIER:** Start from the beginning.

20 **DR. MICHAEL PENNELL:** Yeah, yeah. All right. So
21 I had a comment about the dose response modeling for the cancer data. They
22 used the multistage model which has been the traditional mechanistic model for
23 carcinogens. But in recent years, I've experienced that the EPA has considered

1 alternative approaches where you use different approaches to fit the observed
2 data and then you use the one in your extrapolation approach.

3 For example, this happened in the assessment of 1-
4 Bromopropane. So there, they had a few different dose response models and
5 then used Bayesian model averaging to obtain a benchmark dose estimate that
6 was averaged across those models. Also, this model averaging approach has the
7 advantage that it better addresses model uncertainty.

8 So, I felt that in light of what they've done in more recent
9 years, moved away from just always using the multistage model, I feel that some
10 discussion is needed on why they decided here to again just restrict their
11 attention to the multistage model. And that's it.

12 **DR. KENNETH PORTIER:** Yeah, Michael, that's a
13 good point. I usually pick up on that, and I didn't get to the dose response
14 appendix to check that out. But yeah, we've commented on that in the past. Dr.
15 Gilbert?

16 **DR. KATHLEEN GILBERT:** I just wanted to ask the
17 last reviewer to write up that as a recommendation and send it to me. That
18 would be much appreciated.

19 **DR. MICHAEL PENNELL:** Will do.

20 **DR. KENNETH PORTIER:** Any additional comments
21 on Question 5.5? Dr. Apte. Dr. Apte, your phone might be muted. You're
22 unmuted in Webex. In your case, your computer might be muted. There you go.

23 **DR. UDAYAN APTE:** Yeah, it was my iPad.

1 **DR. KENNETH PORTIER:** Okay. We can hear you
2 now. Well, we were hearing you. Now we've lost you again. Dr. Apte, if
3 you're speaking, we're not hearing you. Seems like we're having a few more
4 technical problems this afternoon than we've had before. I'll wait for Dr. Apte
5 to reconnect. Dr. Rowlands?

6 **DR. CRAIG ROWLANDS:** Yeah, hi. I just wanted to
7 go back to the mode of action briefly just to make, I guess, really a
8 recommendation. These four different modes of action were reviewed in the risk
9 evaluation, and that's just for the liver. And of course, kidney has its own. And
10 so when we're going through all that information, it's very helpful to have this
11 laid out very concisely in a table. And I like adverse outcome pathways, so for
12 molecular initiating event, each key event, then you have your adverse outcome.

13 And for each one of those key events, list the positive
14 studies -- and of course, everything needs to go through a systematic review for
15 quality. So list the positive studies, their quality, and the dose response, the
16 negative studies, their quality, and the dose response, and then include the dose
17 response for the cancer induction of tumor response.

18 That gives one of the ability to just look across everything
19 very clearly and see, do the doses match? Did they overlap right in the right
20 ballpark? And what is the support for the key events based on positive, negative,
21 the quality panel that's on each one of those?

22 It's very helpful to do that, and especially when we have
23 four of these we have to balance in our heads. I think that's an important -- and I
24 know I brought this up in the earlier reviews, so I hope this starts to become sort

1 of a standard approach to laying out modes of actions. That's how everyone else
2 does mode of action. When you read the literature, you go down to risk
3 assessments, they're going to have it laid out that way. It's very helpful to the
4 reviewers to see that, so I just wanted to make that recommendation.

5 **DR. KENNETH PORTIER:** Thank you, Dr. Rowlands.
6 If you could write that up and send that to Dr. Gilbert, we'd appreciate that. And
7 we might leave it in this section or we might put it in Question 7 which talks
8 about improvements for the general structure. Let's see if Dr. Apte's been able
9 to reconnect.

10 **DR. UDAYAN APTE:** Can you hear me now? Yeah,
11 I'm here. Can you hear me?

12 **DR. KENNETH PORTIER:** Yeah, now we can hear
13 you.

14 **DR. UDAYAN APTE:** Oh, okay. So you did not hear
15 any of the stuff that I said before, I'm assuming.

16 **DR. KENNETH PORTIER:** No. No, you disappeared
17 right after you said something about iPad. Boom. You were gone.

18 **DR. UDAYAN APTE:** Okay. All right. So I got rid of
19 them now. My comment is essentially related to dose response and cancer
20 endpoints. So I'll just list introductory (inaudible) comments in the bladder
21 cancers. So, in general, I was trying to figure out from the document, which was
22 not very clear, what is the most sensitive cancer of PCE? Is it the liver cancer or
23 is it something else? So there's a lot of discussion about liver cancer.

1 The previous IRIS document also has a lot of discussion
2 and I agree with Dr. Willhite that it kind of seems like they've sort of carried that
3 over. But if you consider the exposure information, the lowest possible doses,
4 and try to connect them to a cancer endpoint, what is the most sensitive
5 endpoint? And that is not really clear in this document. Is it the liver cancer? Is
6 it the kidney or is it the bladder cancers? That's what I would like to know.

7 **DR. KENNETH PORTIER:** This is Ken Portier. What
8 I hear in addition to that was that the strength of the evidence for that particular
9 cancer is human relevant, and the issue with the liver cancers was maybe the
10 evidence is not as strong. But liver cancer is the -- it may produce the lowest
11 POD, but if it's done in a framework that we're less confident that it's an actual
12 human cancer or carcinogen, the EPA cancer guidelines basically say you can
13 kind of bypass that and go to the next one. And I think that's part of the issue
14 here is we kind of need to see that discussion go on.

15 **DR. UDAYAN APTE:** Can I -- This is Dr. Apte again.

16 **DR. KENNETH PORTIER:** Yeah, sure.

17 **DR. UDAYAN APTE:** As far as the mode of action is
18 concerned, I think that the discussion from the liver cancer standpoint was pretty
19 good. They discussed PPAR-alpha and its relevance or nonrelevance, and they
20 also discussed about the [alpha]-2[mu]-globulin in kidney and its relevance or
21 nonrelevance. They did bring up studies related to DNA methylation, which is
22 basically epigenetics.

23 These mechanisms are now being understood, and this is a
24 relative newer mechanism that we are understanding. So, from that discussion, I

1 think they concluded that there is not much evidence or relatively less evidence
2 for cytotoxicity. But the epigenetic change seems to be a very relevant
3 mechanism. It is not a rodent-specific mechanism like PPAR-alpha, so I think
4 that should be considered.

5 Then I also was wondering about genotoxicity and its
6 connection to cancer. They clearly mention that there is this one study that
7 showed this massive effect after inclusion of the -- essentially an S9 fraction, so
8 metabolism plays a role.

9 And so, I heard a lot of discussion here about that being
10 relatively less relevant for the endpoint, and I was wondering why that was the
11 case. I couldn't understand. Maybe I've missed something there. And so, I
12 would like to know either from the panelists or from EPA, are we considering
13 genotoxicity as strong evidence or not, relevant evidence?

14 **DR. KENNETH PORTIER:** I see Dr. Gilbert's hand up,
15 Dr. Rowland's hand's still up, and Dr. Barone wanting to comment. I'm going
16 to go back to Dr. Gilbert as the lead first and see if she wanted to comment on
17 this.

18 **DR. KATHLEEN GILBERT:** Actually, I think I'd
19 rather hear from Dr. Barone before I make my comment.

20 **DR. KENNETH PORTIER:** Okay. Well, let Craig --
21 did you put your -- yeah, he put his hand down. Okay. Dr. Barone, you have a
22 statement or a question?

23 **DR. STAN BARONE:** Yeah, a couple clarifications. We
24 did attempt a metanalysis of the epi studies, both new and old. That's in

1 Appendix F and described in Appendix F. There was not a consistent finding for
2 the kidney cancers, unlike what was said before by Dr. Willhite. We also looked
3 at, again, in the mode of action analysis, each of the tumor types including the
4 blood tumor types. And there's evidence for genotoxicity there as well as the
5 kidney cancer, as was indicated by several of the panelists.

6 The most sensitive cancer is the mononuclear cell
7 leukemia, MCL, and there's, again, discussion of the relevance or the
8 interpretation uncertainty about MCL as well. I haven't heard much discussion
9 of the MCL data by the panel, and I would hope that you would also weigh in on
10 that in your deliberations.

11 **DR. KENNETH PORTIER:** Thank you. Does anyone
12 want to weigh in on the MCL?

13 **DR. KATHLEEN GILBERT:** I don't remember seeing
14 a lot on the MCL in the section.

15 **DR. KENNETH PORTIER:** Dr. Rowlands?

16 **DR. CRAIG ROWLANDS:** Yeah. If I recall -- now,
17 this is in the Fischer 344 rat, right? And this is a strain-specific disease really.
18 You don't see it in many other animal models or other rat strains for that matter.
19 It has a very high, spontaneous, pretty commonly occurring leukemia
20 background as very high in this and at least a fairly high mortality rate when you
21 get to the end of an 18-month cancer bioassay. In fact, it gets up closer to like 30
22 percent, even as high as over 60 percent in background rates, especially in males.

23 So the problem with that is that you're trying to look at the
24 increased leukemia, and I think Stan already said that this was some controversy

1 to whether this even has relevance for humans. We don't know the mode of
2 action paralysis induced to the Fischer rat. But when you have such a high
3 background rate, it changes from study to study. You often don't see reproduced
4 effects, and you have to really see an increase above a very high background.

5 So, it's not a very good model at all. It's a Fischer rat-
6 specific leukemia with a questionable relevance to humans. We don't know the
7 mode of action, so actually, I would be very reluctant to try and base some sort
8 of a risk estimate for humans off of that model. It's almost the same problems
9 we have with the mouse liver tumors. What relevance does it have to humans
10 that's a real problem? That's it.

11 **DR. KENNETH PORTIER:** Thank you. No, thank
12 you. That's a good point. Dr. Gilbert?

13 **DR. KATHLEEN GILBERT:** Okay. So I admit, I'm a
14 bit lost here. A lot of people don't like the liver tumor model. They prefer the
15 kidney or the bladder, and we just heard from Dr. Barone that the kidney
16 epidemiological studies are not that consistent. So, I'm trying to figure out what
17 I'm going to say in here, what our recommendation is going to be.

18 And then we have Dr. Willhite's suggestion that the whole
19 thing needs to be redone. I think that, if there is any evidence of the MOA, it is
20 genotoxic. So, the selection of a low-dose linear model seems appropriate. Can
21 we say that? Or are we going to say that we need to redo the section before we
22 come to any conclusion? I would like to hear from some other people on the
23 committee about this.

1 **DR. KENNETH PORTIER:** I'd be interested. Did you
2 get a chance to look at Appendix F, Kathleen?

3 **DR. KATHLEEN GILBERT:** No. I missed that
4 appendix. Sorry.

5 **DR. KENNETH PORTIER:** Yeah, and I did too. So,
6 I'm wondering if maybe at this point, we can kind of pause this discussion and
7 give you and me a chance to kind of review Appendix F. And we'll come back
8 to that the first thing in the morning just to see if new insights have occurred,
9 whether it's changed our conclusions or strengthens our conclusions. Dr. Lash?

10 **DR. LAWRENCE LASH:** Yeah. I was just going to
11 comment that, first of all, I think Dr. Willhite made a very persuasive argument
12 and collected a large number of citations that really provide support for the
13 conclusion that the bladder and kidney -- it shouldn't be ignored. I think,
14 additionally, typically in citing the studies from Dekant's group from the late
15 '90s, that there's strong chemical evidence of the generation of genotoxic
16 metabolites.

17 So, I think the question that Dr. Gilbert raised about, you
18 know, what should we say regarding the low-dose linear extrapolation? I think
19 the support for that, and I think the points that Dr. Willhite made, I think, were
20 very persuasive that we need to consider this as a target and it shouldn't be
21 ignored. And I think the relevance to humans has to be considered. So, when
22 you deal with the MCL data or the mouse liver data, you have to consider how
23 well it translates. So that's it.

1 **DR. KENNETH PORTIER:** Dr. Grant, I saw your hand
2 go up and then go down again.

3 **DR. STEPHEN GRANT:** Yeah. I was going to
4 comment a little bit, but I just don't want to be reiterating myself. I think there's
5 pretty strong evidence of genotoxicity in kidney, but we'd really like it to apply
6 to liver because that will be a more protective way of interpreting the data. And
7 there must be some -- I'm reiterating myself -- if it can be genotoxic, probably
8 will be genotoxic and there will be differences based on microenvironments and
9 things like that and the amount of metabolites.

10 The real issue, and this is one thing I hadn't brought up
11 earlier, is that the issue with the mouse is the question of whether the PPAR-
12 alpha data basically satisfied the condition of being the only mechanism.
13 Because that would basically say that's not relevant to humans. If it seems to be
14 a contributor, well then probably the -- we're basically mandated to assume that
15 the main mechanism is genotoxicity because that's what's been best associated
16 throughout the last 50 years with cancer.

17 And again, we also can say it's been fairly well
18 established in kidney, not so well established in liver, perhaps because of this
19 confounding situation. The other problem is that, when we bring in leukemia, I
20 usually shy away from -- yes, leukemia and lymphoma are cancers, but they have
21 their own mechanisms. And so the problem with them is that it's harder to
22 extrapolate to other cancer types if you're using blood cancers as the paradigm.

23 **DR. KENNETH PORTIER:** Thank you. Good points.
24 The other thing I wanted to make sure we do is kind of check Dr. Willhite's

1 references against the epi studies that were reviewed in the metanalysis to see if
2 they're the same or similar, because I know Dr. Willhite cites this stuff, but he
3 didn't do a metanalysis. So, if it's the same studies and EPA went the next step
4 to the metanalysis, I really want to have some opportunity to look at that and
5 integrate that into my thinking.

6 So I think, at this point, this may be a good point to kind
7 of stop with Question 5.5. I'm going to make a note to kind of come back to it
8 first thing tomorrow morning and I'll encourage the lead and associates to look
9 at Appendix F. Let's factor that back into the answer to Question 5.5. Is that
10 acceptable, Dr. Gilbert?

11 **DR. KATHLEEN GILBERT:** Yes, that sounds fine.

12 **DR. KENNETH PORTIER:** Okay, good. Let's move
13 onto Question 5.6. And then let's see. We'll hopefully take a break at that point
14 once we complete 5.6. 5.6 is other aspects of the human health hazard
15 assessment, and Ruthann Rudel is the lead on that. Ruthann?

16
17 **CHARGE QUESTION 5 (5.6)**
18

19 **MS. RUTHANN RUDEL:** Hello. How's everybody
20 doing? It's been a long day. Luckily, I think that 5.6 is relatively quick. I can
21 tell you a little bit about what I've received from some of the members and then
22 we can see if they want to fill things out. But basically, two members basically
23 had questions of extending what we've already been talking about, questioning
24 the liver tumor endpoint, and I think that most of the things that I saw in there,

1 I've heard already. But I'm going to let them extend those comments if they
2 wish to.

3 And then two committee members asked for a more robust
4 and concise summary. This is really hard to do, I have to say. But a summary
5 was in Section 3.2 when you're describing a noncancer toxicity from chronic
6 exposures, and each paragraph about each endpoint cites multiple studies and it's
7 difficult to determine which effects among them EPA considers most important
8 and that this recurs in some of the POD paragraphs as well.

9 Let's see. On Page 300, the recommendation or question
10 is to specify what action is being taken in the dose response assessment to
11 address the genetic variability and susceptibility, which is described on that page.
12 Another detail, which is on Line 6455, to clarify that the IRIS 2012 assessment
13 used the Chiu and Ginsberg PBPK model, you may have talked about that during
14 the PBPK section. So that's what I have, and we can see if anybody in the group
15 wants to extend those or add.

16 **DR. KENNETH PORTIER:** Let me go down the list.
17 Dr. Apte, anything to add?

18 **DR. UDAYAN APTE:** No.

19 **DR. KENNETH PORTIER:** Thank you. Dr. Barton?

20 **DR. CHARLES BARTON:** No, I don't. Thank you.

21 **DR. KENNETH PORTIER:** Dr. Bruckner?

22 **DR. JAMES BRUCKNER:** Nothing else.

23 **DR. KENNETH PORTIER:** Dr. Johnson?

1 **DR. MARK JOHNSON:** Yeah. I made this comment
2 earlier, but I'll make it again. On Page 301, Line 7842 to 7850, it just wasn't
3 clear to me why EPA sought to adjust the occupational data for residential
4 exposure scenario for noncancer effects. So, if that can be clarified -- that's my
5 only comment. Thank you.

6 **DR. KENNETH PORTIER:** Mark, send a quick note
7 like that to Ruthann so she can include it. Dr. Lash?

8 **DR. LAWRENCE LASH:** Yes, hi. I don't have too
9 much to add because I think, as was pointed out, a lot of comments made here
10 relate to comments that were made in earlier charge questions under 5. But I just
11 want to emphasize a couple points that I found interesting here, because it asked
12 us to comment on characterization of assumptions and uncertainties. And what I
13 noticed here was that there are actually a couple of places where comments were
14 made that sort of supported the concerns.

15 I mean, it even said there was a comment about the PPAR-
16 alpha for the MOA in Section 3.2.3.2.4 that it stated that observed liver toxicity
17 may have reduced significance to the majority of human populations, which I
18 kind of thought that was a very vague understatement. So the inconsistencies
19 between uncertainty statements and then conclusions made, because then a little
20 later, it talks about the potential high risk subpopulations, some that have fatty
21 liver disease and diabetes and so on. And to me, they note the uncertainty but
22 then make a conclusion anyway and disregard it.

23 That was, I think, about it because some of the other
24 comments also come up, they're kind of broad general that extend since we were

1 asked -- this question asked about uncertainties and quality, characterization of
2 quality. And I kind of have an overall issue with that and I bring that up in
3 Charge Question 7.-something with regard to how the discussions with regard to
4 identifying datasets of low, medium, and high qualities. So I think we can
5 discuss that later. That's it.

6 **DR. KENNETH PORTIER:** So, Larry -- Ken Portier.
7 Kind of a quick follow-up question. So you see a disconnect between the
8 discussion -- or the identification of uncertainties, and then later utilization of an
9 uncertain fact in the conclusions, right, how should EPA handle that instead? I
10 mean, what's your thinking on what might be the right way to --

11 **DR. LAWRENCE LASH:** Well, I mean, in the case that
12 I cited here, I actually quoted, I think, the section where it said -- and this is in
13 the comments I sent to Ruthann. The document says that its consistent effects
14 were only observed in rodents and the potential influence of certain MOA that
15 are highly active in rodents, that is PPAR-alpha, suggests that observed liver
16 toxicity may have reduced significance to the majority of humans. And then it
17 says, however, susceptible subpopulations such as those with liver disease may
18 still be of high risk of liver toxicity from sustained PCE exposure.

19 So, the problem I have here -- and this is just one example.
20 There were two others that I cited elsewhere where it seemed like the evaluation
21 understates an uncertainty. You know? Because I think this is really an
22 understatement, because I think the huge body of literature says that there's no
23 significance for humans if this is the main MOA.

1 And I don't think there's good evidence for -- you know,
2 there's some evidence for some metabolites of PCE such as TCA and potentially
3 DCA causing epigenetic changes. But there's not really good evidence for
4 genotoxic effects of MOA. So what are you left with? So I think just saying
5 "may have reduced significance" is really kind of fudging it, and then going
6 ahead and using this. And I think there's a couple of others. So does that kind
7 of express what I mean there?

8 **DR. KENNETH PORTIER:** Yeah. Right now, I'm
9 hearing --

10 **DR. LAWRENCE LASH:** I was just going to say that
11 there are other --

12 **DR. KENNETH PORTIER:** Larry.

13 **DR. LAWRENCE LASH:** I'm sorry?

14 **DR. KENNETH PORTIER:** I was just going to say,
15 what I'm hearing you say is, they didn't make a conclusion on uncertainties.
16 And then they won't act on that conclusion. So they state the uncertainty and
17 move on, and you're never sure, well, what do they conclude about that
18 uncertainty? Does that mean we don't use it? Or does that mean we're just
19 going to use it and somehow ignore the uncertainty? I think that's part of what
20 I'm hearing you say. Is that right?

21 **DR. LAWRENCE LASH:** Right. It doesn't seem like
22 the -- but I think in this specific case, actually, it's more than an uncertainty. I
23 think the conclusion that's made or the moderation of the conclusion saying that,
24 well, this may have reduced significance to the majority of human population, I

1 think, is really an understatement of the lack of significance, that it's not reduced
2 significance. There's really no significance. You know?

3 There are other examples where they say an uncertainty,
4 like particularly in the exposure sections where there's a number of cases that I
5 noted elsewhere, where there's questions raised about the completeness or the
6 accuracy of exposure datasets where they'll say that the EPA has low or medium
7 confidence in the dataset or that they used a model rather than data because there
8 were no data and that, therefore, this may underestimate or overestimate the true
9 exposure. But then we have high confidence in the conclusion. So, there's
10 disconnects all over the place. That's what I'm saying.

11 **DR. KENNETH PORTIER:** Yeah. Okay. Thank you.

12 **DR. LAWRENCE LASH:** Okay. Thank you.

13 **DR. KENNETH PORTIER:** Ruthann, I hope you got all
14 of that.

15 **MS. RUTHANN RUDEL:** Yeah, yeah. I mean --

16 **DR. KENNETH PORTIER:** Let me keep going down
17 the list.

18 **MS. RUTHANN RUDEL:** Oh. Can I just ask him a
19 question?

20 **DR. KENNETH PORTIER:** Yeah, Ruthann. Go ahead.

21 **MS. RUTHANN RUDEL:** Well, I guess I want to
22 reiterate Ken's question. This is not my specific area of expertise, but if they're
23 saying that PPAR mechanism is not relevant to humans but it is relevant to non-

1 alcoholic fatty liver disease or something like that, is that what that section is
2 saying, do you think?

3 **DR. LAWRENCE LASH:** You're asking me? Larry?

4 **MS. RUTHANN RUDEL:** Yeah.

5 **DR. LAWRENCE LASH:** I mean, that's what I -- what
6 I'm taking it as is that there's some acknowledgement. And rather than saying
7 that there's no relevance to humans, which I think is really the case, what it's
8 saying is that there's reduced relevance for the majority of the population, but
9 then it's saying that there may be subpopulations that have liver disease who will
10 be particularly susceptible because of --

11 **MS. RUTHANN RUDEL:** Do you think that's true?
12 Are you saying that you don't think that's true or you don't know?

13 **DR. LAWRENCE LASH:** I don't think you have any
14 evidence to conclude that. That's why I'm saying that the conclusion, it doesn't
15 match the evidence. No. I mean, I kind of understand -- if there are other MOAs
16 for which there's evidence, I suppose you can conclude that -- and it's maybe the
17 way this is worded.

18 But if you cite -- if you say that potentially these
19 subpopulations that have fatty liver disease or whatever could be susceptible
20 whereas the majority of the population is not. But I think you have to invoke
21 other mechanisms, not the PPAR-alpha. So I don't think there's proper
22 acknowledgement of the large database of literature probably dating back 30
23 years that has gone over this.

1 **MS. RUTHANN RUDEL:** So you think that there's a
2 strong literature to say that PPAR mechanisms are not relevant, even for humans
3 that have liver disease or other liver problems?

4 **DR. LAWRENCE LASH:** I mean, I don't know that
5 that's been looked at. I don't know if someone else might know. But pretty
6 much, the response in humans is so much diminished compared to rodents that
7 the conclusions that I've seen and I recall from a number of either peer review
8 groups similar to this, or other review documents, but this mechanism is really
9 like the [alpha]-2[mu] in kidney that's male rat-specific. And the humans just
10 don't amount the same type of response. Even though humans have homologous
11 proteins, they just don't do the same thing. So, yeah, I don't know of any
12 evidence for this.

13 **MS. RUTHANN RUDEL:** Yeah. Okay. I'm trying to
14 just -- we can talk about it, I guess. I'm just trying to figure out whether your
15 comment is about that you disagree with their characterization of the actual
16 evidence or just the way they're treating the uncertainty, I guess.

17 **DR. LAWRENCE LASH:** Ah. Well, it's kind of both I
18 guess.

19 **MS. RUTHANN RUDEL:** Uh-huh.

20 **DR. LAWRENCE LASH:** But it's certainly with regard
21 to this specific question, which is I interpreted that what we were all asked is
22 how the assumptions and uncertainties were presented and discussed. But I
23 didn't feel, in this case, that the uncertainty was adequately put into account in
24 the conclusion. Yeah.

1 **MS. RUTHANN RUDEL:** Yeah. Okay, thank you.

2 **DR. LAWRENCE LASH:** Sure.

3 **DR. KENNETH PORTIER:** I think I'd like to ask Dr.

4 Apte, because I think he wants to comment on this as well. And then Dr.

5 Willhite's had his hand up. And then, Dr. Barone, I see your hand up. Dr. Apte?

6 **DR. UDAYAN APTE:** Yeah. So I just want to comment

7 a couple things there. I totally agree with Dr. Lash about the PPAR-alpha

8 relevance to the human situation. That's pretty well established. However, I

9 think there is a great need to disconnect that from the non-alcoholic fatty liver

10 disease issue. That's nothing to do with PPAR-alpha.

11 I mean, in humans, the mechanisms are being investigated

12 and that doesn't have to do anything with PPAR-alpha activation or whatnot.

13 There might be some PPAR-alpha activation that you see in rodents with

14 (inaudible), but that's not considered of the relevant mechanism of this disease

15 which will affect close to 30 percent of U.S. population within the next 20 years.

16 So this susceptibility of this specific population to PERC

17 is independent of the PPAR-alpha mode of action. It is mainly to do with two

18 things. One, that these individuals generally tend to be heavier, have more

19 adipose tissue, they have increased BMIs because these diseases are associated

20 with obesity. And because of the way PERC ADME works, this will make these

21 individuals more susceptible. So that uncertainty has to be thought about. That

22 is one thing.

23 The other thing is NAFLD is a multisystem disease. It

24 involves liver as the main issue if you do pathology but generally is also

1 associated with type 2 diabetes, immune reactions, things like that. In fact, a
2 recent consortium of liver doctors is going to rename this disease as MAFLD,
3 metabolism associated fatty liver disease rather than non-alcoholic. But the
4 change will take place within a year, I think.

5 We need to sort of kind of separate these two things and
6 comment on that. So the mode of action for PPAR-alpha is kind of a separate
7 issue than susceptible -- increase of individuals with non-alcoholic fatty liver
8 disease. And that mechanism of action is different. That has nothing to do with
9 PPAR-alpha.

10 **DR. KENNETH PORTIER:** Thank you, Dr. Apte. Dr.
11 Willhite, did you want to add to this or start a new comment?

12 **DR. CALVIN WILLHITE:** No, I want to just put in one
13 point before you go looking at Appendix F. I believe that's what we were
14 directed to. This paper was not among the 13 that I counted up for kidney
15 cancer, but this is a very interesting paper. The first author is Ma, M-A, and it
16 was in the *Journal of Environmental and Public Health*. The title is
17 "Association Between Residential Proximity to PERC Dry Cleaning
18 Establishments and Kidney Cancer in New York City."

19 It's not a controlled study, obviously. But the important
20 things that are stated here in this from the Department of Epidemiology and
21 Biostatistics, University at Albany School of Public Health. Those are the
22 authors. The conclusion is Perchloroethylene, PERC, is commonly used as a dry
23 cleaning solvent and is believed to be a human carcinogen with occupational
24 exposure resulting in elevated rates of kidney cancer. That's about as clear a

1 conclusion as I've seen, and it's not from Calvin's just quick look at it or a
2 metanalysis, but it's reviewed here. And that's all I had to say about that.

3 Thanks.

4 **DR. KENNETH PORTIER:** Thank you. Dr. Barone,
5 clarifying question or statement?

6 **DR. STAN BARONE:** Yeah, a couple of clarifying
7 questions. One is the potency of PPAR-alpha in mice and rats. When we have
8 liver tumors in both rats and mice, is the PPAR-alpha causal? That's one
9 question, necessary and sufficient. And the other is I've heard a number of
10 panelists say that PPAR-alpha's not relevant to humans, and Dr. Lash actually
11 spoke to the levels of PPAR-alpha in humans a moment ago.

12 And I wonder, again, in the cases of statins, which are
13 PPAR-alpha agonists, there's sensitive subpopulations to statins with folks who
14 cannot take statins because of liver toxicity. I'm curious to hear though, do we
15 need to consider a susceptible population who may have higher expression levels
16 of PPAR-alpha, and may have toxicity due to PPAR-alpha mechanisms?

17 **DR. KENNETH PORTIER:** Dr. Apte jumped right on
18 that. Dr. Apte?

19 **DR. UDAYAN APTE:** Oh, I guess my hand was up
20 already. But I'll go ahead and say something anyway. I was going to say a few
21 things. Well, so the relevance of PPAR-alpha to the humans, that is specifically
22 about when we talk about liver. Other tissues in human body of course have
23 PPAR-alpha. It does respond to PPAR-alpha agonists, and that's why we have
24 lipid-lowering drugs like (inaudible) and others that actually work.

1 However, the human liver has significantly less PPAR-
2 alpha as mentioned before than rodent livers, and that's where the relevance of
3 mode of action comes into question. So, when it comes to PPAR-alpha in
4 humans who -- in other organs, yes, it is there. And it is actually responding too.
5 It's in enough quantity and it does respond to its ligands. So that's one thing.

6 About the statins, the hepatic toxicity of statins is a
7 conundrum to be putting it mildly. It is one of the idiosyncratic reactions, I
8 think. I need to look it up, but I don't think we know the mechanism that clearly.
9 And most people who take statins are recommended to have a liver enzyme
10 check or liver function test done every certain months to make sure statins are
11 not affecting.

12 The question whether those people should be considered a
13 susceptible population to PERC, I would say yes only if there is a demonstrated
14 liver problem. You know, that doesn't mean that every person who takes statins
15 should be considered a susceptible population. I think if you have somebody
16 who is on statins and there is a demonstrated liver problem, yes, that person
17 might be more susceptible to additional chemical injury. But normally, people
18 taking statins who are not actually showing any signs of injury, I'm not very
19 certain that will qualify as a susceptible population. That's what I want to say.

20 **DR. KENNETH PORTIER:** Thank you. Dr. Lash?

21 **DR. LAWRENCE LASH:** Yeah. I was going to say that
22 the sensitivity to statins and why some people can't take -- and I think it's correct
23 that the mechanism really isn't well known or well characterized. But I didn't

1 think it had to do so much with the liver function, per se, or certainly PPAR-
2 alpha. But I think it's just not poorly characterized. That was it.

3 **DR. UDAYAN APTE:** Yeah, that's right. This is Dr.
4 Apte. It doesn't seem to be related to PPAR-alpha.

5 **DR. LAWRENCE LASH:** Yep.

6 **DR. KENNETH PORTIER:** Okay. Ruthann, any
7 additional comments or you think we're done with this question?

8 **MS. RUTHANN RUDEL:** Yep, I think we're done.

9 **DR. KENNETH PORTIER:** I think it's time for a
10 break, folks. I have 4:05. We're running a little over a half hour behind
11 schedule, which is okay, but let's go ahead and take our 15-minute break and
12 return at 4:20 Eastern please. Thank you.

13 **DR. YVETTE SELBY-MOHAMADU:** Thank you.

14
15 **[BREAK]**

16
17 **DR. KENNETH PORTIER:** Okie-doke. I have 4:20.
18 Let's reconvene. I think we've completed all of the discussion on Question 5
19 with the exception of 5.5. We're going to return tomorrow morning once we
20 reviewed the Appendix F material. I'm writing a note to myself. And I'll ask
21 for Tamue Gibson to remind me as well when we start tomorrow morning.

22 I'd like to go ahead and move onto the discussion, the risk
23 characterizations in Question 6. Dr. Selby-Mohamadu, would you read in the
24 question?

CHARGE QUESTION 6: RISK CHARACTERIZATION

DR. YVETTE SELBY-MOHAMADU: Sure. Thank you. Question 6, Risk Characterization -- EPA concludes that PCE poses a hazard to environmental aquatic receptors with algae being the most sensitive taxa. Environmental risks were assessed using risk quotients and the number of days that a concentration of concern was exceeded. EPA evaluated potential risks to workers and ONUs, consumer users, and consumer bystanders. For noncancer effects, EPA used a margin of exposure which is the ratio of the hazard value to the exposure value. For cancer, an IUR for liver and lung tumors was used to evaluate chronic cancer risks for occupational scenarios.

Question 6.1: Please comment on the characterization of uncertainties and assumptions including whether EPA has presented a clear explanation of underlying assumptions, accurate contextualization of uncertainties and, as appropriate, the probabilities associated with both optimistic and pessimistic projections, including best-case and worst-case scenarios.

DR. KENNETH PORTIER: Thank you. Dr. Johnson has the lead on this question. Dr. Johnson, this is kind of a broad question covering environmental cancer, noncancer workers, ONUs, consumers, and bystanders.

DR. MARK JOHNSON: Yes sir.

DR. KENNETH PORTIER: Lead on.

CHARGE QUESTION 6 (6.1)

DR. MARK JOHNSON: Okay. I have a lot to read, so just bear with me for a moment. I had to switch phones. Okay. All right.

There was a few comments about the fact about terminology. Be careful about that we're really looking at hazards, not risk. Risk, by definition, is a probability of an adverse event. And sometimes there's some language that we use that suggests that we really know something about the magnitude that we exceed in the RQ or HQ. There's some language in certain places that I can give you more specifics on where, when you're below that unity, there is no risk. I think most of us would agree that there probably is some probability of an adverse event, even if you're below one. But that's just semantics.

Okay. I'm going to read some of these comments. Since occupational user and consumers exposed to PCE through both dermal and inhalation routes, aggregate exposure needs to be determined. Use the model for both dermal inhalation exposure together, as individual models increase uncertainty of this highly exposed population.

It's also important to run a model with and without PPE, such for occupational nonusers and bystanders usually do not use respirators and gloves, respectively to better understand the risk of these individuals. Bystanders could be the sensitive population such as children, because children's brains are very vulnerable to their immature detoxifying system. Therefore, the

1 model should be adjusted accordingly to properly evaluate the risk of children
2 following exposure to TCE.

3 Presentation of this section is quite dense. It's just not
4 clear which risk estimates are based on stronger evidence than others. The
5 occupational dermal estimates are a bit less certain because the data inputs do not
6 come from a transparent method in the document. The PPE estimates are
7 reasonable, giving the data uncertainty presented accordingly. Some efforts
8 combine risk from inhalation and dermal routes, likely should be done since
9 individuals can conceivably be exposed simultaneously from both routes of
10 exposure. It is unrealistic to model them separately.

11 The consumer risk estimates are not presented as nearly as
12 clearly as it could be. I believe EPA is using the points of departure from Table
13 4-2 for acute risk of these estimates, but it's not certain. The PODs for consumer
14 exposure possibly could be different than the PODs for occupational exposure
15 because duration exposure may be influencing the PODs, even in the case of
16 acute endpoints, particularly to understand a little better the estimates of
17 exposure for high intensity users and whether those are reasonable. If they are
18 more uncertain, then that should be highlighted.

19 Regarding environmental assessments, there seems to be a
20 disconnect between the problem formulation and the draft risk assessment.
21 While the problem formulation appears to provide conservative assumptions
22 regarding fate and receptor identification, the DRE simply states that receptors --
23 that is, terrestrial and media-like sediments -- will not be considered. It's still

1 unclear how literature studies have been excluded and when they were found
2 acceptable in the problem formulation document.

3 Upon conducting a word search using worst-case, there's
4 only one occurrence in a 667-page document and is not in the risk
5 characterization section. Consequently, worst-case scenarios have not been
6 provided in this draft risk assessment. One committee member has evaluated,
7 while uncertainties are briefly discussed for modeling scenarios of exposure, the
8 worst-case or even 90th percentile estimates are not provided. The
9 recommendation is to provide those worst-case scenarios.

10 For environmental hazard assessment, worst-case
11 scenarios would include sublethal effects, typically for development. Weight of
12 evidence is only provided for human health sections hazard and not in risk
13 characterization. Had a weight of evidence evaluation been conducted for
14 environmental hazard, it would be clear that effects noted in vertebrates by this
15 human health section can be used in read-across for environmental hazards. The
16 recommendation is to provide weight of evidence assessments for the
17 environmental hazard.

18 And specifically, Page 316, Lines 8200 to 8205, when
19 using a peer review model or not, assuming that oral data are equivalent to
20 inhalation data, it's fundamentally flawed. There is confidence in the exact dose
21 from the compound to the target where there is certainty which metabolite is
22 responsible for the effect. I think that's supposed to be uncertainty.

23 Otherwise, the use of a PBPK model is preferred, but
24 there's still inherent uncertainty associated in what they choose. Consider there

1 is certainty when using a model throughout the extrapolation. Oral data are not
2 equivalent to inhalation data. I think I have quite a few comments here. I'll
3 continue.

4 EPA did not address volatilization pathway to inhalation
5 exposures to small burrowing mammals and biosolids. I think we discussed that.
6 The first sentence -- this is incorrect -- is written on Page 457 when EPA did not
7 calculate hazards to terrestrial invertebrates instead of intellect organisms.
8 That's just an editorial. But the major issue is not. The overall section in risk
9 characterization is largely divided in five major subsections: environmental risk,
10 human health risk, assumptions of key sources, and uncertainty for risk
11 characterization, and other risk-related considerations and risk conclusions.

12 This particular charge question is primarily focused on
13 sections 4-3, 4-4, but also in 4-5. The environmental risk characterization
14 explains procedures for calculating and estimating exposure levels in different
15 COUs, duration exposure, and gives statistics on calculated RQ values.
16 Uncertainties and assumptions are basically discussed, but for the example, the
17 use of measured values where available versus model data are discussed.
18 Validation of the model data are discussed as well. This seems clear and doesn't
19 raise any concerns.

20 The human health risk characterization evaluation gives a
21 brief overview of Section 4.3.2.1, included with the statement, major
22 uncertainties include this section of cancer endpoints for IUR selection,
23 inconclusive human evidence for a few health domains. This is quite an

1 understatement. It probably needs additional discussion here in reference to
2 where else these issues are discussed in this evaluation.

3 Regarding occupational risk considerations, the evaluation
4 clearly identifies two areas of uncertainty, mainly dermal exposures and PPE
5 uses across OECs, although the brief discussion here seems logical and
6 appropriate to reference to where else in the evaluation these issues are
7 discussed. It should be done in more depth.

8 Discussions of dermal exposures and how uncertainties
9 are considered seemed logical in keeping with both clinical properties of PCE as
10 well as the desire to be protective, human health discussions of PPE usage are of
11 a continuing concern. And we've had this, I think, for other chemicals. Primary
12 for lack of data to evaluate such usage during different OES.

13 Nonetheless, it is appropriate if the evaluation reports
14 MOEs, both with and without, for use in OES. For consumer use, however,
15 MOEs are only calculated without PPE use. While the rationale for no PPE use
16 for consumers seems reasonable, evaluation could add the use of PPE and
17 recalculate MOAs to demonstrate the beneficial impact of PPE use.

18 Alternately, simple reference to MOE calculations for
19 different OES, with and without PPE, can be discussed with their unreasonable
20 risk identified for consumer use scenarios, again, to demonstrate the potential
21 impact of PPE use.

22 Under the subsection of "other risk-related
23 considerations," the issue of susceptibility or highly exposed subpopulations
24 briefly discuss these issues are discussed elsewhere as well, and some cross-

1 referencing would be helpful. The issue of susceptible subpopulations is a
2 special consideration for TSCA and is one that's always discussed for which
3 little specific data are available. Evaluation clearly notes some of the factors that
4 may enhance susceptibility. Use a default uncertainty factor of 10 to account for
5 this. Such an approach is standard and appropriate.

6 Table 2-5, the limited TRI report of requirements make
7 this charge estimates of low quality. Allowing 25 thousand pounds per user to
8 go unreported leaves entirely too much slop in the assessment and evaluates less
9 than 325 million pounds annually. 1200 facilities using just under this limit
10 would constitute 10 percent of the total use. This may sound like a large number
11 of businesses, but the estimated number of dry cleaning facilities in the U.S.
12 exceeds 32 thousand. And the estimated auto repair shop exceeds 230 thousand.
13 The 1200 is less than 5 percent of those business use categories.

14 The possibility of manufacturing facilities operating more
15 than 350 days a year is less in probability that the operations occur on less than
16 350 days per year. Thus, the statement in the uncertainty section is misleading.
17 These operational data should be readily available from industrial manufacturers
18 and other significant commercial users. These data should be required of all
19 major users. That would allow a probabilistic determination of operating days
20 per year.

21 If those data are not available, then assuming a five-day
22 work week, two-week turnaround is a more conservative estimate. That would
23 represent 250 days of operation. It should be noted that other DREs for
24 chlorinated solvents assume 270 days of operation, which is far lower than the

1 350 used for PCE and is closer to the 250-day estimate. But it still may be too
2 high. Processing as reactant, formulation, industrial processing also have PCE
3 discharge days in excess of 250 days a year with no supporting data.

4 The use of high production volume is not protective of
5 environment or human health. High centiles reduction must be used in the
6 absence of data. Adhesive sealants, while it's true that evaporation is not
7 accounted, neither is partitioning of PCE vapor back into surface waters. That
8 uncertainty must also be captured for this COU and for others where agency
9 downplays wastewater releases due to lack of evaporation estimates, like wipe
10 cleaning.

11 And the last one is the maskant for milling. The entire
12 uncertainty section points out problem with parsing of data among users if there
13 are no data for industries in this absence of data to indicate releases to all media,
14 the exception should assume 100 percent discharge to water. This comment
15 applies to COUs in facilities where they're reporting releases to environmental
16 media. Further, in each case where there are no reporting, the risk determination
17 should be that unreasonable risk cannot be ruled out, not that unreasonable risks
18 are not found. This is an important aspect of risk assessment. And that's all I
19 have.

20 **DR. KENNETH PORTIER:** Thank you, Mark. So, as
21 I'm listening to this, they kind of jump around. I'm assuming, or I'm hoping,
22 that when you write this up, there'll be more of an organization. You know, a
23 dichotomy between the environmental and human health and then the human
24 health among the worker ONUs and consumer groups. Kind of break that out.

1 **DR. MARK JOHNSON:** Yeah, absolutely. That's an
2 excellent recommendation. I will do that. I was literally receiving comments up
3 until this morning, so that's why it kind of jumps around.

4 **DR. KENNETH PORTIER:** No, no, I realize that. And
5 I'm going to go through the group and see what other -- you know, kind of trawl
6 through the group and see what other comments we can put in. I'll just kind of
7 remind the group that we're focusing here on the risk characterization.

8 So, I kind of was listening for the stuff that would link
9 them back to Chapter -- what is it? Chapter 5? No. Yeah, Chapter 5. And I
10 heard a lot of stuff that ties back to hazard. For that list, it maybe ties into the
11 actual risk characterization. With that comment, I'll move on. Dr. Cobb, do you
12 want to add anything to this?

13 **DR. GEORGE COBB:** I have nothing to add. Dr.
14 Johnson did a great job reading all of my comments in, and I appreciate him
15 doing that.

16 **DR. KENNETH PORTIER:** Dr. Hossain?

17 **DR. MUHAMMAD HOSSAIN:** I don't have additional
18 comments. Johnson covered my comments that I sent to him. Thank you.

19 **DR. KENNETH PORTIER:** Dr. Lash?

20 **DR. LAWRENCE LASH:** Yeah, same thing that my
21 comments were all covered. So, I have nothing to add there.

22 **DR. KENNETH PORTIER:** Dr. Meliker?

23 **DR. JAYMIE MELIKER:** Yeah, I just have one point.
24 I thought Dr. Johnson did a really nice job. My main point is Table 4-112 is this

1 large summary table in the risk characterization, and that's where I think it
2 would be helpful to have some estimates of uncertainty or certainty in there of
3 where there's more confidence, in which of these risk estimates. We go through
4 this very large table for different occupations for -- I'm looking at it here. It's
5 got risk estimates for non-PPE, risk estimates with PPE, it's got workers, it's got
6 ONUs. And then I think, further on, I think there's a section with consumers.

7 It would just be nice for there to be some description there
8 of where EPA feels they're most confident because it's just a lot of data that had
9 to be thrown out. And I don't think there's equal confidence in all of the data.

10 **DR. KENNETH PORTIER:** That's a good point, Dr.
11 Lash. Thank you. Oh, yeah, Dr. Meliker.

12 **DR. JAYMIE MELIKER:** Yeah, no. That was me.
13 That was Dr. Meliker.

14 **DR. KENNETH PORTIER:** That was Meliker. Yeah.
15 Behind myself. It's been a long day so far. Dr. Schlenk?

16 **DR. DANIEL SCHLENK:** Yeah, Ken. And also to
17 follow up, at least when I teach risk assessment here, risk characterization is
18 about characterizing the uncertainty that you have. And I think that's what the
19 question is supposed to be answering. It's a little bit tough because, you know,
20 you have exposure uncertainties and you have hazard uncertainties. So, it's
21 tough to group that logistically, at least in a format, unless you go back to those
22 sections.

23 So that's, I think, why you're seeing some of the exposure
24 and hazard components there. Those are the uncertainties that are basically

1 being discussed. And I think, at least in my reading of it, a lot of those
2 uncertainties are not fully discussed in the characterization section as they should
3 be, particularly the worst-case scenarios. I think those are definitely lacking, so I
4 just want to add that in in terms of the comment. But Mark addressed everything
5 that I had said. Thanks.

6 **DR. KENNETH PORTIER:** So, Dan, before you go, if
7 what you say is true, that's the goal of the risk characterization, why do you do
8 the uncertainty and assumption discussions in the individual exposure and hazard
9 sections? Shouldn't the risk characterization be more an integration of that
10 uncertainty?

11 **DR. DANIEL SCHLENK:** Yes, yeah. Yes. Definitely.

12 **DR. KENNETH PORTIER:** That's what I was trying to
13 get at.

14 **DR. DANIEL SCHLENK:** It is an integration, but it's
15 also the section typically where you do weight of evidence and uncertainty
16 analysis as well. So you discuss the worst-case scenarios. I mean, that's
17 generally where you put that information, at least in a section in the
18 characterization study, at least in the assessments that I've seen anyway.

19 **DR. KENNETH PORTIER:** Yeah. And that's why I
20 kind of like Dr. Meliker's comment, because to me, if you can go into that table
21 and say, these are the ones we have confidence in, we've integrated the
22 uncertainties, we've looked at the strength of our assumptions and we feel
23 confident in these or much less confident in those, to me, that's an integration
24 and that's a risk characterization.

1 **DR. DANIEL SCHLENK:** Agreed.

2 **DR. KENNETH PORTIER:** Good point. Okay.

3 **DR. DANIEL SCHLENK:** Agreed, agreed. I think the
4 point, in a perfect world, what you would have is a percentile reading if you had
5 probabilistic assessments where you'd have a 20th percentile degree of certainty,
6 a 50th, and a 90th percentile in terms of overlay. That's kind of where you
7 would see that. But, you know, that's in a perfect world.

8 **DR. KENNETH PORTIER:** Yeah. And I'm going to
9 inject an article that I read recently that talked about weight of evidence that kind
10 of does that in a what might be called semi-quantitative way. But I'll kind of
11 save that for Section 7 because it's not specific to this.

12 Better move on. Dr. Willhite? Calvin, your phone must
13 be muted. You're off of Webex, but we still don't hear you.

14 **DR. CALVIN WILLHITE:** You can hear me now, can't
15 you?

16 **DR. KENNETH PORTIER:** I can hear you now.

17 **DR. CALVIN WILLHITE:** I just have a question on
18 this slide here. And it's right above the shaded box. The sentence reads: for
19 cancer, an inhalation unit risk for liver and lung tumors was used to evaluate
20 chronic cancer risk for occupational scenarios. Is that sentence accurate? I
21 thought we had a mouse liver and we had rat leukemia. Is that sentence correct?
22 That's all I had to question.

23 **DR. KENNETH PORTIER:** Dr. Johnson?

1 **DR. MARK JOHNSON:** Oh, I'm sorry. My hand is up
2 for another reason. I just want to dovetail on your comment real quick, Ken, is
3 that I've seen risk assessments done in past where they've semi-qualitatively
4 done uncertainty using high, medium, and low or plus signs. But anyway, let's
5 get to Dr. Willhite's question. Maybe someone from EPA?

6 **DR. KENNETH PORTIER:** Yeah, because I don't
7 remember anybody mentioning lung. Dr. Lee or Dr. Barone?

8 **DR. STAN BARONE:** We'll have to check on that. I
9 think that might be a mistake.

10 **DR. KENNETH PORTIER:** Yeah. I thought so too. I
11 think it's not lung tumors that we're looking at.

12 **DR. STAN BARONE:** No, I think it's held over from
13 carbon tet and it's a mistake.

14 **DR. KENNETH PORTIER:** And it's not just yours
15 because the committee looked at this earlier as well, and somehow we missed
16 that as well. So good catch, Calvin. Dr. Anderson?

17 **DR. HENRY ANDERSON:** Yeah, I just have a quick
18 question. Throughout all of this -- I mean, upfront, there's a fair amount of time
19 put in to estimating a number of workers. And they're exposed and then the
20 ONUs in the risk here, I mean, the estimates of those numbers are pretty
21 uncertain as well, I would say. So, where in this whole process does the number
22 of workers come into play?

23 **DR. KENNETH PORTIER:** That's another good
24 question that we'll turn to EPA for a comment. Dr. Barone or Dr. Lee?

1 **DR. STAN BARONE:** In the risk evaluation rule, it's
2 one of the criteria that's mentioned for risk determination. It's also a
3 consideration we do where we can determine the number of workers for the
4 exposure scenarios. It is a critical aspect to future risk management if
5 unreasonable risk is found in calculating the excess lifetime cancer risk.

6 **DR. HENRY ANDERSON:** Okay.

7 **DR. KENNETH PORTIER:** So that's just going to add
8 another risk characterization and kind of an uncertainty evaluation, because we
9 do have quite a bit of uncertainty in the numbers of workers, ONUs, and
10 consumers exposed. Dr. Kissel?

11 **DR. HENRY ANDERSON:** And we really have pretty
12 good data --

13 **DR. KENNETH PORTIER:** Go ahead, John.

14 **DR. HENRY ANDERSON:** -- about workers and I'm
15 concerned that, in the methods you have to get workers, that really includes
16 ONUs. And so what's done is you then say, oh, ONUs are these additional
17 people, when in fact, they may already be counted in the worker workforce. But
18 it might be helpful upfront when you describe how you go about doing the
19 numbers, say that those numbers don't really impact the risk characterization or
20 other issues that are really important information to have in subsequent responses
21 by EPA to this set DOE so that you can just set that aside and say, okay, that
22 comes into play later.

23 **DR. KENNETH PORTIER:** Thanks, Henry. John
24 Kissel?

1 **DR. JOHN KISSEL:** Yeah. So I'm interpreting this
2 notion of uncertainty and clarity here somewhat broadly, but I have this problem
3 and I've confirmed that other people have it also. In attempting to check the
4 consumer dermal exposures, the spreadsheet, which is supplemental document
5 19, is protected in a way which does not give us access to the guts of the file.
6 So, we can't actually see what the calculations are. And I wonder if EPA could
7 correct that and distribute a file that we can actually read so that we could look at
8 the calculations.

9 **DR. ALAN KAUFMAN:** Yeah. This is Al Kaufman. It
10 looks like columns H through P, I think, are hidden. If somebody could unhide
11 those and then re-protect the sheet, that would be great.

12 **DR. KENNETH PORTIER:** Dr. Barone?

13 **DR. STAN BARONE:** Yes, we'll check on that and
14 follow up with Tamue. I did want to make a clarification for one of the previous
15 comments that Dr. Anderson mentioned. ONUs are workers. They are workers,
16 so please don't think that they're not part of the worker population. They're not
17 the users in the direct proximity; that's our assumption. But they are workers in
18 that condition of use.

19 **DR. HENRY ANDERSON:** Yeah. No, I understand
20 that. But what I was saying, is the data you use to estimate the number of users
21 and ONUs -- I'd have to go back. I think you do, and you have a table that
22 estimates the number of ONUs and the number of workers.

23 **DR. STAN BARONE:** We do.

1 **DR. HENRY ANDERSON:** And it's unclear to me from
2 that dataset how you get the ONUs that would be in a company that's different
3 from total workers. I think my question really is, are these two separate
4 populations in these industries in the counting? I don't remember the database
5 you use. But most of those are -- it's like going and getting the taxes paid. It'll
6 be the total workers in a workforce and that would be both. So, I'm just
7 wondering -- it doesn't probably matter -- are you potentially double-counting
8 individuals?

9 **DR. KENNETH PORTIER:** Yeah. Henry, my way of
10 thinking is it's workers equal OUs plus ONUs so that you use the generic term
11 "workers" and they're the industry count, but then there's the OUs that are
12 exposed differently from the ONUs. And maybe it may be that we need to look
13 more carefully at the terminology used throughout to ensure that, when you're
14 talking about the worker who has hands-on with the chemical, that we use the
15 term OU, occupational user.

16 I don't think you're usually generically computing the risk
17 to workers in general in this evaluation. You're usually looking at risk to OUs,
18 risk to ONUs, and risk to consumer users as three separate non-overlapping
19 populations. And I think, Dr. Anderson, your concern is to make sure that that's
20 clear on these counts upfront when you're reporting the industry breakdown and
21 the potential individuals who would be impacted by this risk evaluation. Is that
22 correct?

23 **DR. HENRY ANDERSON:** It's more that the base
24 document that's used -- I would have to go back. It's been a while since I looked

1 at it. I mean, it's such a big document. Up front, there's a database, a federal
2 database, that's used to estimate or that reports the number of workers in various
3 categories. And I thought those really were all workers. We separate those
4 workers into workers and ONUs, but I think in the estimation of how many
5 workers there are and ONUs, I don't see how you get the ONUs because the
6 ONUs are -- our definition of that is they have to be some -- they're really people
7 who are working on the floor.

8 It isn't an employee of the company that happens to be
9 there during -- their fiscal staff or writing checks or things like that, those are too
10 far removed, I think, to consider them ONUs. I'll have to open up the document
11 again.

12 **DR. KENNETH PORTIER:** Point taken. Look at it
13 because I think --

14 **DR. HENRY ANDERSON:** It's not what they are. I
15 understand what they are. It's how we want to separate them that I'm not sure
16 how you estimate that -- what's the basis of numbers? Where are you getting the
17 numbers for the ONUs? And are those then subtracted from the total workforce
18 of a company?

19 **DR. KENNETH PORTIER:** I see Mr. Macek. Mr.
20 Macek, was your hand up? Did you want to add a comment?

21 **MR. GREG MACEK:** Yeah, hi. This is Greg Macek
22 with the EPA Risk Assessment Division. The number of workers estimates were
23 in the area that I was responsible for. So we used a top-down type approach to
24 estimate workers. And as Dr. Barone said, workers includes two categories:

1 workers and the ONUs. So, the top-down approach involved accessing
2 databases from the census bureau, Bureau of Labor Statistics, and that included
3 data by occupation codes for the various -- by NAICS codes.

4 And those occupation codes had enough detail that we
5 looked at the description and used our judgment to indicate which categories
6 were representative of the workers in which were representative of the ONUs.
7 So, we were able to obtain averages for a site within that NAICS code which we
8 had mapped to the occupational exposure scenarios that we assessed, and so we
9 had those per site averages for those two categories and then multiplied by the
10 number of sites to get the totals of workers and ONUs.

11 So we did pay, I think, good attention to making sure we
12 had separated out the estimates for workers and ONUs for each of the
13 occupational exposure scenarios. It's in that appendix. I could be glad to
14 provide any more explanation or information on the approach we used. But I'm
15 glad you're making a comment so it draws attention to that area of the analysis
16 that we did.

17 **DR. HENRY ANDERSON:** The only reason, partly,
18 why I'm asking about that is, when I looked at the manufacturing sampling list,
19 that seemed to have what I would think are either non-ONUs or ONUs, like the
20 management staff and things like that. So, it wasn't clear. If you feel like there
21 is a table somewhere in the NAICS codes, which of those did you characterize
22 and say I'm going to count those as an ONU in this particular worksite area?
23 And maybe they're in -- I've just been through it all.

1 **MR. GREG MACEK:** Yeah. In the appendix, we try to
2 provide examples. You know, we provided a few examples. Of course, there's a
3 lot of detail with these estimates if, when you look at each of the OESs that we
4 included in the scope, I guess there are over 20 different ones. So, there is a lot
5 of detail.

6 But the appendix in the risk evaluation, we wanted to
7 include the details of a few examples to illustrate how we analyzed the
8 occupation codes for a particular OES to make the judgments of worker versus
9 ONU. And also, there was some detail in the supplemental. I'd be glad, before
10 tomorrow, to look that over and maybe I could shoot an email to Tamue to list
11 the appropriate references in the document so you can take a look at those.

12 **DR. HENRY ANDERSON:** That'd be great.

13 **MR. GREG MACEK:** Sure.

14 **DR. KENNETH PORTIER:** Yeah. Thank you, Greg.
15 That would be wonderful.

16 **DR. HENRY ANDERSON:** Don't need to kill yourself
17 trying to do it.

18 **MR. GREG MACEK:** Yeah, no. I think it'd be easy
19 just looking at what we already prepared and just highlighting --

20 **DR. HENRY ANDERSON:** Give me the page numbers,
21 yeah.

22 **MR. GREG MACEK:** -- yeah, where you could find it.

23 **MS. TAMUE GIBSON:** Thank you.

1 **DR. KENNETH PORTIER:** Yeah. I want to take a
2 little break here. We originally planned to go to 5:00, and I have a couple of
3 minutes before 5:00. And I'd really like to see a show of hands of those
4 committee members who kind of have to leave at this point. I know of at least
5 one that had a conflict. If I have too many hands, we may have to consider --
6 because it's my goal to at least go through 6.2 today. Dr. Macek, you can put
7 your hand down. Okay. I'm only seeing two hands up of charter members.
8 DFO is --

9 **DR. HENRY ANDERSON:** How much time are you
10 past again?

11 **DR. KENNETH PORTIER:** Half hour.

12 **DR. HENRY ANDERSON:** A whole hour?

13 **DR. KENNETH PORTIER:** No, no. Half hour.

14 **DR. HENRY ANDERSON:** Half hour? Okay.

15 **DR. KENNETH PORTIER:** I think we're going to have
16 to go with 5:30, and then we're going to call it quits.

17 **DR. HENRY ANDERSON:** Makes sense. Yeah.

18 **DR. KENNETH PORTIER:** Well, a hand went down,
19 so I've only got one hand now of a charter member. I think we still have
20 quorum, so we can kind of proceed. Thank you for that.

21 Back to Dr. Johnson, any additional comments on this?
22 Anyone on the panel or Dr. Johnson? I think we've had some good discussion
23 on this. I don't see any new hands popping up, so let's go ahead and move onto
24 Question 6.2. Let's read it into the docket. Dr. Selby-Mohamadu?

CHARGE QUESTION 6 (6.2)

DR. YVETTE SELBY-MOHAMADU: Yes. Question 6.2: please provide information on additional uncertainties and assumptions that EPA may not have considered or adequately presented.

Question 6.3: please comment on whether the information presented supports the findings outlined in the draft risk characterization question.

Question 6.4: please comment on the applicability and completeness of the underlying data used to support the risk characterization and the sensitivity of the agency's conclusions to analytic assumptions made.

DR. KENNETH PORTIER: So, Dr. Johnson, you had the lead on 6.2. Proceed.

DR. MARK JOHNSON: Right. Okay. We'll start with environmental hazard. The evaluation notes that we only have data from three species of algae. Although some of us did a survey of ecotox database, and there are some other data for some other, I guess, aquatic plant organisms. I think there's some information on diatoms out there that might help. But there was concern about the fact that we're basically wondering how representative these three species of the data from three species of algae are to the total algal population, or for that matter, aquatic plants in general. It remains unclear if that's a real concern.

1 One reviewer notes that various species of algae can quite
2 substantially in their sensitivity to environmental toxicants. And that may be a
3 consideration that could be more explicitly described in certainly the analysis
4 section. The other aspect also, again -- it dovetails the previous comment -- is
5 that EPA intended to protect algae or aquatic plants in general. If that's a
6 concern, you may want to expand that section as well.

7 There are no data supporting the supposition that
8 sediment-dwelling invertebrates are at similar risk to aquatic-dwelling insects,
9 nor the data suggests that PCE concentrations will be the same in sediments and
10 water. The DRE will be incomplete until toxicity data are included for sediment-
11 dwelling organisms. There are several additional uncertainties and assumptions
12 that the EPA has not properly considered. For example, dermal exposure based
13 on age and gender, which does represent actual dermal absorption of TCE at the
14 surface area of the hand of each individual is different if their body weights are
15 not similar.

16 Therefore, risk characterization of dermal exposure, the
17 EPA should go with body weights to determine toxicity of TCE to dermal
18 exposure which will reduce the certainty of risk via dermal exposure. With
19 regard to cancer, IUR values are based on liver and lung tumors. Really
20 problematic because evaluation is not convincingly argued that liver and lung are
21 significant cancer sites in humans. I think that was touched on earlier.

22 Here's an example of uncertainties yet to be examined by
23 the committee. The PEC (phonetic) has a log K_{ow} of around 3. This means
24 there is a thousand times more likelihood of absorbance from aqueous media into

1 biota. This compound is quickly metabolized, which is likely a reason why
2 bioaccumulations occur in fish. However, organisms of limited
3 biotransformation or metabolism would likely accumulate this compound.

4 Algal estimates were 100 to 300 in the problem
5 formulation, given the likelihood of accumulation within (inaudible) of the
6 invertebrates. Trophic transfer is a possible uncertainty.

7 Wastewater-dominated streams has not been considered as
8 a worst-case scenario due to climate change, water reuse practices in arid
9 regions. There may be very limited dilution of ethylate discharges in these areas
10 and they should consider that as a worst-case scenario.

11 In addition, estimates of discharge are primarily through
12 direct non-POTW discharge rather than from wastewater treatment. It's unclear
13 why the agency used a WT module in E-FAST. Their recommendation is to use
14 direct discharge input of E-FAST without the WTP module.

15 Some consumer use, likely scenarios to be associated with
16 chronic exposures because of high frequency of the activity or because of
17 elevated indoor air levels from use and storage in the home. Chronic cancer risk
18 should be estimated for consumer use scenarios. Chronic and cancer risk.

19 Excuse me. Workers live in vicinities of these facilities which are omitting, and
20 also consumers need to be considered commutatively in aggregate, including
21 ambient air, solar vapor, occupational consumer exposure.

22 Facilities and neighborhoods where PERC is being omitted
23 use -- are they the same neighborhoods and HECs where TCE and methylene
24 chloride are also being omitted? There's some mixture potential here.

1 Exposures in risk need to be considered across these chemicals since these
2 chemicals have similar toxic effects and may act additively to endpoints such as
3 the nervous system, liver effects, CYP activation, and other reproductive and
4 developmental effects.

5 And the last one is uncertainties inherent in treating oral
6 data equivalent to inhalation needs to be exclusively stated. Those should not be
7 treated equally. Okay, that comment was made earlier. And that's all I have.

8 **DR. KENNETH PORTIER:** Thank you. Dr. Cobb,
9 comments?

10 **MARTIN ALVARADO CORTES:** I think he said he's
11 done, Ken. His stuff was read into the record.

12 **DR. KENNETH PORTIER:** Yeah, I think he was also
13 the one that had to leave at 5:00. Dr. Hossain?

14 **DR. MUHAMMAD HOSSAIN:** Hi. I think Johnson
15 covered my comments. But the comment is only about the carpet area for
16 (inaudible) exposure. In other -- the area of PPAR chemical that we did before --
17 is that the EPA used the standard carpet area for men and women, but we didn't
18 find that type of information in this DRE for this particular chemical.

19 So, I think it will be better with that or the dose number in
20 this DRE, that would be helpful. Otherwise, they should go by the body weight
21 because the carpet area of hands should be changed based on the body weight.
22 That's all.

23 **DR. KENNETH PORTIER:** Thank you. Please send
24 that comment to Dr. Johnson. Dr. Schlenk?

1 **DR. MARK JOHNSON:** I think you missed Larry
2 again, Ken.

3 **DR. KENNETH PORTIER:** Oh. Why do I miss Dr.
4 Lash? Dr. Lash.

5 **DR. LAWRENCE LASH:** I guess it's a short name, so
6 it's easy to miss -- Lash. But anyway, no, I think Dr. Johnson pretty much
7 shared my comments. I mostly focus on the -- I just found it striking that there
8 was a fair bit of talk about the algae susceptibility and how wide a variable it can
9 be and the whole uncertainty of how representative these three species.

10 And I recall from the TCE document, there were a lot
11 more data for a lot more species. So, some sort of qualitative comparison
12 could've been made to get some idea as to the representativeness. That was
13 really my key issue here. That's it.

14 **DR. KENNETH PORTIER:** Thank you. Dr. Schlenk?

15 **DR. DANIEL SCHLENK:** Mark got all my stuff. I'm
16 good.

17 **DR. KENNETH PORTIER:** Thank you. Dr. Willhite?
18 Calvin, I think your phone's on mute. You're unmuted on Webex.

19 **DR. CALVIN WILLHITE:** I have nothing to add.

20 **DR. KENNETH PORTIER:** Okay, nothing to add.
21 Thank you. I typically agree with Dr. Lash. I think they remembered there is
22 some verbiage that talks about a species other than algae, algae being the most
23 sensitive. So there is some of that conversation in there. Whether it's adequate
24 is another matter. Any additional comments? Dr. Anderson?

1 **DR. HENRY ANDERSON:** Just to show my ignorance,
2 is the mode of action for the algae all the same? What I'm looking for is PCE to
3 get an agent to use against blue-green algae that will not affect others. Get rid of
4 our toxic algae.

5 **DR. KENNETH PORTIER:** Does anybody want to
6 adjust that? Dr. Schlenk?

7 **DR. DANIEL SCHLENK:** It's funny if you -- again,
8 this is why I asked the question about the Medaka study that was done on the
9 developmental aspects. If you take that number, the LOEC that they had from
10 the developmental tox assay, divide it by 10, which is what you would normally
11 do because you don't have an NOEC -- or I'm sorry, divide it by 2 to an NOEC,
12 and then take the safety factor on that, it actually comes out to be almost the
13 same number as what you see in algae.

14 So, I think that's, again, a critical study that was deemed
15 acceptable but then unacceptable later on. But it gives you a number that's very
16 similar to what the algae number is.

17 **DR. HENRY ANDERSON:** Okay. Thank you.

18 **DR. KENNETH PORTIER:** Dr. Blystone?

19 **DR. SHERI BLYSTONE:** Yeah. There were comments
20 in there about cumulative exposure or exposure across chemicals that may have a
21 similar endpoint adverse effect. And while I appreciate that -- that would be
22 really nice to do -- I think that's hugely complex and raises lots of issues. Again,
23 that seems to be bigger than a single chemical at this point. And we can lump

1 that into discussions for further down the line about what's a good way or how
2 could EPA do that.

3 **DR. KENNETH PORTIER:** Thank you. Any
4 additional comments? I thought I saw a hand go up, but then it went down, so I
5 was trying to figure out who it was. Dr. Johnson, did you get all of that?

6 **DR. MARK JOHNSON:** Yes sir. I believe I did.

7 **DR. KENNETH PORTIER:** Good. At this point, I have
8 10 after the hour. I'll ask Dr. Schlenk, who's the lead on 6.3, whether he thinks
9 we can kind of complete that in another 20 minutes. Dr. Schlenk?

10
11 **CHARGE QUESTION 6 (6.3)**
12

13 **DR. DANIEL SCHLENK:** Yeah, I'm pretty sure I can
14 read that into the record. I didn't get a whole lot of comments on it actually, so
15 basically, it's a page and a half which has been broken up into sections. So, I
16 would say within five minutes, I could read that.

17 **DR. KENNETH PORTIER:** Okay, great. So, before we
18 do that, let me turn to EPA and see if they have any additional comments or
19 questions on our response to 6.2.

20 **DR. STAN BARONE:** Not at this time.

21 **DR. KENNETH PORTIER:** Okay. So let's move onto
22 6.3. Comment on whether the information presented supports the findings
23 outlined in the draft risk characterization section. Dr. Schlenk is the lead. Dr.
24 Schlenk?

1 **DR. DANIEL SCHLENK:** Okay. The conclusion
2 subsection of the risk characterization section, Section 4.5, briefly outlines the
3 conclusions that presents various summary tables. For environmental risk,
4 Summary Table 4-110 shows RQ values in calculated days of exceedance
5 derived from modeling data. Data from Table 4-110 was used and set for 11
6 specific use categories. Concentrations of concern were provided for acute
7 toxicity, chronic toxicity, and algal toxicity. Derivation of these values has been
8 discussed in Question 3 in uncertainties and Question 6.1 and 6.2.

9 Risk quotients greater than unity were used to indicate
10 risk, or hazard really. In all use categories, RQs were greater than 1 for algal
11 toxicity -- this is for the 11 specific categories from 110 -- were greater than 1
12 for algal toxicity in many cases for chronic toxicity, although many of these did
13 not exceed the 20-day limit imposed by the agency or exposure necessary to
14 elicit their responses.

15 In Section 5, determination of risk was provided and Table
16 5-1 focused on environmental risk. However, for risk determination, Table 5-1
17 subcategories of PCE used was provided. And in contrast to Table 4-110,
18 conclusions of known reasonable risk was provided by the agency.
19 Consequently, there seemed to be a disconnect between what was provided in
20 Table 4-110 and that provided in Table 5-1.

21 So the recommendation there would be that there needs to
22 be some consistency between what's actually discussed in Section 4 and in
23 Section 5 in terms of the use category evaluations. Additionally, the statement
24 that additionally there was no PCE toxicity available for amphibians is at best an

1 error. The problem formulation includes data from McDaniel that shows
2 abnormality for two amphibian species at 7.8 and 7.9 milligrams per liter.
3 Again, these data should be used in the assessment. Any additional amphibian
4 data for PERC should be incorporated.

5 For human health exposure, EPA disavowed those
6 consumer dermal exposure calculations in the DRE based on methodological
7 error and promised to revise them for the final version of the DRE. All
8 consumer dermal risk estimates in the DRE should therefore be considered
9 unsupported.

10 For human health risk, the first section on OES considers
11 risk both with and without PPE use and shows detailed lists of MOE values plus
12 and minus PPE use for each OES. That's Table 4-112. Consumers and
13 bystanders are considered separately, and MOU values are listed for each
14 condition of use for Table 113. The information in these tables concisely and
15 accurately summarizes the conclusions in the evaluation. As this section was not
16 meant to provide rationale for choices or express the degree of confidence for
17 uncertainty, it achieves a simple goal of presenting the risk characterization
18 results.

19 The criteria for concluding environmental risk greater than
20 1 and those for concluding acute or chronic noncancer MOE and cancer risk are
21 explained elsewhere. Addition of a simple cross-referencing statement to where
22 these criteria are explained might be helpful. EPA estimated human health risks
23 from both potential cancer and noncancer endpoints following acute and chronic

1 PCE exposure. Several animal studies support the health concerns of
2 neurotoxicity, kidney, liver, immunotoxicity and developmental toxicity.

3 And following acute chronic exposure to PCE, one
4 committee member noted that NOAEL or LOAEL was used to determine
5 chronic cancer or non-cancer risks, but no NOAEL or LOAEL doses were
6 properly presented in the DRE. Since doses for NOAEL and LOAEL are varied
7 with species and exposure route, this member recommended that EPA should
8 present NOAEL and LOAEL doses routes in animal species in a tabular form in
9 the DRE.

10 Another member thought the MOE for non-cancer and the
11 IUR for cancer were appropriately used for risk characterization. Here, as in
12 other DREs, the agency lists exposure reduction factors when PPE is used,
13 something the committee has expressed reservations about in the past. However,
14 if they're going to be presented anyway, they should be put in context noting that
15 they are the least effective form of protection and should be the protection of last
16 resort after engineering controls or other safeguards are not feasible. And that's
17 all I got.

18 **DR. KENNETH PORTIER:** Thank you, Dan. Dr.
19 Hossain, anything to add?

20 **DR. MUHAMMAD HOSSAIN:** No, I have nothing to
21 add. Dr. Schlenk already covered my comment here. Thank you.

22 **DR. KENNETH PORTIER:** Thank you. Good. Dr.
23 Kissel?

1 **DR. JOHN KISSEL:** I'm sorry. I was distracted. The
2 consumer dermal risk is unsupportive. Was that stated?

3 **DR. KENNETH PORTIER:** Yeah, he had a general
4 statement of that.

5 **DR. JOHN KISSEL:** Yeah, okay. That's all that I need.

6 **DR. KENNETH PORTIER:** Thank you. Dr. Lash?

7 **DR. LAWRENCE LASH:** Yes, I'm here. So yeah, I
8 think my comment was covered. The main point I made here, I think, was just to
9 make the document more useful, so cross-listing would be helpful. And I think
10 that's a pervasive issue with the huge document. So that was the only other
11 point. Yeah.

12 **DR. KENNETH PORTIER:** Thank you. Dr. Willhite?

13 **DR. CALVIN WILLHITE:** Nothing to add.

14 **DR. KENNETH PORTIER:** Thank you. Dr. Vorhees?

15 **DR. CHARLES VORHEES:** No. Dr. Schlenk put my
16 comments in. I'm good.

17 **DR. KENNETH PORTIER:** Okay. Dr. Anderson?

18 **DR. HENRY ANDERSON:** Yeah, I just thought there
19 could be some asterisks or footnotes, again, about the PPE use that, really, the
20 PPE is most effective for short-term kind of emergency use reduction. So, the
21 data that we see for 15-minute sampling and things like that, those are really
22 utilized in suggesting whether or not the PPE should be warned for specific types
23 of activities.

1 The assumption that the total exposure that you're going
2 to expect workers to wear PPE continuously all the time, I think, is wrong. And
3 it would probably be good to put in there at least a footnote or something, again,
4 just reminding the reviewer that, as previously said, that the PPE is the last
5 choice that is most appropriate for the short-term or emergency use. And if
6 we're near the end, I just want to remind you, Ken, that I won't be on the call
7 tomorrow. So, don't ask me to comment or vote.

8 **DR. KENNETH PORTIER:** No, I have that marked
9 down, Henry. You're already marked.

10 **DR. HENRY ANDERSON:** Yeah. I won't be turning
11 my computer on. I may get in late if you run long, but I think that's unlikely.

12 **DR. KENNETH PORTIER:** Thank you. Any
13 additional comments on this last issue of the presentation of the information
14 supporting the draft risk characterization section? I'm not seeing any hands
15 going up. It may be a function of fatigue more than anything else. Dr. Schlenk,
16 any last comments?

17 **DR. DANIEL SCHLENK:** No, I think I got everything.

18 **DR. KENNETH PORTIER:** Good. Okay. All right.
19 This ends the work that we had clarified for the committee to do today, and I
20 think it's a good time -- we're about 20 minutes over which is surprising to me,
21 given that at one point, we were at least an hour behind our agenda. But I
22 appreciate the committee being increasingly efficient as we -- highly correlated
23 with fatigue, right? Higher fatigue, higher efficiency.

1 At this point, I will turn it over to the DFO for any final
2 comments before we end the meeting. We will begin again tomorrow morning
3 at 10:00 with Question 6.4. Tamue?

4 **MS. TAMUE GIBSON:** Okay. Thank you, Dr. Portier.
5 Can you hear me?

6 **DR. KENNETH PORTIER:** I'd already muted myself,
7 but yes. You're welcome.

8 **MS. TAMUE GIBSON:** Okay. Okay, great. All right.
9 So thanks for everyone, the committee and the public, for listening online. We
10 greatly appreciate it. This ends today's Day 3 portion of the peer review
11 meeting, and the meeting has been adjourned. Thank you.

12 **DR. KENNETH PORTIER:** Goodbye, everyone.

13
14 **[MEETING ADJOURNED FOR THE DAY]**
15

1 **MS. SARA WILSON:** Good morning. Welcome to the
2 fourth and final day of the meeting on the U.S. EPA peer review draft -- or peer
3 review of the draft risk evaluation for Perchloroethylene. Battelle is an EPA
4 contractor providing meeting support for this hearing, which to that is being
5 recorded. I will now introduce Tamue Gibson, the designated federal official.

6
7 **OPENING OF MEETING - DAY 4**

8 **MS. TAMUE GIBSON:** Thank you. Good morning and
9
10 I am Tamue Gibson, your DFO. It is my pleasure to open the fourth and final
11 day of this four-day online meeting for the Science Advisory Committee on
12 Chemicals. This is the peer review of EPA's draft risk evaluation for
13 Perchloroethylene.

14 This week's Webex host meetings have all gone very well.
15 However, if you encounter any problems with audio or video transmission today,
16 please refer to our TSCA SACC website, which is www.epa.gov/tsca, T-S-C-A,-
17 peer-review. For members of the press, EPA media relations staff are available
18 to answer your questions specifically about the meeting, so I would ask that you
19 please address all your questions to Mr. Ken Labbe. And his email address is L-
20 A-B-B-E.Ken, K-E-N@epa.gov. As noted in our announcements about the
21 SACC meeting, the agenda times are approximate.

22 Overall, the Committee sessions are going very well, and I
23 thank all of the peer reviewers for your contributions to this meeting. And I also

1 would like to thank the public for their participation. I now turn the meeting
2 over to our chair, Dr. Portier.

3 **DR. KENNETH PORTIER:** Good morning. Welcome,
4 Committee. Welcome, public, to this third and final day meeting of the SACC
5 on the draft risk evaluation of Perchloroethylene. As we've done in the previous
6 days, we're going to start with a roll call of members. Dr. Anderson we know is
7 working on COVID-19 work, so we'll start with Dr. Barton.

8 **DR. CHARLES BARTON:** Here.

9 **DR. KENNETH PORTIER:** Dr. Bennett?

10 **DR. STEVEN BENNETT:** I am here.

11 **DR. KENNETH PORTIER:** Dr. Blystone?

12 **DR. SHERI BLYSTONE:** Good morning.

13 **DR. KENNETH PORTIER:** Dr. Bruckner? Dr.

14 Bruckner?

15 **DR. JAMES BRUCKNER:** I think I answered again for
16 the wrong person. I'm here, too.

17 **DR. KENNETH PORTIER:** Thank you. Dr. Cory-
18 Slechta?

19 **DR. DEBORAH CORY-SLECHTA:** I'm here.

20 **DR. KENNETH PORTIER:** Dr. Davies?

21 **DR. HOLLY DAVIES:** I'm here.

22 **DR. KENNETH PORTIER:** Dr. Doucette?

23 **DR. WILLIAM DOUCETTE:** Present.

24 **DR. KENNETH PORTIER:** Dr. Gilbert?

1 **DR. KATHLEEN GILBERT:** I'm here.

2 **DR. KENNETH PORTIER:** Dr. Johnson?

3 **DR. MARK JOHNSON:** I'm here.

4 **DR. KENNETH PORTIER:** Dr. Kaufman?

5 **MR. ALAN KAUFMAN:** I'm here. Good morning,

6 everyone.

7 **DR. KENNETH PORTIER:** Good morning. Dr.

8 Kissel?

9 **DR. JOHN KISSEL:** Here.

10 **DR. KENNETH PORTIER:** Dr. Rowlands? Dr.

11 Rowlands?

12 **DR. CRAIG ROWLANDS:** Sorry. One more mute.

13 I'm here.

14 **DR. KENNETH PORTIER:** Ruthann Rudel?

15 **MS. RUTHANN RUDEL:** Hi, I'm here.

16 **DR. KENNETH PORTIER:** Dr. Schlenk?

17 **DR. DANIEL SCHLENK:** Here.

18 **DR. KENNETH PORTIER:** All of the charter

19 committee is here. Dr. Apte?

20 **DR. UDAYAN APTE:** Here.

21 **DR. KENNETH PORTIER:** Dr. Cobb?

22 **DR. GEORGE COBB:** I am here.

23 **DR. KENNETH PORTIER:** Dr. Daniels?

24 **DR. MICHAEL DANIELS:** I'm here.

1 **DR. KENNETH PORTIER:** Dr. Grant?

2 **DR. STEPHEN GRANT:** I'm here.

3 **DR. KENNETH PORTIER:** Dr. Hossain?

4 **DR. MUHAMMAD HOSSAIN:** I'm here.

5 **DR. KENNETH PORTIER:** And not to be left out, Dr.

6 Lash?

7 **DR. LAWRENCE LASH:** I am here.

8 **DR. KENNETH PORTIER:** Dr. Lin?

9 **DR. ZHOUMENG LIN:** I'm here.

10 **DR. KENNETH PORTIER:** Let's see. Dr. Meliker

11 should be here this morning. Dr. Meliker?

12 **MS. TAMUE GIBSON:** He'll be in in the afternoon.

13 **DR. KENNETH PORTIER:** Oh, the number is in the

14 afternoon. Okay. He's not here this morning.

15 **MS. TAMUE GIBSON:** Yes.

16 **DR. KENNETH PORTIER:** Dr. Roby:

17 **DR. KATHLEEN ROBY:** Good morning. I'm here.

18 **DR. KENNETH PORTIER:** Dr. Vorhees?

19 **DR. CHARLES VORHEES:** Here.

20 **DR. KENNETH PORTIER:** Dr. Willhite?

21 **DR. CALVIN WILLHITE:** Here. And I must tell you I

22 must leave promptly at your 3:00.

23 **DR. KENNETH PORTIER:** Well, we're shooting for

24 that, Calvin. Dr. Pennell?

1 **DR. MICHAEL PENNELL:** Here.

2
3 **COMMITTEE MEMBERS FOLLOW UP FROM THE PREVIOUS DAY**

4 **DR. KENNETH PORTIER:** Good. Okay. All present
5
6 and accounted for. So yesterday, we got through all of Question 5 and half of
7 Question 6. At this point, I'll ask the Committee are there any comments, follow
8 up to yesterday's discussion? I think there was something about Question 5.5 --

9 **MS. TAMUE GIBSON:** Yes.

10 **DR. KENNETH PORTIER:** -- related to the cancer
11 hazard assessment and the EPI meta-analysis. And I wondered if we could kind
12 of review or talk about that. I think Dr. Willhite, you wrote some comments on
13 that? I don't know if others went back and looked at them.

14 **DR. KATHLEEN GILBERT:** I did. This is Kate
15 Gilbert. I also looked at the comments.

16 **DR. KENNETH PORTIER:** Well, let's start with you,
17 Dr. Gilbert, since you're the lead on that question if I remember correctly. Oh,
18 no. Dr. Lash is the lead on it. No --

19 **DR. KATHLEEN GILBERT:** No, I'm the lead.

20 **DR. KENNETH PORTIER:** You're the lead. Okay.
21 Dr. Gilbert.

22 **DR. KATHLEEN GILBERT:** Okay. So I looked at the
23 Appendix F, and I just want to say that the EPA is to be commended for what I
24 thought was a really comprehensive and detailed description of the studies

1 looking at the connection between PCE and cancer in human and animals. And I
2 apologize for missing Appendix F in my preparation for the Question 5.5.

3 So in the epidemiological studies described in Appendix
4 F, the Agency kept using the expression “suggested but limited” to describe the
5 association between PCE and multiple cancer types, including lung, liver, breast,
6 and kidney cancer. The Agency performed a meta-analysis of five EPI studies
7 on kidney cancer, which showed no association or a weak association between
8 the incidence of kidney cancer and PCE exposure. Even more limited was the
9 evidence linking PCE to other kinds of cancer, including bladder and esophageal.

10 One exception was NHL where several studies showed an
11 elevated risk for PCE. However, we heard from Dr. Grant yesterday about why
12 blood cancers have unique characteristics that make it difficult to generalize
13 what you see in them to other kinds of cancer. In the animal studies, the most
14 common results following PCE exposure was the incidence of liver cancer,
15 followed by kidney cancer.

16 Bottom line, I concluded that the assessment by the
17 Agency in the DRE regarding the connection between PCE and cancer was as
18 accurate as possible given the data and that the choice of liver cancer for the dose
19 response analysis was also the best choice given the data. That’s all I have.

20 **DR. KENNETH PORTIER:** Thank you. Does anyone
21 else want to comment on that? Raise your hand. Dr. Grant?

22 **DR. STEPHEN GRANT:** I just sent comments to that
23 effect to Dr. Gilbert, and basically, we are completely in accord.

1 **DR. KENNETH PORTIER:** Thank you. Anyone else
2 want to kind of add in on that? Maybe I should ask Dr. Gilbert if this -- the end
3 of 5.5, you expressed some concern about knowing where the conversation had
4 landed. Does this kind of help you in terms of being able to write up
5 recommendations and discussion to Question 5.5?

6 **DR. KATHLEEN GILBERT:** Well, I'd still like to hear
7 from Drs. Lash and Willhite about this. I think they were the ones who were
8 raising the most concerns. So as far as I'm concerned, this is fine. But I would
9 like to hear what they have to say.

10 **DR. KENNETH PORTIER:** Dr. Willhite or Dr. Lash?

11 **DR. LAWRENCE LASH:** Hi, this is Larry. Yeah. I
12 think we've kind of come a ways with this section, so I guess the main concern --
13 and this comes up again in later discussions. It really comes down, I think, to the
14 issue of biological plausibility, and I understand the need for having data -- dose
15 response data and so on to support calculations. But I think the issue is the
16 biological plausibility and for humans as opposed to for other species. But I
17 think we certainly incorporate a lot of that. That's all I have.

18 **DR. KENNETH PORTIER:** Okay. Dr. Lash, are you
19 going to revisit your comments and kind of make some clarifications and get that
20 back to Dr. Gilbert so she can incorporate that? Dr. Willhite, did you want to
21 comment?

22 **DR. CALVIN WILLHITE:** Just very briefly. What I'd
23 recommend is that the EPA follow its guidance, and, specifically, the cancer
24 guidelines state, exceptionally -- that is carcinogenic to humans -- "may be

1 equally appropriate with a lesser weight of epidemiologic evidence that is
2 strengthened by other lines of evidence. It can be used when all” -- and I want to
3 emphasis -- “it can be used when all of the following conditions are met.”

4 There’s four conditions that must be met. One, there is
5 strong evidence between human exposure and either cancer or the key precursor
6 events of the agent’s mode of action but not enough for causal association.
7 Second point, there is extensive evidence of carcinogenicity in animals. Third
8 point, the modes of carcinogenic action and associated key precursory events
9 have been identified in animals. And the last, there is strong evidence that the
10 key precursory events that precede the cancer response in animals are anticipated
11 to occur in humans and progress to tumors based on biological information.

12 If one looks at each of those four points, save for perhaps
13 the last one, there is strong evidence that the key precursory events that precede
14 the cancer response in animals are anticipated to occur in humans and progress to
15 tumors based on biological information. Each of the others we have biochemical
16 and genotoxicity, and, of course, we have the extensive evidence of
17 carcinogenicity in animals. And we don’t necessarily expect species
18 concordance. However, the mode of action in kidney is fairly well-described.

19 Therefore, what I would ask as part of our -- in my written
20 comments is EPA step through its own cancer guidelines, address each of those
21 points, and clarify why they are selecting mouse liver, with all of its problems,
22 and why -- and if you don’t select mouse liver, what you have is F344 rat
23 leukemias, which appear to have a very high background. So you’ve got such
24 complex problems with the animal models that now you’re left with only the

1 human data. So at any rate, I would recommend that EPA step through each one
2 of those items that are listed under the paragraph beginning with the word
3 “exceptionally.” And that’s all I have to say.

4 **DR. KENNETH PORTIER:** Dr. Grant?

5 **DR. STEPHEN GRANT:** Okay. Bear with me. I’m
6 actually going to read something that I just sent to Kathleen. “Based on my
7 looking at Appendix F and overall, I would conclude that although a mode of
8 action of genotoxicity is better established for kidney cancer than liver cancer, it
9 does provide proof of principle that PCE is capable of acting as a mutagenic
10 carcinogen.

11 “As long as the evaluation is driven by liver cancer and is
12 largely based on rodent data, it is critical that the data be evaluated based on the
13 contribution of PPAR alpha activation. If it is reasonable that this mechanism
14 accounts for all of the liver cancer in the rodent models, than it is problematic to
15 extrapolate these data to humans. We’d have to check, but I’m pretty sure that
16 EPA policy requires assuming a linear no-threshold model in the case of a mixed
17 mode of action. And the possibility could exist that you could try to correct it for
18 the contribution of PPAR alpha, but I think that’s probably asking too much.”

19 So that’s my conclusion, and that is that the evidence isn’t
20 as strong as we would like. There is evidence for another mechanism that does
21 not translate well to humans, and the question is how do we deal with that. Do
22 we drop liver and move to something else, or do we assume that even if the two
23 are 50/50 that it’s still best to use the liver data for the POD? Thanks.

24 **DR. KENNETH PORTIER:** Dr. Lash?

1 **DR. LAWRENCE LASH:** Yeah. Just a brief thing. I
2 just want to say that I think what Dr. Willhite provided is very useful because it
3 gives a specific action recommendation. And I think it goes along with what I
4 said that you have to have the biological plausibility. And that's what's missing
5 with, I think, the liver data and the leukemia. So I support his comments. That's
6 all.

7 **DR. KENNETH PORTIER:** So what I'm hearing you
8 say, Dr. Lash, is that at least in the DRE maybe the discussion on the plausibility
9 for these two cancers -- the animal observations being plausible in humans -- that
10 discussion needs to be enhanced. That would be the recommendation here -- that
11 if they're really going to go -- both you and Dr. Grant said the same thing. If
12 they're going to go with liver cancer, that relevance discussion needs to be
13 increased for liver cancer. And if they're not going to go with leukemia, the lack
14 of relevance or the -- I think in the case of the leukemia, the lack of power for
15 determining a significant effect in animals needs to be discussed.

16 **DR. LAWRENCE LASH:** Yes, for sure. And in fact, I
17 even noted in one of my early -- my comments yesterday -- I forget which
18 specific section -- that the evaluation at one point notes -- but I thought it
19 understated the potential issue by saying that it would potentially reduce
20 significance for the PPAR responses. So I don't think they dealt with the
21 justification in their rationale very well. So yeah.

22 **DR. KENNETH PORTIER:** Dr. Grant, your hand's still
23 up.

1 **DR. STEPHEN GRANT:** Yeah. I just wanted to say I
2 was a little confused because the section on liver cancer then invoked the TCA
3 draft evaluation. And basically, if we're sticking with liver as the main driver of
4 our evaluation, then I don't think we can simply refer to the TCA evaluation.
5 We have to bring more of that into this evaluation because it is the evidence for
6 using -- for genotoxic mode of action in liver.

7 **DR. KENNETH PORTIER:** Okay. That's a good point.
8 I have a question on the kidney epidemiology stuff. I just reread the discussion
9 in Section F 1.5. The recent studies that are quoted and that find no association
10 are not done in dry cleaning populations. They're done in electronics. They're
11 done in aircraft manufacturing. And we know in some of those populations that
12 the volatiles are more of a mixture than a PCE or PERC specific exposure, which
13 kind of Dr. Willhite alluded to yesterday as being one of the strengths of
14 examining especially kidney cancer effects in dry cleaning. Can you comment
15 on that, Dr. Grant, Dr. Lash?

16 **DR. STEPHEN GRANT:** I have to think about it.

17 **DR. KENNETH PORTIER:** Okay. To me, that was
18 one of the issues that I was looking to see addressed. The epi data is what the epi
19 data is, and the epi studies covered in the IRIS assessment tended to focus on the
20 dry-cleaning populations. And the newer studies don't tend to focus on dry
21 cleaning. It's other populations, which brings up that whole issue of when you
22 don't find an association but you're dealing with a less than powerful exposure
23 measurements in the epi study. Then kind of weight of the evidence goes down.
24 Dr. Bruckner's got his hand up. Jim?

1 **DR. JAMES BRUCKNER:** Hi, I just wanted to reiterate
2 that in my experience the evidence for the genotoxic mode of action, of course,
3 is much stronger in kidney than in liver. There are other mechanisms that
4 probably offer to liver beyond the PPAR. There's hypomethylation of some of
5 the oncogenes. There's, of course, hepatocellular death and proliferation.
6 There's inflammation. There's oxidative stress.

7 So there's all these other mechanisms that appear to be
8 occurring in liver. Some may be occurring in kidney. But just the weight of
9 evidence in my mind says genotoxicity -- if it's a mechanism in liver, we don't
10 have very good evidence of that. But we do have good evidence in kidney. So
11 just wanted to add that.

12 **DR. KENNETH PORTIER:** So that helps in
13 establishing hazard and MOA, but it doesn't necessarily help in the establishing
14 a point of departure. And the problem is the kidney is useful in establishing
15 hazard. Then you go to the liver to establish the point of departure. And I think
16 that's the concern that we're talking about here. Dr. Lash?

17 **DR. LAWRENCE LASH:** Yeah. I was just going to
18 add -- because you made the point of Appendix F and the electronics workers
19 with presumably mixed exposures -- and I recall in something that Dr. Willhite --
20 one of the documents that he sent out that there was something about that there
21 were studies with mixed exposures but where they actually determined and
22 specified the specific component that was PCE. But also, I wanted to say that
23 looking through Appendix F, which summarizes -- or is supposed to summarize
24 the epi studies and other studies since the 2012 IRIS document, that it doesn't

1 seem to include, I believe, what Dr. Willhite sent and listed other studies -- that
2 there are additional studies that seem to have more positive associations for
3 bladder and kidney than are summarized in that appendix. So I think that's
4 important that there are additional studies that he identified.

5 **DR. KENNETH PORTIER:** Well, we'll include them,
6 then. Dr. Gilbert?

7 **DR. KATHLEEN GILBERT:** Well, I think the point
8 was brought up yesterday is were those studies included in the bibliography of
9 the studies that the EPA looked at? And they may be not mentioned in the text,
10 but were they part of the overall examination? And I don't know the answer to
11 that.

12 **DR. KENNETH PORTIER:** I think that was why Dr.
13 Barone in our administrative meeting this morning was asking that those
14 references be included so that they can double check that they were examined
15 but were deemed inappropriate for some reason. And I think the issue we're
16 bringing up here is that, if those were deemed inappropriate, maybe that needs to
17 be added to the discussion in Section F 1.5 so that it's clear that they were looked
18 at but then assessed not appropriate. Dr. Grant?

19 **DR. KATHLEEN GILBERT:** Can I just make a point?

20 **DR. KENNETH PORTIER:** Oh, I'm sorry. Sure.

21 **DR. KATHLEEN GILBERT:** I totally agree with you,
22 but then it raises the issue for many other aspects of it where we -- people find
23 papers, and we don't know if they were included or if they -- do they need to be -
24 - does everything need to be described in the DRE?

1 **DR. KENNETH PORTIER:** I'm going to come back to

2 --

3 **DR. KATHLEEN GILBERT:** -- results or --

4 **DR. KENNETH PORTIER:** Katherine, I'm going to
5 come back to that in Question 7.3 when we look at other ways --

6 **DR. KATHLEEN GILBERT:** Okay.

7 **DR. KENNETH PORTIER:** -- to improve the
8 document. I've got some suggestions on how to kind of improve the weight of
9 evidence discussion to bring in a little bit more of that. I don't think they all
10 have to be discussed, but we have to get a better picture of how much was looked
11 at and how much was assessed as adequate, not adequate, how much was
12 assessed as high, medium, and low quality, those kinds of things.

13 It's hard to get a handle on that stuff, and I think that's
14 kind of part of the quality review and the weight of evidence discussion in the
15 DRE that we continue, as a Committee, to comment on.

16 **DR. KATHLEEN GILBERT:** Good point.

17 **DR. KENNETH PORTIER:** Dr. Grant?

18 **DR. STEPHEN GRANT:** Well, now I have three things
19 I have to comment on. The first is that part of being a systematic review is that
20 you have to account for all of the literature, and that's really what we're talking
21 about here is we have to know whether it was considered. Then we can go on
22 and determine whether it was considered properly. But what we can't do is our
23 own searches and then say, "Oo, look. I found something that they didn't know
24 about." We need to know right away whether they knew about it already.

1 The other thing is I have thought about the issue of
2 looking at different worker populations. And yes, it is problematic to use data on
3 people who are less exposed. And this is one of the problems with our data
4 source, which is the open literature, and one of the factors that goes into the open
5 literature is novelty, which is -- having worked in tobacco, I've actually
6 published studies where people have said, "Why are you doing that again? Why
7 are you beating that dead horse?"

8 So it may well be that, at the moment, it's easier to fund
9 studies into other source of PCE than it is dry cleaners because it's felt that that's
10 been mined properly. Again, it comes back to maybe there has to be some way
11 for a group like this to recommend -- and this is an RFA -- on generating data
12 that we feel is very important for regulatory concerns.

13 Last thing, it came up again, despite my refuting it earlier
14 in the week, that there are other mechanisms that work in the liver. There may
15 be, but the only one that has extensive evidence is PPAR alpha activation.
16 There's a couple of papers on epigenicity, and there's a couple of papers of
17 cytotoxicity, certainly not enough to say, "Oh, well, they're well-established
18 mechanisms." Although, the DRE does say that -- that there's lots of evidence
19 for this being a mixed mechanism.

20 Cytotoxicity and epigenetic can both be secondary to
21 genotoxicity and we just heard oxidative stress, which can also induce
22 genotoxicity. I'm now going to read -- "want to reiterate the evidence that
23 cytotoxicity and epigenetics as mechanisms independent of genotoxicity is so
24 weak that it is a vast over interpretation to use them as evidence that PCE has

1 multiple mechanisms of carcinogenicity. At best, I think those mechanisms
2 should be mentioned in a cautionary way as potential other mechanisms.”

3 **DR. KENNETH PORTIER:** Thank you, Dr. Grant.
4 Anyone else want to comment on this? I see Dr. Barone has his hand up. He
5 wishes to make a comment or ask a clarifying question. Dr. Barone?

6 **DR. STANLEY BARONE:** One of the comments -- and
7 this follows on Dr. Willhite’s comments from yesterday and the comments by
8 the lead this morning, Dr. Gilbert. As it relates to what studies we evaluated, if
9 you look at the supplement on our data evaluation, you’ll see what studies we
10 evaluated. And at least one of the studies that Dr. Willhite mentioned -- I believe
11 it was the Ma study -- did not have -- did not receive -- it received a low ranking
12 and wasn’t carried forward for dose response analysis because it actually didn’t
13 have good exposure characterization. It was just proximity to a PCE source, no
14 characterization of exposure. So it was hard to actually use for dose response.

15 So again, I think if the Committee could look at the
16 supplemental file and cross walk what references they think are new, if there’s
17 something we haven’t already evaluated, we definitely want to evaluate it in
18 response to the recommendations. And if you think we got the evaluation
19 wrong, we’re, of course, wanting to hear your comments and recommendations.

20 **DR. KENNETH PORTIER:** Thank you. I think we’ve
21 had enough discussion on this. There’s opportunity in our comments here, if the
22 Committee wants to do a little bit of additional work and add that to the minutes,
23 that’s probably acceptable, especially as regards to arguing whether certain
24 literature citations are included or are properly included or excluded. If there’s

1 some discussion on that, we'll put that into the minutes. Dr. Gilbert, I think I'm
2 going to end the discussion on this, and let's move on with today's agenda, if
3 that's okay. Any final comments?

4 **DR. KATHLEEN GILBERT:** That's fine. I think I
5 have everything I need.

6 **DR. KENNETH PORTIER:** Thank you. Okay. I think
7 we're at Question 6.4 under risk characterization if I remember correctly. We
8 read it into the docket yesterday, but let's go ahead and kind of read 6.4 back in
9 again so that we can begin our discussion. I'm not sure who's reading this
10 morning.

11
12 **CHARGE QUESTION 6 (6.4)**

13 **DR. MARI LEE:** This is Mari Lee. I'm on again today.
14
15 So Question 6.4, please comment on the applicability and completeness of the
16 underlying data used to support the risk characterization and the sensitivity of the
17 Agency's conclusions to analytic assumptions made.

18 **DR. KENNETH PORTIER:** Thank you. And Dr.
19 Cobb, you have the lead on this.

20 **DR. GEORGE COBB:** Yes, Ken. That's correct. So
21 first of all, thanks to all of the discussants for participating in this. We've
22 divided this into two different sections: an environmental health section and a
23 human health section, just for clarity. These comments also feed into 11

1 working recommendations, which I'm not planning to read in today unless you
2 want them read in today.

3 **DR. KENNETH PORTIER:** Those recommendations
4 will be in the bulleted slide for our draft 0, right?

5 **DR. GEORGE COBB:** Correct.

6 **DR. KENNETH PORTIER:** Good.

7 **DR. GEORGE COBB:** They're already in what we
8 drafted up. So the first thing that's kind of overarching is that exposures to PCE
9 through legacy issues will influence both human health and environmental health
10 releases and exposures. And they've not been evaluated, and the discussants
11 agreed that this evaluation's really incomplete until those aspects have been
12 incorporated somehow.

13 Now, going on to the environmental health aspects, it's
14 unclear to the Committee how literature studies have been excluded in Section
15 3.1, even though they were found to be acceptable during the problem
16 formulation. As an example, the developmental toxicity done for vertebrate fish
17 using the Japanese medaka seemed to be teratogenic or seemed to show
18 teratogenesis at a low concentration, deemed acceptable and then discarded
19 somehow between problem formulation and here. And it's really critical to have
20 as much data as possible when considering these sublethal endpoints. And this
21 feeds back into what Dr. Johnson lead us through in Question 3.1.

22 Also -- and there are page numbers for all this. I'm not
23 going to read all the page numbers -- but statements about ambient
24 environmental concentrations of PCE exceeding concentrations of concern is

1 misleading in several places. There's so few downstream monitoring data that
2 it's really difficult to draw any inferences from the monitoring data. Statements
3 linking releases to upstream monitoring stations or monitoring stations in vastly
4 different parts of a watershed really should be removed or qualified very
5 specifically as to what those distances of removal are.

6 On the exposure side, it's unclear why the MPDS
7 monitoring data was not evaluated using the EFAST models -- not used to
8 evaluate the EFAST models, excuse me. And it's also unclear why municipal
9 discharge data from the DMR was also not used in the exposure assessment.
10 Also related to water, central tendencies of concentrations is really not what the
11 Agency should be doing. In the absence of monitoring data, high centile
12 concentrations are really what's needed to be used and considered in these
13 assessments.

14 I will give a line number, 9908. There's a statement in the
15 document that PCE was detected moderately, and then the sentence ends. And
16 then it starts, "However, PCE was not higher than the detection limit." Now,
17 that doesn't make any sense because, if it's detected, it can be not higher than the
18 detection limit. So there's some wording problems with those kinds of things
19 that need to be cleaned up. That may be a minor point, but it's something that
20 needs to be cleaned up.

21 Omission of general population exposures really needs to
22 be addressed in this assessment or some kind of comprehensive statement about
23 the assessments that are being done in other agencies -- other aspects of the
24 Agency really need to be included to give an overall picture of what's being

1 done to address the items or the exposures and risk that are not covered in this
2 DRE. I found it really difficult to resolve the fact that there were no
3 unacceptable risks from adhesives when adhesives were predicted to have the
4 highest releases to the environment. And that's line 10624 compared to Table
5 2.2 on page 67. So in fact, there were unacceptable risks found for other things
6 but not for the adhesives, even though adhesives had the highest releases. So
7 some rationale for why that was the case should be provided.

8 Risk quotients, in Section 5.3, need to be revised to
9 include the concentrations of concern that are based on the more robust analysis
10 that were discussed in Question 3. And also, as we saw in some other DREs or
11 assessments, care needs to be taken to ensure that if more than one facility's
12 discharging to a common wastewater treatment plant or a common stretch of a
13 river those need to be added. They can't be considered separately, especially if
14 they're discharging to a single treatment plant.

15 There are likely to be additional acute and chronic risks
16 determined once the more robust concentrations of concern are considered, as we
17 discussed in Question 3. In Table 4-110, the low number of days of exceedance
18 in the table, again, are difficult to justify, given the high mean aqueous
19 concentrations of Perchloroethylene that are reported. That's really the case
20 because the data analysis can't really be evaluated -- at least I couldn't find a
21 way to evaluate it. The probabilistic dilution model output and input is what's
22 going to drive those exceedances. And without an understanding of the
23 underlying functions of streamflow, the distribution shape of the streamflow and
24 the release distributions, it's really hard to determine whether that was done

1 appropriately. And I will say -- and I usually don't say this, but even if those
2 data were available, I don't think we would have time to adequately evaluate that
3 aspect.

4 It's also unclear in that table what the risk quotients
5 represent. Are they risk quotients that are averages? Is it some overlap of the
6 PDM probability of exceedance with a hazard value? I'm just not quite clear
7 what that is. So some explanation of that should be made. We've also talked
8 about average risks and average 7Q10s really tend to minimize risk quotients and
9 probably should be using higher centile values than that.

10 Staying in that table, there are some things that kind of
11 bother me, and there's been a little bit of discussion about this among the group.
12 And maybe there's a disagreement, but we've got chronic exceedances for
13 invertebrates at several places. And there's a specific one, 10 -- excuse me,
14 110000317194, where exceedances are predicted to occur on 70 percent of the
15 modeled days. So I think that's 14 of 20 days. And the risk quotient is 7.2. And
16 I get it that 14 days isn't 20 days for the chronic exposure. But with a risk
17 quotient of 7.2, I start to question whether there's not actually a risk there.

18 Furthermore, there are instances in this table where there
19 are between 60 and 80 to 80 percent of the days -- so somewhere between 12 and
20 18 days of exceedance -- with risk quotients over 100 at times. And there's no
21 risk identified. And I specifically think that that's a problem that somehow
22 needs to be addressed. And there are several instances where this is true, and
23 I'm not going to go through all of them.

1 There's also a statement on page 469 that the EPA
2 identified environmental risk for a condition of use. And given the uncertainties
3 in the data, the EPA does not consider the risk to be unreasonable. So that
4 represents an inappropriate use of uncertainty. If the uncertainty is high, you
5 can't say there's no risk. You have to gather the data to then reduce that
6 uncertainty. So if your risk quotients are greater than one and you've got high
7 uncertainty, that high uncertainty can't, in my estimation, given you a
8 justification for unreasonable risk. Data is the only thing that can do that for
9 you. And there are a couple of instances of that type of thing.

10 One thing that we didn't discuss as a group -- I added
11 afterwards, and I apologize to the group for this. On page 467, the term "aquatic
12 organisms" is used in that paragraph several times, and it's used pretty vaguely.
13 And I know the Agency was under a lot of pressure in writing this document, but
14 I think it's worth looking at that and writing that paragraph specifically to the
15 types of aquatic organisms that you're addressing.

16 Then one comment from some of the folks on the human
17 health side related to the environmental health aspects was that a data gap
18 appears to be related to algae exposures to PCE. And it is clearly noted in the
19 evaluation that there are three species of algae and that they have exposures and
20 recognition that algae -- that sensitive algae species -- sensitivity of algae species
21 can vary greatly. So the question really is how reasonably representative are
22 those three species. And some careful analysis of that, maybe even if it's
23 qualitative, could give a real support for the fact that those algae species are

1 representative of all algae. And as we heard yesterday, perhaps even aquatic
2 macrophyte. So those are things that we need to address.

3 Going on to human health, the DRE provides a thorough
4 discussion of sources of human health information, including those that are used
5 in previous assessments, such as those done by the EPA and ATSDR. And the
6 studies concluded after those assessments were identified and examined to see
7 whether human health data contained in those studies would impact the
8 conclusion of the previous human health assessment. In term of completeness,
9 the underlying human health data, there are some data gaps.

10 The EPA uses standard default assessments from their
11 stated policies to address those data gaps, but there are some things that maybe
12 need to be addressed. The EPA chose to use hepatocellular carcinoma for the
13 mouse and a cancer endpoint for departure -- point of departure calculation. A
14 linear extrapolation is used based on the policy of applying this to situations
15 where there's evidence of genotoxicity as part of the mode of action or where
16 little is known.

17 There are a couple of concerns with this. And I think this
18 goes directly to some of the things that were just being discussed last time. Is
19 mouse liver cancer appropriate when there are more -- there are really no
20 supporting data? There are very little data to support the conclusion that certain
21 Perchloroethylene metabolites can act by genotoxic mechanism, so really left
22 with a linear extrapolation based on the lack of mode of action information.
23 Such a default particularly for test organism that may have limited relevance to
24 humans does not inspire much confidence.

1 Then going to lung tumors, there's no evidence of this in
2 humans, despite the occurrence of multiple -- occurrence in multiple species of
3 rodents. Extrapolation to human without supporting mechanistic data is
4 problematic. Another comment is regarding the assumptions to support the risk
5 characterization and sensitivity. DNA damage is used as a biomarker for
6 assessing health risks to occupational chemicals. In Section 3.2.3.3.1, the EPA
7 mentioned that PCE may increase micronuclei and DNA damage in workers
8 exposed to PCE, but no stronger evidence was found to support that particular
9 statement.

10 The Agency also mentioned on page 271 that TCE caused
11 DNA breakdown in mouse liver and kidney after IP injection of TCE. There's
12 no reference provided. There was a study in 1999 that did a similar type of
13 design and did not find any DNA damage in liver, even with a higher dose of
14 TCE. So it's really hard to conclude that DNA damage was caused by TCE.
15 With that, those are the comments that I had received, and I will pass the torch
16 back to Ken.

17 **DR. KENNETH PORTIER:** Dr. Cobb, you mentioned a
18 page number in the DRE that -- and I checked it at the time. And I didn't see
19 your comment. Can you mention that page number again? It's back midway in
20 your presentation. I'm sorry.

21 **DR. GEORGE COBB:** Ken, can you tell me what it was
22 referencing?

1 **DR. KENNETH PORTIER:** Environmental hazard.

2 And you talked about a paper or a discussion to terrestrial -- I think it was
3 terrestrial stuff. I think you said 467. But that can't be because that's not the --

4 **DR. GEORGE COBB:** There's a 407 and a 469 in here.

5 **DR. KENNETH PORTIER:** 469 talks about
6 manufacturing. 407, you said?

7 **DR. GEORGE COBB:** 407 is a table.

8 **DR. KENNETH PORTIER:** Right. Is that the one you
9 were referring to? The point I wanted to make is you need to double check those
10 pages to make sure the reference is right.

11 **DR. GEORGE COBB:** Ken, I will double check and
12 cross-reference all those pages to make sure they're correct.

13 **DR. KENNETH PORTIER:** Yeah. Because I think one
14 of them, you were saying something, and I'm looking at the table. And it's like
15 that doesn't match up with what he's saying. Dr. Gilbert?

16 **DR. KATHLEEN GILBERT:** I think Dr. Cobb did a
17 great job, and I don't have anything to add.

18 **DR. KENNETH PORTIER:** Thank you. Dr. Hossain,
19 anything to add?

20 **DR. MUHAMMAD HOSSAIN:** I have nothing to add,
21 and Dr. Cobb cover everything very nicely.

22 **DR. KENNETH PORTIER:** Thank you. Dr. Kissel?

23 **DR. JOHN KISSEL:** So I'm struggling a bit with what
24 topics fall under what questions because there seems to be a lot of overlap. But I

1 would say, with respect to completeness of data use, I think the fact that EPA
2 does not have an occupational bystander category reflects lack of use of some
3 underlying data as there is certainly very good data for the people that cohabitate
4 in buildings with dry cleaners are exposed to PCE. And they're not covered
5 here. So I would consider that a lack of completeness.

6 Another topic which also falls under other questions is the
7 literature use. So when I independently just decided to think about dermal
8 absorption of Perchloroethylene, I went and did a literature search. And I came
9 up with some references that I think are valid that somehow got washed out in
10 EPA's review. And that may reflect differences in how those things are used and
11 what the criteria are. I think that's an issue of the -- also, it's a bit hard to
12 evaluate how EPA evaluated that literature.

13 The bibliographic document has got a huge list of stuff,
14 and it's presented in a way that makes it hard to parse. The individual
15 documents can be judge either on topic or off topic across different topic areas,
16 so you have to search all of them. It would be nice if that bibliography was
17 organized in a way where everything is listed in alphabetical order and then
18 there's columns which indicate where they're considered on topic or off topic or
19 not evaluated so one could more completely understand.

20 But even in the case of things that are judged on topic, if
21 you then search in the DRE, they aren't cited and appear to have been ignored
22 even if they were on topic. So I think there are issues about some things -- at
23 least within my neck of the woods in the dermal absorption literature, I think
24 some useful stuff got left out. So those are my comments for 6.4.

1 **DR. KENNETH PORTIER:** Thank you, Dr. Kissel. Dr.
2 Lash?

3 **DR. LAWRENCE LASH:** Dr. Cobb covered everything.
4 My comments had primarily focused on perceived data gaps, so he covered that
5 very nicely. And I don't have anything to add, then. Thanks.

6 **DR. KENNETH PORTIER:** Dr. Schlenk?

7 **DR. DANIEL SCHLENK:** George got all my
8 comments.

9 **DR. KENNETH PORTIER:** Dr. Willhite?

10 **DR. CALVIN WILLHITE:** Nothing to add.

11 **DR. KENNETH PORTIER:** Dr. Grant, I see your hand
12 up.

13 **DR. STEPHEN GRANT:** Yeah. Hello, I'm going to
14 reiterate a point I made earlier in the week that, as biomarkers go, micronuclei is
15 just about as good as there are. I would say chromosome aberrations are better
16 established. Bonassi et al 19 -- sorry, 2007, "an increased micronucleus
17 frequency in peripheral blood lymphocytes predicts the risk of cancer in
18 humans." Murgia et al 2008, "Validation of micronuclei frequency in peripheral
19 blood lymphocytes as early cancer risk biomarkers in a nested case control
20 study."

21 These are combinations of a Nordic combined study, an
22 Italian study which had a number of different investigators, and then it was
23 confirmed in a Baltic study. Micronuclei are a way of telling that someone is on
24 the pathway to cancer and at much greater cancer risk. And, in fact, I don't even

1 like using cancer risk because it predicted cancer incidents in a perspective
2 fashion. Bottom line, everybody, the data doesn't get any better than that, so we
3 have to respect it.

4 **DR. KENNETH PORTIER:** Yeah. Dr. Grant, that
5 comment may be more useful when we talked about that a couple of questions
6 back. So we'll be thinking about maybe putting that in a different place. I think
7 that's good support. Anyone else? Dr. Cobb, your hand's up.

8 **DR. GEORGE COBB:** Well, I was just going to say that
9 last comment -- if Dr. Grant could send me those references, I think I captured
10 what he was saying. But we probably need to address whether to put both Dr.
11 Grant's comments -- and I forget who sent me the other comment -- both in or if
12 we just move them both to a separate section or how to handle that. But I don't
13 want to have conflicting information in the cancer section and then this
14 uncertainty come back and say something different, if you agree, Ken.

15 **DR. KENNETH PORTIER:** Well, that's one of my jobs
16 when I reread this stuff. I look for those discrepancies. It might be that Dr.
17 Grant's comment might fit better on Question 5.5 where we actually discussed
18 the cancer hazard and the evidence. And I know we talked about mitochondrial
19 effects at that point. Dr. Rowlands?

20 **DR. STEPHEN GRANT:** Excuse me. Was that Dr.
21 Lash who wants me to send it?

22 **DR. KENNETH PORTIER:** Dr. Cobb, the lead.

23 **DR. STEPHEN GRANT:** Okay. Thanks.

24 **DR. KENNETH PORTIER:** Dr. Rowlands? Sorry.

1 **DR. CRAIG ROWLANDS:** That's okay. So yeah. It's
2 interesting the studies on the micronuclei -- and I think that's an important
3 observation. But I guess in addition to the paper citing where there were an
4 association between micronuclei and, I guess, incidence of all cancers, what is
5 the validation? We here about this often in science that we have a great
6 biomarker now. And then as it goes to a longer study and actual validation
7 protocol, it actually doesn't really -- it's not as good as everyone thought it
8 would be.

9 So I think it's important that we also provide the evidence
10 that this micronuclei is actually really predicting incidence of cancer, what kinds
11 of cancers, and what chemicals have actually been shown to (audio skip) nuclei
12 and then are associated with specific cancer. I think those are all very important
13 points.

14 **DR. KENNETH PORTIER:** I think that's a good
15 general point, and it almost sounds like a document that needs to be created in
16 support of all of these TSCA risk assessments. So I'm going to try to capture
17 that one. Dr. Johnson?

18 **DR. MARK JOHNSON:** Yeah. I just want to respond
19 to the comment that Dr. Grant made. I agree. However, there are some
20 exceptions. And those exceptions may be compounds that are through the oral
21 route and where a metabolite is not responsible. It's the parent. So in those
22 cases, sometimes the liver will transform it to a metabolite, and it's the parent
23 that's genotoxic. And then the common assay in the liver is probably going to be
24 more useful in those cases.

1 I know we were fooled a couple times in cases of -- I can't
2 say it now -- interpacket recirculation where the gut microbiome was responsible
3 for reducing actually a metabolite to a more genotoxic one. And we saw it in the
4 liver. Didn't really see it in the blood in the bone marrow. So I just thought I'd
5 throw that out there. I don't know if it applies in this case or not.

6 **DR. KENNETH PORTIER:** Dr. Grant?

7 **DR. STEPHEN GRANT:** The studies that I'm
8 referencing are not occupational studies. They are based on accumulations of
9 data from photogenetic testing labs. And basically, they're not looking at
10 induced -- necessarily induced micronuclei. We can always assume that there
11 must be an inducing agent. But I believe there are endogenous mechanisms. But
12 the bottom line was the baseline burden of micronuclei -- your frequency was
13 predictive of the future incidence of cancer.

14 **DR. KENNETH PORTIER:** Dr. Hossain, I saw your
15 hand go up and go down. Did Dr. Grant steal your comment? Dr. Cobb, your
16 hand is still up. Dr. Willhite?

17 **DR. CALVIN WILLHITE:** Yes, sir. As to the
18 comment about whether the parent compound or the metabolites that I just heard,
19 there's a paper by Nijhuis, N-I-J-I-H-U-I-S, from 2010. They conclude, "From
20 the weight of evidence from mutagenicity studies, there are no indications that
21 PCE -- that is the parent -- that PCE is genotoxicity. There's abundant evidence
22 that the mutagenicity and carcinogenicity of PCE exposure are mediated by its
23 metabolic products." And these are mutagenic in pore sign, renal, epithelial

1 cells, salmonella, et cetera. The important thing here is the parent compound is
2 not genotoxic. It is the metabolite. Thank you.

3 **DR. KENNETH PORTIER:** Dr. Hossain? Sorry. I was
4 muted. I thought I was unmuted. Dr. Hossain, you're muted in Webex. There
5 we go.

6 **DR. MUHAMMAD HOSSAIN:** Yes, can you hear me?

7 **DR. KENNETH PORTIER:** We can kind of hear you.
8 There's a lot of background noise.

9 **DR. MUHAMMAD HOSSAIN:** Hello?

10 **DR. KENNETH PORTIER:** Yes, I can hear you now.

11 **DR. MUHAMMAD HOSSAIN:** Okay. I think Dr.
12 Grant is right about the micronuclei, but there's a real concern about the data for
13 the DNA BMA. Only one study done with mouse found it caused DNA damage
14 by PCE. But similar study was done with other workers to reproduce the data.
15 They used different concentration of doses and 100, 500, or 1,000 milligrams per
16 kilo, similar conditions. But they didn't find any DNA damage in liver with
17 100,000 milligram per kilo. So this is very difficult to conclude whether PCE
18 caused DNA damage leading to cancer. Thank you.

19 **DR. KENNETH PORTIER:** Thank you. Back to Dr.
20 Grant.

21 **DR. STEPHEN GRANT:** Well, I thank everyone. I
22 tried to hold back during this panel, but now we're having fun. The issue with
23 micronuclei is that they are certainly -- they indicate mutagenicity but not by
24 ways that aren't indicative of DNA damage, believe it or not. Because it is a

1 chromosomal mechanism, there are two kinds of micronuclei, those that have a
2 centromere -- and we basically think that they fell off the spindle. So there are
3 agents that we would then call aneugens that cause aneuploidy. They might not
4 touch DNA at all. The other thing that you get are micronuclei that are pieces of
5 chromosomes, and those are the products of chromosome breaks.

6 One of the issues -- I'm now saying something that I,
7 again, wasn't going to bring up. But the issue with leukemia and lymphoma is
8 something called illegitimate BBK (phonetic) recombination, and that can result
9 in chromosome breaks simply because you can't resolve the break you make
10 when you splice together the immunoglobulin genes, for example. So there are
11 things where you can interfere with enzymes or interfere with the spindle, and
12 you get what is a mutagenic effect without ever interacting with the DNA itself.
13 And these things do contribute to cancer, and they may be more important than
14 we want to give them credit for because we now like to think of mutagens as
15 things that cause point mutations. That is very limited view.

16 **DR. KENNETH PORTIER:** Thank you. Dr. Willhite, I
17 see your hand's still up. Okay. Any additional comments? Thank you for that,
18 Dr. Grant. Dr. Cobb, I think we're ready to move on. Any final comments
19 before I turn to EPA?

20 **DR. GEORGE COBB:** Ken, I think I captured all of
21 that. If Dr. Grant and Dr. Kissel could just make sure to read this part when I
22 send it back around, I want to make sure I've captured their stuff appropriately.

23 **DR. KENNETH PORTIER:** Thank you. EPA, do you
24 have any comments to make or clarifying questions?

1 **DR. MARI LEE:** Not at this time.

2 **MR. JAMES BRESSETTE:** This is Jim Bressette EPA.

3 **DR. KENNETH PORTIER:** Yeah.

4 **MR. JAMES BRESSETTE:** Okay. I forgot to unmute
5 the first time. Referring back to the Spencer 2002 study on the Japanese
6 medaka, when that was brought up on Day 1, we went back into our data quality
7 supplemental, and we found an anomaly that's an error where the same study is
8 listed twice -- first time in occurrence of the supplemental. It shows an
9 unacceptable ranking, and then the exact same study in the same supplemental --
10 which is shouldn't occur twice -- shows it has a ranking of high. And dug a little
11 deeper. The second one appears to be -- the high ranking appears to be a
12 reevaluation of that first unacceptable ranking where it got put to high. I'm
13 going to reevaluate it, and it will be integrated into the risk assessment as
14 appropriate.

15 **DR. KENNETH PORTIER:** Thank you. So the
16 Committee has had at least one impact so far. Great. I think at this point let's go
17 ahead and move on to Question 6.5. Dr. Lee, would you read that in, please?

18
19 **CHARGE QUESTION 6 (6.5)**

20 **DR. MARI LEE:** Question 6, risk characterization
21 continued, EPA provided separate risk estimates for chronic inhalation exposures
22 using the key human hazard/assessment endpoint of neurotoxicity using
23 occupational HECs, i.e. assuming 1.25 cubic meters per hour inhalation rate.
24

1 Question 6.5, please comment on whether EPA sufficiently characterized and
2 evaluated considerations for the effects of differing breathing rates on risk
3 estimates, especially in the context of occupational scenarios. Additionally,
4 please provide any suggestions for adjusting risk estimates from other 24-hour
5 PBPK-derived HECs for occupational scenarios (Draft PCE Risk Evaluation:
6 Appendix G and Supplemental file number 16: “Assessment of Occupational
7 Exposure and Environmental Releases for PCE,” and Appendices B-C contained
8 therein.)

9 **DR. KENNETH PORTIER:** Thank you. Dr. Lash, you
10 have the lead on this.

11 **DR. LAWRENCE LASH:** Yes. So this I think, unlike
12 the questions that we’ve just been discussing, is a lot more restrictive and
13 specific in its focus. So hopefully it shouldn’t take too long.

14 So basically, when I approached this, I sort of also looked
15 to see where breathing rate -- did basically a document search and found where
16 this is referred to and how it’s dealt with. So that’s where I started off. So I
17 noted that in Section 3.2.5.3.2, which is a subsection entitled “Noncancer PODs
18 for Chronic Inhalation Exposure” -- and I’ll just quickly paraphrase it, not read
19 it, but it’s in the text that I’ll submit.

20 The document talks about workers, epidemiology studies
21 of dry cleaning and laundry workers exposed to PCE, and it notes that in order to
22 account for the presumed increase breathing rate of workers -- and I assume --
23 my assumption is that they’re presuming that there’s an increased breathing rate
24 just due to the exertion doing work that they do. And they’re assuming it’s ten

1 meters cubed over eight hours as opposed to 20 meters cubed over 24. And so
2 they're saying this is how they account for the increased rate.

3 And they additionally derived eight-hour occupational
4 HECs using eight-hour LOEC values from the original studies. They also
5 derived 12-hour values. And so I thought -- to me, this seemed reasonable to try
6 and account for the anticipated breathing rate. And they conclude that this did
7 not influence the calculated values.

8 They subsequently in Section 4.4.1 -- so now moving to
9 the risk estimation section. The evaluation stated in discussing specifically
10 potentially exposed or susceptible subpopulations. So they talked about different
11 factors such as human physiological factors, and this included breathing rate,
12 body weight, tidal volume and so on, as well as all the other typical factors such
13 as age, biological sex, genetic polymorphisms, pre-existing health status and so
14 on.

15 This is kind of -- it's a particular focus of TSCA, but I
16 think it's also an area that we presume a lot but we don't have a lot of direct
17 information on -- a lot of supporting data. So the document states that most but
18 not all of these factors are expected to be covered by the inclusion of a 10X
19 uncertainty factor. So this, I think, is reasonable, and it's also standard
20 procedure. The only question I noted was you could model some of these factors
21 and put data into PBPK models and get more precise estimates or predictions of
22 consequences for the exposure.

23 So also there was -- the Agency mentions some
24 uncertainties about susceptible populations, but there are no calculations made

1 for this. And we note, for example, conditions such as pregnancy, genetic
2 polymorphisms, obesity, kidney and liver illness, and these could be -- we could
3 input parameters, again, into models and get more precise -- I think a more
4 precise discussion of the potential impact. The charge question also directed us
5 to Appendix G of the evaluation, which is subtitled "Chronic Inhalation Risk
6 Estimates Using Occupational HECs." And there was a summary table, Table
7 Appendix G.1, that lists chronic inhalation risk estimates for all the OESs.

8 So I was looking, and I did not see how this -- how
9 breathing rate differences could be taken into account. They talk about risk
10 estimates with and without respirators. And there's a presumption that, based on
11 the discussion from the Section 3.2.5.3.2, that higher breathing rate for workers
12 is taken into account. But I think some clarification would be helpful for that.

13 Also, a Committee member noted that it would be useful
14 to, in this table -- to have exposure -- there's no exposure duration found for the
15 repackaging scenario, so that should be added into the table to make it more
16 complete. The charge question also asks us to look at supplementary file 16,
17 which is entitled "Assessment of Occupational Exposure and Environmental
18 Releases for Perchloroethylene." And it had two specific appendices, Appendix
19 1 -- Appendix B that has equations for calculating acute and chronic non-cancer
20 and cancer inhalation exposures, and Appendix C, which had sample
21 calculations. And I could not find anything that specifically showed
22 incorporation of breathing rate into exposure estimates.

23 So we came up with three specific recommendations. One
24 was -- the first one is that PBPK model based on human concentrations under the

1 eight or 12 hours after exposure to PCE should be run for risk estimation for the
2 various OESs; second, that a model can be used -- a PBPK model, again, can be
3 used to simulate effects of factors that may determine susceptible populations,
4 and these factors would include altered breathing rate and/or pulmonary tidal
5 volume due to exercise or pre-existing lung disease; two, altered physiology due
6 to age, sex, or physiological states such as pregnancy in females, pre-existing
7 disease such as diabetes, liver, kidney disease and, three, genetic polymorphisms
8 such as those known for CYPs and GSTs, which are important for PCE
9 metabolism. And then, finally, Table Appendix G.1 should be revised to include
10 calculation of HECs for the repackaging OES, which seem to be omitted. And
11 that was all I had.

12 **DR. KENNETH PORTIER:** Thank you, Dr. Lash. Dr.
13 Hossain, anything to add?

14 **DR. MUHAMMAD HOSSAIN:** Actually, I don't have
15 anything to add. Dr. Lash, I think, presented all the comments I provided to him.
16 And clearly we have the concern about the susceptible population. We don't
17 have enough data to how you can do a better prediction for this population. The
18 needs of this population need -- we need to make it more than two -- with each of
19 individuals to see how these individuals are sensitive to PCE. And that would
20 be, I think -- we need to go that way.

21 **DR. KENNETH PORTIER:** Thank you. Dr. Willhite,
22 anything to add?

23 **DR. CALVIN WILLHITE:** Yes, sir, a question. At
24 page 574, there's a presentation of different regulatory values. One of those

1 values is the permissible exposure limit, which is 100 parts per million with a
2 ceiling concentration of 300 parts per million. The question to us says, "Please
3 comment on whether EPA sufficiently characterized and evaluated factors on
4 risk estimates, especially in the context of occupational scenarios." As much as I
5 looked through the document, I don't see -- assuming we take the mouse liver as
6 the carcinogenic endpoint -- carcinogenic risk estimates for either the federal
7 PELs or the California PEL, which is 25 parts per million. Is that in this
8 document? Thank you.

9 **DR. KENNETH PORTIER:** So you're kind of saying in
10 addition to the point of departures that EPA has calculated risk for you'd want to
11 see risk calculated for occupational -- current occupational safety thresholds?

12 **DR. CALVIN WILLHITE:** I think that's appropriate to
13 do. Thank you.

14 **DR. KENNETH PORTIER:** Okay. I think, Dr. Lash,
15 that's kind of another recommendation. You might want to consider working
16 with Dr. Willhite to get the wording right. I don't think that was done in this
17 document, and I don't think we've seen it done in any of the previous risk
18 assessments either for probably multiple reasons that Dr. Anderson would
19 comment on if he were with us today. Dr. Bruckner?

20 **DR. JAMES BRUCKNER:** Yes. I was just going to say
21 that on Section -- or Question 5.3, we were going to address some of the
22 susceptible population factors that could be input into the models. And so I'll
23 include a section there, and then that can serve as support or cross-reference for
24 what Larry's going to be doing here.

1 **DR. KENNETH PORTIER:** Good point. I think Dr.
2 Lash mentioned something about the use of PBPK models. And I was sitting
3 there thinking how would that be done? But really, if you think about inhalation
4 rate as one of those factors that gets involved in a model sensitivity analysis,
5 understanding how the estimated HEC changes with minor changes in inhalation
6 rate would be useful input into this question. And I think Dr. Lin was the one
7 that mentioned that he felt they had done a good sensitivity analysis, but
8 someone would have to go back into the Chang paper and kind of extract out that
9 value to be able to answer this question. Dr. Lin?

10 **DR. ZHOUMENG LIN:** Hi, Dr. Ken. Yes, the other
11 day I mentioned about the sensitivity analysis that this paper described it is low
12 co-sensitivity in the analysis. Basically, they then the impact of the change of
13 each parameters on the outcome of interest, including four selected dosimetric.
14 This is standard sensitivity analysis that is commonly used in this field. This is
15 called a local, one-time sensitivity analysis.

16 In this group, by Dr. Cho (phonetic), later on, two years
17 ago, they published a small advanced sensitivity analysis method. It's global
18 sensitivity analysis. The difference is, in this paper, the local sensitivity analysis
19 does not consider potential correlations between parameters.

20 In the latest paper published by this lab in 2018, global
21 sensitivity analysis, they kind of consider the sensitivity, also the potential
22 correlations between parameters. So they can basically rank the sensitivity of all
23 parameters. So this is something of the sensitivity in this paper. Thank you.

1 **DR. KENNETH PORTIER:** So are they -- you mean
2 they're taking into account things like inhalation rate might be correlated or body
3 weight might be correlated with age? Certainly youth inhalation rates and
4 elderly inhalation rates may not be the same of those of the kind of middle-aged
5 worker. Dr. Lin is that -- yeah.

6 **DR. ZHOUMENG LIN:** You mean inhalation rates are -
7 - so my understanding is that inhalation rate parameter was used in the
8 calculation of human equivalent dose used in that equation described in the TIA
9 document. This parameter in the model is just one parameter. And then,
10 basically all they did is -- by changing these parameters by either 1 percent or 5
11 percent or 10 percent, and then kept other parameters the same. And then they
12 ran the model and then calculate the four dosimetrics.

13 And then there is an equation presented in this paper that
14 can calculate the coefficient. So it does not determine the potential association
15 between this inhalation rate with other parameters such as age, body weight,
16 others -- not for this local sensitivity analysis. For local sensitivity analysis, each
17 percentivity of each parameter is evaluated independently.

18 **DR. KENNETH PORTIER:** All right. Okay. Now, I
19 understand. Gotcha. Anyway, there's the opportunity to do that with the model.
20 Any additional comments? Dr. Daniels?

21 **DR. MICHAEL DANIELS:** Yeah. I was just going to
22 say that's kind of -- the local sensitivity analysis that was done in kind of the
23 original 2011 paper without the correlation is something that sometimes gets
24 critiqued also in, like, Monte Carlo sort of sensitivity analysis where you have

1 priors on all these parameters. And typically, you have tens or 20s of
2 parameters, and they're all assumed independent, which is not going to be the
3 case. So with this recent development in the literature that Dr. Lin mentioned, if
4 they could kind of -- that might be something that they could kind of tweak in
5 terms of some of the PBPK modeling that would be helpful. Because doing
6 them in isolation -- it's very hard to not do them one at a time because getting
7 that correlation is harder than even figuring out kind of what individual kind of
8 estimates potentially should be or individual parameter values should be. But it
9 might be something worth kind of the EPA checking into. That's all.

10 **DR. KENNETH PORTIER:** Thank you. Dr. Lash?

11 **DR. LAWRENCE LASH:** Yes. I just wanted to clarify
12 a comment I made about using --imputing PBPK into -- into a PBPK model
13 differing breathing rates. So this could be -- reflect some of my ignorance about
14 this. But it seemed to me in the statement I was quoting from Section 3.2.5.3.2
15 where it talks about the anticipated increased breathing rate of workers, which I
16 assume -- or anybody, say, exercising or exerting where it looks like it's about
17 50 percent because it says ten meter cubed over eight hours as opposed to 20
18 meter cubed over 24.

19 So the idea or -- and it could be that this was done because
20 they talk about -- the evaluation talks about inputting values and modeling. And
21 their concluding statement was, "These additional derivations did not result in
22 any change to the uncertainty factors." So what I'm wondering if maybe it's
23 potential that some other process has saturated -- so increasing the breathing rate
24 doesn't end up having a net effect on delivery of inhaled PCE or whatever. But

1 if that's the case, or something to that effect, a little more explanation to clarify
2 that would be helpful. So that was all I wanted to add.

3 **DR. KENNETH PORTIER:** Good point. Dr. Bruckner,
4 your hand's still up.

5 **DR. JAMES BRUCKNER:** Yes, sir. I just wanted to
6 mention again -- and there are issues in Ginsburg's original paper. When they
7 did their local sensitivity analysis, breathing rate or alveolar or ventilation rate
8 had the greatest impact, along with, like you'd expect, cardiac output or
9 pulmonary blood flow and blood-air partition coefficient. So each of those
10 factors had a pronounced influence on just the level of parent compound that was
11 absorbed into the body and entered the bloodstream.

12 **DR. KENNETH PORTIER:** So Dr. Bruckner, before
13 you go, I think the big question here is whether minor changes in that breathing
14 rate would result in more than a tenfold factor of change in the HEC or enough
15 of a change in the HEC that the ultimate risk estimate would change by what
16 we're accounting for in the uncertainty factor. One of the concerns is that some
17 of these factors -- minor changes could be more than what we're accounting for,
18 which would mean, for example, an individual who has high breathing rate or
19 maybe an individual with poor cardiac performance might move from the tail of
20 the standard worker population to become part of a PESS population that we
21 need to consider. And part of the thing that I struggle with is that we throw in a
22 three or a tenfold uncertainty factor, and we're assuming that that covers the
23 normal population. But we're never quite sure how spread the normal
24 population is. Do you follow what I'm saying?

1 **DR. JAMES BRUCKNER:** I do. I recall from just some
2 direct measurement studies -- thank you -- Astrine (phonetic) or some old papers
3 that -- some Scandinavian studies that were done years ago where they just had
4 subjects exercising at different rates. I remember the most pronounced
5 differences in exercise or breathing rate, cardiac output produced -- pronounced
6 changes in those produced no more than perhaps a 30 percent change in arterial
7 blood concentrations of a series of volatile organic compounds, if that helps. It
8 didn't produce as much of a change as I expected it might -- that is people
9 exercising at different levels.

10 **DR. KENNETH PORTIER:** I think that's very useful
11 information that somehow it needs to be incorporated into the PESS discussion,
12 which we're going to talk about after the break here, because that helps us to
13 establish kind of what's a normal range and then helps then to focus what
14 extreme condition might move an individual, a worker -- an occupational worker
15 or a non-user in this case to be considered not part of the norm. And what I'm
16 hearing you say is that at least with a lot of these physiological parameters that
17 the threefold or tenfold uncertainty that we assign to the risk in the normal
18 population probably covers a lot of tailed distribution physiology, if that's
19 correct.

20 **DR. JAMES BRUCKNER:** That's correct. That's my
21 impression. I was surprised to see that it didn't have more of an effect. But I'll
22 see if I can find some of those old papers that we could depend upon for this.

23 **DR. KENNETH PORTIER:** Thank you. Dr. Lash, your
24 hand is up.

1 **DR. LAWRENCE LASH:** No, no. I just forgot to put it
2 down. Sorry.

3 **DR. KENNETH PORTIER:** Okey-doke. Dr. Lin?

4 **DR. ZHOUMENG LIN:** Thank you. I just want to have
5 a final comment about the local versus global sensitivity analysis of the PBPK
6 model. Just now, another colleague mentioned about global sensitivity analysis.
7 I think it's okay to suggest that if they had done global sensitivity analysis that
8 would be better. But I will not produce as a required revision. This is because,
9 as far as I know in this field, sensitivity analysis is considered required to
10 perform before publishing a PBPK model. But typically, local sensitivity
11 analysis is considered adequate if a paper reports local sensitivity analysis
12 regarding -- this is adequate. So I would say this is recommendation but not a
13 requirement. Thank you.

14 **DR. KENNETH PORTIER:** Thank you. Dr. Bruckner,
15 your hand's still up. I didn't know if you wanted final comment or you just
16 hadn't put your hand down. Hand's gone down. Any final comments after Dr.
17 Lin's final comment? I'm not seeing any. Dr. Lash, it's been a good discussion.
18 Anything else you wanted to close out with before I turn to EPA?

19 **DR. LAWRENCE LASH:** No, I just needed from Dr.
20 Willhite text for his comment. But that was it. Otherwise, I think I got
21 everything.

22 **DR. KENNETH PORTIER:** So I'll turn to EPA and ask
23 are there any clarifying questions or comments?

1 **DR. MARI LEE:** This is Dr. Lee. No, no clarifying
2 comments at this time.

3 **DR. KEITH JACOBS:** This is Keith Jacobs. I just have
4 one quick comment. Just to clarify, I think that maybe we -- as was pointed out,
5 we need to better explain the process on what was done. There seemed to be a
6 lot of discussion about us saying "No changes," and then there was talk about the
7 uncertainty factors.

8 That was kind of just us -- just a, like, FYI statement. The
9 change in the breathing rate did result in 35 percent lower MOEs. And that's
10 why in the Appendix G I indicate -- I think it's in orange -- where basically the
11 risk conclusions change, where you have a different -- maybe you have risk
12 using the occupational HEC that you didn't before. So if the Committee thinks
13 that using that made sense, we may incorporate that appendix into the normal
14 occupational risk section, not just as an appendix and actually use that. That's
15 all.

16 **DR. KENNETH PORTIER:** Thank you. I think at this
17 point in our agenda we're due for a break. We're a little bit early. I have 11:35,
18 but let's go ahead and take a 15-minute break. If anyone on the Committee is
19 experiencing some of the phone issues breaking up, you might want to consider
20 using the communicate button in Webex to disconnect your audio and then have
21 them call you back in and reconnect. That's what I'm going to be doing here in
22 just a second because I've been getting a breakup of some of the conversation.
23 So we'll be back at ten minutes to noon. Thank you.

24 **MS. TAMUE GIBSON:** Thank you.

1 [BREAK]

2 **DR. KENNETH PORTIER:** Let's reconvene. By my
3 clock I have 11:50. At this point, we're going to move on to the discussion of
4 Question 6.6., if Dr. Lin would read that into the docket, please.

5 **MS. TAMUE GIBSON:** Excuse me, Dr. Portier. Dr.
6 Cobb has a comment in regard to Charge Question 6.4.

7 **DR. KENNETH PORTIER:** Dr. Cobb? Not sure Dr.
8 Cobb got back yet.

9 **MS. TAMUE GIBSON:** There he is.

10 **DR. KENNETH PORTIER:** Yeah.

11 **DR. GEORGE COBB:** Hey, Ken. I'm sorry. I took my
12 phone to a different room and left it. So full disclosure. Hey, just a real quick
13 comment, when we were talking about 6.4, at the end the Agency made a
14 comment about the medaka study getting removed and then accepted back in.
15 My comment is I encourage the Agency to really look through all of that data
16 again because every study that was accepted was based on nominal exposure
17 data. So all of those studies have a criteria by which the Agency probably
18 should have rejected them. So it's going to be very hard to justify rejecting
19 studies based on some minor problem. And that is my only comment.

20 **DR. KENNETH PORTIER:** Thank you, George. It's
21 an issue we've talked about in the past for other chemicals as well where the
22 studies report nominal doses and only few of them actually go in and confirm the
23 delivered dose. And for a couple of those studies, the delivered dose can often

1 be quite different than the nominal dose, which can have a big effect on
2 subsequent PODS. So it is an important point.

3 **DR. GEORGE COBB:** Yeah. Ken, that was standard
4 practice when these studies were done, so I'm not necessarily trying to trash the
5 studies. That's just how things were done. But if you're going to accept them,
6 then you kind of have to broaden what you're going to accept, in my estimation.
7 And that would increase the robustness of the dataset, honestly.

8 **DR. KENNETH PORTIER:** Okey-doke. So Dr. Lee,
9 can we move on to Question 6.6?

10
11 **CHARGE QUESTION 6 (6.6)**

12 **DR. MARI LEE:** Question 6.6, the Frank R. Lautenberg
13 Chemical Safety for the 21st Century Act, amended TSCA, states that
14 "potentially exposed or susceptible subpopulations," PESS, are considered in the
15 risk evaluation process. Question 6.6, has a thorough and transparent review of
16 the available information been conducted and led to the identification and
17 characterization of all PESS, Sections 2.4.3, 3.2.5.2, and 4.4.1? Do you know of
18 additional information about PESS that EPA needs to consider? Additionally,
19 has the uncertainty around PESS been adequately characterized?

20 **DR. KENNETH PORTIER:** Dr. Gilbert, we've kind of
21 relied on you quite a bit in this assessment. Thank you for volunteering. You're
22 the lead on Question 6.6.
23

1 **DR. KATHLEEN GILBERT:** I'm not sure I

2 volunteered. Okay.

3 **DR. KENNETH PORTIER:** What's that?

4 **DR. KATHLEEN GILBERT:** I said I'm not sure

5 "volunteer" is exactly the word I would use. So as far as the PESS, the Agency
6 lists all the potential factors that might increase sensitivity and provides a
7 rationale for why they may impact susceptibility. These factors included altered
8 physiology, for example, age; pregnancy; sex; pre-existing diseases like diabetes,
9 liver, or kidney disease; obesity or genetics, for example, genetic polymorphisms
10 in CYPs that may implement PCE metabolism. Plus, in the case of lipophilic
11 PCE, people with more adipose tissue, such as pubescent and adult women, may
12 retain PCE and thus be exposed to a sustained higher level of a chemical.

13 Also unique to PCE, the Agency describes that people
14 with existing liver or kidney disfunction or a neurological problems related to
15 vision or pattern recognition may be at increased risk for PCE induced toxicity.
16 Also, they discussed at potential greater risk are pregnant women, the developing
17 fetus and newborn infants. The PESS characterization in this, as in previous
18 draft risk evaluations, is pretty pro forma.

19 As noted by one discussant, there is unfortunately seldom
20 much in the way of direct data available to confirm that a particular
21 subpopulation is indeed more susceptible to injury from exposure and therefore
22 provide a rationale for driving risk assessment evaluations. While the rationales
23 for including all of these potential factors as impacting susceptibility are clear,
24 specific data demonstrating the altered susceptibility are generally not available.

1 This obviously creates uncertainty, which is incorporated into the uncertainty
2 factors that are used to calculate the various PODs.

3 I want to thank the discussants. They sent me a lot of
4 good comments. One discussant thought that co-exposure to other toxicants,
5 such as TCE, that could increase PCE toxicity should be addressed in this
6 section. And I'm going to ask if this discussion wants to expand on this and
7 perhaps state whether this concern rises to the level of a recommendation.

8 Another discussant did not think that the Agency had done
9 a good job at evaluating or distinguishing the potentially exposed population
10 from the susceptible subpopulations. They pointed out that the SS are people
11 that may require more protective overall acceptable limit in order to keep them
12 safe from the effects of the chemicals. They also made an interesting point that
13 if exposure levels are primarily set from animal data, there may be little evidence
14 of the human range of response. In such a case, there should be more discussion
15 on what the range of normal might be, and potential contributing factors should
16 be considered or at least additively to create a unique uncertainty factor for the
17 agent in question. And I'm going to ask this discussant if they want to say
18 whether this rises to the level of a recommendation.

19 The major concern of at least three discussants and a
20 public commenter was the potential insufficiency of a 10X uncertainty factor.
21 The 10X uncertainty factor for human intraspecies variability is thought to
22 account for most of the factors affecting exposure susceptibility. The Agency
23 acknowledges that it's unable to account for all possible PESS considerations.

1 Although the 10X is probably sufficient to account for
2 most biological mechanisms of increased susceptibility, it's not clear that it's
3 sufficient to encompass developmental effects of PCE exposure. This is
4 especially true in view of the potential overestimated POD for developmental
5 toxicity that we talked about with regard to Question 5.1 yesterday. There is
6 evidence that certain chemicals, including bisphenol A, arsenic, dioxin lead, and
7 TCE, can induce developmental toxicity at levels that do not cause maternal
8 toxicity. In some cases, the differential sensitivity can be in the log range. If
9 that is the case for PCE, obviously a 10X factor could not be sufficient to
10 encompass both increased sensitivity due to developmental exposure, as well as
11 all the other human intraspecies variability.

12 So at this point, I only have one recommendation, but that
13 may change after we hear some more from the discussants. And that
14 recommendation is, if the section on the PCE induced developmental tox as
15 discussed in Question 5.1 is altered to generate a lower POD, the uncertainty
16 factor that is thought to account for the increased exposure susceptibility for
17 developmental exposure may need to be adjusted upwards. And that's all I have,
18 so I'm going to turn it over to the discussants.

19 **DR. KENNETH PORTIER:** Thank you. Dr. Grant, do
20 you want to add?

21 **DR. STEPHEN GRANT:** Sure. So I separated the
22 susceptible populations into two groups: one who would be common susceptible
23 groups -- that would be obese. That would be aging. That would be pregnant.
24 And the issue that I had is that, since we really don't know what the protective

1 factor might be in those cases, that perhaps we might take a look at what the
2 percentage of obese people in the population are. Certainly, we don't care about
3 percentage. We want to protect pregnant women, for example, look at the
4 effective age, and basically, we want to assign requirements for protective
5 factors to a population. And then I would probably submit threefold for each
6 factor.

7 What's another way of approaching it in the absence of a
8 lot of data? If we have epidemiological data, these range of normal people, we
9 can actually do an epidemiological factor study and find out what their effect is.
10 But in the absence of that, we basically have to be protective.

11 Notice that we've talked about more than three
12 considerations, and that three would run up to nine-fold. I would say that if we
13 decided that there are more than three protective factors, that tenfold is probably
14 not a good default. Going on a little bit -- so yes, I think that should be a
15 recommendation, to consider each element in a susceptible population as
16 independently necessary of protection.

17 The second thing would be that's all normal. When we
18 talked about polymorphisms, a polymorphism by definition is something that's
19 common in the population, at least 1 percent. There are -- and again, I'm a
20 geneticist, but I think that there are other cases of disease and things where those
21 are going to be rarer. And the question is at what point do we identify people
22 who aren't going to be part of the population -- they're distinct -- but they still
23 need protection? Are they allowed to go out in the world and walk past a plant
24 that produces PCE?

1 So are there such people? Because we're not talking
2 about people that you would find in the normal population. They are rarer and,
3 to some degree, represent a unique population. But should we be looking to
4 identify such populations, and how much further do we go in protecting such
5 populations if we do identify them? In this case, I would say that there are
6 hyper-metabolizers that are rare that the question is are they -- are we creating
7 limits that protect them, or are they so unusual and rare that we can't afford to
8 protect them as we would the rest of the population?

9 I'd also like to mention that I'm in breast cancer. The
10 effective age on breast cancer, the difference in risk between a 35-year-old and a
11 65-year-old is twentyfold. So tenfold, if we're in the metric system, sounds like
12 a good default. But there are common risk factors that are larger than tenfold.
13 That's it for me.

14 **DR. KENNETH PORTIER:** Thank you. Dr. Hossain?

15 **DR. MUHAMMAD HOSSAIN:** Yes. I have a minor
16 comment about the susceptible population. The EPA listed people with poor
17 vision or neurocognitive deficiencies are under susceptible subpopulation. They
18 mention the page number 300. "Neurological endpoints are primarily related to
19 visual functions, pattern recognitions, and memory. Therefore, subpopulation
20 with poor vision or neurocognitive deficiencies may be especially susceptible to
21 these others."

22 I don't think that the people with poor vision or
23 neurocognitive people fall under this category because the susceptibility means
24 that they could have more proxy to this -- PCE could make more toxicity to this

1 population for the developing brain or in children. Children are more susceptible
2 because they have immature de-toxical mechanisms or the ability because they
3 have higher effect. So clearly the PCE can accumulate highly in the fat, so they
4 could have more accumulation and more toxicity. But I don't see that poor
5 vision could influence that susceptibility to the PCE. So I think this statement
6 needs to be corrected. Thank you.

7 **DR. KENNETH PORTIER:** Thank you, Dr. Hossain.
8 Dr. Lash?

9 **DR. LAWRENCE LASH:** Yeah. Dr. Gilbert included
10 all my comments, which weren't that extensive. But I actually just want to
11 comment that the suggestion about potentially having higher uncertainty factor
12 than the maximum default 10 for susceptible population I think is something to
13 consider because it kind of did bother me a bit -- I don't know if "bother" is the
14 right word. But it sort of peaked my interest in that in the comments there was a
15 couple places made where the document or the evaluation concludes that the full
16 uncertainty factor may not include -- or I forget the exact language -- may not
17 account for all susceptibilities and variabilities in populations.

18 And I think when you're dealing with so many potential
19 different types of factors such as the physiological differences, things like
20 breathing rate, lung function, cardiac, renal, liver function, and then you're also
21 dealing with the different occupational exposure scenarios and the potential
22 genetic polymorphism is something to consider. And it may be worthwhile to
23 pursue more -- certainly needs more. I think the point is that the set of vague

1 comment made in the evaluation about this may not be accounted for I think
2 needs further exploration. So that was it.

3 **DR. KENNETH PORTIER:** Thank you. Dr. Roby, we
4 haven't heard from you before.

5 **DR. KATHERINE ROBY:** Yeah. So I don't really have
6 anything new to add, but my comments were included by Dr. Gilbert's
7 statement. But I do very much agree with what Drs. Grant and Lash have just
8 said. It seems that the Agency kind of has agreed that they haven't really
9 considered or that they've been able to account for all of the uncertainty and
10 adding what we know as the range of variability -- especially in some of the
11 endpoint measures, it seems that the factor of 10 really isn't likely to cover the
12 range of possibilities. So I agree with the recommendations that Dr. Grant had
13 also just spoke to. And that's all.

14 **DR. KENNETH PORTIER:** Thank you. Dr. Willhite?

15 **DR. CALVIN WILLHITE:** Yes, sir. As I understand
16 the discussion, it's about whether the intraspecies default uncertainty factor of 10
17 is adequate. There's a paper -- I've cited it in my written comments. The first
18 author is Spearow, S-P-E-A-R-O-W, first initial J. It's from the Cal EPA people
19 in Sacramento. They looked at the genomic and metabolic variation, and they
20 come back with a 27-fold intraspecies uncertainty factor.

21 But there have been some metabolism comparisons
22 between different ethnic groups, notably Asians -- that is Koreans and Japanese,
23 Africans. So there's a range of values there. And what you might want to do is
24 use a data-driven uncertainty factor rather than a default 10.

1 And this is a little bit political, but what you don't -- what
2 the EPA doesn't want to do is suffer from criticism that they didn't have a large
3 enough, quote, safety factor. And there are people out here that make their living
4 off of that. So what I'd do is I'd recommend take a look at that Spearow and the
5 metabolism papers. Let's see if we can't get a data derived uncertainty factor.

6 Thank you.

7 **DR. KENNETH PORTIER:** Thank you. Anyone else
8 on the Committee want to comment? And while you're thinking about that, I'm
9 going to make a comment. I've been thinking about PESS and how these TSCA
10 evaluations address it. And to me, it needs to be looked at as two parts.

11 There's kind of the occupational worker PESS issue, and
12 then there's the consumer PESS issue. So if we look at the occupational
13 workers, the OUs and ONUs, you have to ask yourself, well, what kind of health
14 status scenarios might be covered by an uncertainty factor of 10? And what
15 health status situations might not be? So the question -- you look at things like
16 obesity. We talked about excess fat and the fact that this particular drug may be
17 stored short-term, long-term in fat.

18 So you have to ask, well, is obese workers factored in
19 here? Pregnant female workers factored in here? And I'll put the developmental
20 issue to the side because I really don't know what to think about that. But older
21 workers and how many of those are actually in that -- by older, I'm not just
22 thinking 65-year-old. I'm thinking about do we have workers in this industry
23 that are 70 years old and older.

1 We mentioned poor vision workers. We mentioned
2 reduce liver function -- workers with reduced liver function. If you think about
3 that -- and that was my question to Dr. Bruckner in the sense that I have a feeling
4 that that tenfold factor covers a lot of the variability in these workers, even some
5 of these that have -- that are in the tail of the body mass distributions, that are in
6 the tail of the liver function distribution, maybe even the vast majority of the
7 ages of workers. That's covered in tenfold. I didn't hear anything that kind of
8 pushes them out.

9 Then when you apply that same disease status discussion
10 to consumers, it gets a little bit more uncertain because you don't know the liver
11 status of -- you can't assume they're a healthy worker population, that there's
12 enough health in that individual to be participating in occupational work.
13 Consumers, some of them may have poor vision and be participating in activities
14 that utilize this. And some of them may have liver function deficiencies that are
15 bad enough that they're not in this occupational worker population, but they are
16 utilizing some of these products.

17 I think EPA needs -- what I'm getting at is EPA needs
18 kind of a framework to systematically think through PESS issues, and I don't
19 always see that in the PESS write ups in these three sections. And maybe they
20 need to be thinking about kind of putting that in. And then Dr. Grant's
21 discussion on genetic status -- that opens a whole other door that really has a lot
22 of uncertainty because we don't know distributions of genetic -- and I'll use the
23 phrase defects in quotes -- how in the worker population -- how many or what
24 fraction of that population may have genetic differences that might lead to

1 adverse endpoint affects that normal exposures in normal workers would not
2 occur.

3 But in these genetically different individuals it would
4 occur. And I don't know -- at this point, EPA can just state that's part of the
5 uncertainty, but I don't know if they can quantify that in a way that Dr. Willhite
6 was kind of mentioning. And then the alcohol consumption, which is more of a
7 lifestyle issue -- it impacts health status, but it's a factor that's more lifestyle
8 factor than it is a health status factor.

9 And we know that alcohol consumption may affect the
10 liver functioning, may affect obesity probabilities. Again, somehow figure that
11 into this framework. And that's kind of my comment, and I don't know what
12 you're going to do with that, Dr. Gilbert, except maybe I'll try to write up a
13 paragraph of that to get to you.

14 **DR. KATHLEEN GILBERT:** Okay.

15 **DR. KENNETH PORTIER:** And Dr. Barton? Chuck?

16 **DR. CHARLES BARTON:** Yes, thank you.

17 **DR. KENNETH PORTIER:** There we go.

18 **DR. CHARLES BARTON:** Can you hear me? Can you
19 hear me?

20 **DR. KENNETH PORTIER:** Yes. Yes, I can.

21 **DR. CHARLES BARTON:** Okay. Great. I just wanted
22 to mention I think I provided an article or two regarding the SIP 2E1 range of
23 concentrations between people. And I think it was like 24-fold difference. But I
24 supplied the article, which I don't have anymore. But I think it was when we

1 discussed carbon tet that I supplied the information. But we had a write up, I
2 believe, in carbon tet about that, about the SIP P450 variation that might be used
3 for this. That's all.

4 **DR. KENNETH PORTIER:** Thank you. That's
5 actually a good point. Now, what I would do is I would take that information to
6 my modeler and say, "Well, an individual who's got a different SIP 2E1 status
7 level, how does this impact the parameterization in this PBPK model? And if I
8 change those parameters to low or high levels, what does that do to the outputs,
9 and how does that relate?" And at least I'd have some information to know
10 whether that factor has the potential to move the endpoint outside that 20-fold
11 range.

12 **DR. CHARLES BARTON:** Hypothetically, it should.

13 **DR. KENNETH PORTIER:** You broke up. Please
14 repeat.

15 **DR. CHARLES BARTON:** I said hypothetically, it
16 should. If we can -- I think it would be very good, if we can point it out, to have
17 that modeled or be good information to know.

18 **DR. KENNETH PORTIER:** Yeah. And you would
19 think if it's 20-fold difference, it should show up. But if the model is not
20 particularly sensitive to those SIP effected parameters, it may not have more than
21 a two- or threefold impact. But you're right. It's some information -- it's
22 additional information that could help inform whether you identify those
23 individuals as a potential susceptible subpopulation. Dr. Bruckner?

1 **DR. JAMES BRUCKNER:** I was just going to mention
2 that I was a member of a National Academy committee that assessed what was
3 going on at Camp Lejeune where they had course PERC and trichloroethylene.
4 And just for context, I wrote a fairly extensive review on lifestyle factors and
5 susceptibility that could influence both the toxicity and the carcinogenicity. So
6 I'll provide that. That might be good at least just as a reference -- a good general
7 discussion.

8 **DR. KENNETH PORTIER:** Thank you. Ruthann
9 Rudel?

10 **MS. RUTHANN RUDEL:** Hi, there. Sorry. Took me a
11 while to unmute. I just was going to chime in that I also saw that sort of many
12 factors that would affect susceptibility are talked about, but then it's never
13 incorporated into the assessment beyond the 10X default. And others have
14 provided some information, like Dr. Willhite with the California 27X, and Dr.
15 Barton had previously provided some useful information about that.

16 I don't know if this would be a possibility, but NHANES
17 might be useful to estimate the proportion of the U.S. working age population
18 that's obese. And then also they may have some liver function measurements
19 because there's a lot of clinical measurement on everybody in that study that
20 could -- so that could be a way of sort of getting -- understanding maybe the
21 prevalence and even the range of liver function issues in the working age
22 population. And then in terms of alcohol, it may be a lifestyle factor, but I feel
23 like there has to be some room, I guess, built in for workers to be drinking
24 alcohol because it's sort of very common. Thanks.

1 **DR. KENNETH PORTIER:** Thank you. Dr. Grant?

2 **DR. STEPHEN GRANT:** It's not just very common but
3 socially acceptable. So you can't really require people not to do it and work. I
4 really do --

5 **DR. KENNETH PORTIER:** Dr. Grant, you're breaking
6 up. Can you get a little closer maybe?

7 **DR. STEPHEN GRANT:** -- doing things in an evidence-
8 based way. However, we can't expect that there's going to be evidence for
9 everything, so some things are going to fall back to a default. One of the things -
10 - we usual talk about genetics as something that highfalutin and high and the sky
11 and would it be nice if we had it. There are now common genetic tests --

12 **MS. TAMUE GIBSON:** Dr. Portier, I cannot hear Dr.
13 Grant.

14 **DR. STEPHEN GRANT:** -- if you order them. If you
15 get a 23 and Me profile, it will tell you polymorphisms that affect your
16 metabolism of drugs. We need to --

17 **DR. KENNETH PORTIER:** Dr. Grant. Dr. Grant.

18 **DR. STEPHEN GRANT:** We at EPA need to look at
19 things that can be communicated in that way that actually need to be taken into
20 account for occupational exposure. It may be that unions would be having
21 people take a 23 and Me profile when they start work. Or the companies may
22 want to protect themselves from downstream liability by checking that out as
23 well. I'm not a big advocate of 23 and Me because it's over simplified. But it is
24 out there, and we should make use of it.

1 **MS. TAMUE GIBSON:** He's going to have to repeat it.

2 It was not audible.

3 **DR. KENNETH PORTIER:** Yeah. Dr. Grant, we only
4 got about one out of every three or four words in what you just said. I think
5 you're going to have to maybe log out and log back in again to see if we can get
6 a better connection because you're breaking up.

7 **DR. STEPHEN GRANT:** Okay. I left it on speaker. Is
8 this better?

9 **MS. TAMUE GIBSON:** Oh, there it is. Yes.

10 **DR. KENNETH PORTIER:** Yeah. I'm sorry you're
11 going to have to repeat it.

12 **DR. STEPHEN GRANT:** Okay. No problem. It was
13 just the idea that we usually think of genetics as something far in the future and
14 wouldn't it be nice or, god, I hope that I'm not around when that happens. But
15 the bottom line is it's already here to some degree. You can order a genetic test,
16 and 23 and Me has gotten permission to publish and warn you about the
17 implications of some of the things that they find in your DNA, particularly
18 adverse drug effects, which is you are going to be susceptible. You're going to
19 be an overreactor to this drug.

20 We should be aware of the polymorphisms that they are
21 already including in their tests that might be relevant to some prominent
22 occupational exposures. I know the company would be open to adding things if
23 they can sell it, right -- if it becomes a reason to take the test. Unions might want

1 to protect their workers by having them profiled I'd say before they start work,
2 but most of them are already working. So it would be as a part of checkup.

3 Companies might want to indemnify themselves by
4 identifying people that shouldn't work in particular areas. We should -- I'm not
5 a big advocate of 23 and Me because it's vastly oversimplified, but it's data
6 that's out there, infinitely greater than zero. And it would take some of the
7 uncertainty away for polymorphisms and interesting enzyme genes that we can
8 identify. That's all.

9 **DR. KENNETH PORTIER:** Thank you. Dr. Apte?

10 **DR. UDAYAN APTE:** I have a few comments about this
11 from the NAFLD perspective. So in the document, EPA does recognize that
12 people with fatty liver disease might have more susceptibility. And given the
13 fact that PERC is fat soluble and now we know from PBPK modeling and mouse
14 studies that the adding of PERC and the effects of PERC will change in fatty
15 liver disease; I think it's a very relevant thing to consider for this particular
16 section.

17 And as we know, about 35 percent of U.S. population is
18 considered obese. Close to 70 percent is considered overweight. So if we just
19 stick to the number of obesity there, that's a huge population. And I think with
20 change in fat distribution in the body, you're going to have a significant change
21 in how PERC is dealt with within the body. So right there is a major concern.

22 The second concern is sort of the genetics of it, and there's
23 been some discussion here on this. One of the -- so let me track back a little bit.
24 With obesity, there are several different issues, but one of the major issues is in

1 non-alcoholic fatty liver disease where you have a significant amount of fat in
2 the liver, followed by inflammation. And this fat inflammation combination
3 essentially starts decreasing liver function.

4 There are two endpoints of that. A lot of these patients
5 will actually have liver fibrosis, cirrhosis, and they'll decompensate. That means
6 their liver function will drop, and they'll die of liver failure. Other people will --
7 some people, a relatively less number of patients will actually develop
8 hepatocellular carcinoma liver cancer. These people are clearly at a higher rate
9 of liver cancer. And NAFLD generally exists along with other comorbidities,
10 such as type 2 diabetes.

11 Now, one thing we know about the genetics is that
12 NAFLD is significantly more common in Hispanic population, as well as there is
13 a specific gene mutation or a snip identified in a gene called PNPLA3, which is
14 associated with high NAFLD occurrence and severity of disease. I was just
15 looking up yesterday in Bureau of Labor Statistics and things like that the
16 percent of Hispanics that work in, for example, laundry and dry-cleaning
17 business. And there is a substantial percent. A large part of that is actually
18 women who work there. So I think that right there becomes a special population
19 that we need to be considering for this kind of review where people who are
20 known to have a preponderance of NAFLD and might be actually in
21 occupational settings where they might be exposed to these things.

22 So I just wanted to make these two points, and I would
23 like EPA to consider them when they revise the document. The data on these are
24 available. The data of NAFLD and how NAFLD changes the PBPK model are

1 available. I don't think -- I haven't looked, but I could look up if there are any
2 epidemiology data on specifically NAFLD and PERC. But that is something, if
3 they are not available, that is definitely a data gap that the field in general should
4 be looking at. Thank you.

5 **DR. KENNETH PORTIER:** Thank you. Dr. Apte, you
6 bring up a good point because I was sitting there thinking if 80 percent of people
7 were overweight, then the definition of the worker population should include
8 those 80 percent. So that overweight status in a sense should be accounted for
9 by the standard -- the inputs that go into the model or into the assessment that
10 account for the fact that, you know, the vast majority of workers are going to be
11 overweight. And if 40 percent have some aspect of fatty liver disease, maybe
12 that should be figure into the standard, not considered -- because when you start
13 talking about 40 percent, that's a big chunk of the standard population. That's
14 not an exceptional subpopulation. It is a significant fraction of the population.
15 And I struggle with those issues there. Dr. Apte?

16 **DR. UDAYAN APTE:** Yeah. Absolutely. I mean, I'm
17 very concerned about the 40 percent number. That is very real. Most of these
18 studies have shown that anywhere between 35 or 40 percent of Americans are
19 now considered obese. And that is also associate with lower socioeconomic
20 status. People are more likely to be working in environments where PERC
21 might be present. So that's kind of gathering a perfect storm. And yes, we
22 should be very concerned about that.

1 **DR. KENNETH PORTIER:** But in the sense, EPA's
2 standard safety issue should cover those conditions and not leave them to
3 potentially exposed susceptible subpopulations, if it's that big of a fraction.

4 **DR. UDAYAN APTE:** Right, right.

5 **DR. KENNETH PORTIER:** That's the point I'm trying
6 to make.

7 **DR. UDAYAN APTE:** Yes. I see what your point is. So
8 they're not really any more PESS. They're really the normal population, and we
9 need to factor that in. That's what you're trying to say. And I agree with that,
10 and that's -- go ahead.

11 **DR. KENNETH PORTIER:** Yeah. No. Yes, we agree.

12 **DR. UDAYAN APTE:** Yeah. And that's absolutely true,
13 and I struggle with this all the time from several different perspectives, not only
14 from environmental risk assessment perspective but things like drug
15 development perspective, too, because we model things in normal conditions
16 when we are really trying to sell the stuff to a large population which is not
17 normal. So exactly the same way, here we are trying to do risk assessment for a
18 large population. Maybe a significant chunk of this is not just logically normal.

19 **DR. KENNETH PORTIER:** Yeah. It just reminds me I
20 did a study back in the mid-2000s looking at body weight distributions from
21 NHANES. EPA uses the 70-kilogram body weight, but when you actually look
22 at that distribution, you find a very significant fraction of the population that's
23 over 80 kilograms or even 82 kilograms, male and female.

1 **DR. UDAYAN APTE:** Absolutely. If you consider just
2 the normal population, 70 kilogram is really historic standard that comes from
3 somewhere in the '50s probably. The average weights, if you consider now, are
4 not. We talked about 40 percent obesity, but that's different. That's considering
5 the BMI of more than 30. But a lot of people who are not clinically obese are
6 actually overweight, and they're not in that 70-kilogram category anymore. The
7 change in demographic has to start figuring out and factor it into the discussions
8 as we go forward.

9 **DR. KENNETH PORTIER:** Yeah. I just saw Dr.
10 Barone's hands go up. I'm sure he wants to kind of clarify something or ask a
11 question. Dr. Barone, before I go to Dr. Grant and Ruthann.

12 **DR. STANLEY BARONE:** Yeah. Just on the body
13 weight issue, we continually look at NHANES data, and the body weight -- body
14 mass issue does lead to corrections and updates in the exposures factors
15 handbook. So we have moved away from the 70-kilogram man to the 80-
16 kilogram man. That is included in some of the calculations.

17 I'm a little unsure what the recommendations are in this
18 conversation. I'm not trying to interject too much, but I hope we can get some
19 kind of summary because I'm not sure, other than using a 10X factor for human
20 variability and using the 95th percentile for our exposure estimates and risk,
21 what you're recommending we should do in addition.

22 **DR. KENNETH PORTIER:** We'll come back to that.
23 Dr. Grant and then Ruthann. Dr. Grant?

1 **DR. STEPHEN GRANT:** Well, to address what Dr.

2 Barone just said, I think one suggestion is to identify those factors that increase
3 susceptibility and either measure them, which is what we'd like to do, or assign a
4 default protective factor per factor, per element of the susceptibility equation.

5 And again, what I'm thinking is it doesn't have to involve too many factors, and
6 I guess we have to describe what the default would be -- and I assume threefold -
7 - to go beyond what we're using now, which is a tenfold factor. And one of the
8 things -- the reason I put up my hand is simply to indicate that, yes, there's a
9 considerable portion of the American population who is larger than they should
10 be, myself included. But also, it's confounded by the fact that they're also older.

11 So there is, in some of these risk factors, there's
12 concordance between them. So you can't even really expect them to be
13 independent. They're going to occur together at greater frequencies than you'd
14 expect.

15 Well, take it one step further, and the question really
16 comes -- and I did mention this before when I said, if you do epidemiology and
17 you have an endpoint, you'll get some idea of what the range in the human
18 population is. But if we're extrapolating from mice, then we're assuming some,
19 quote/unquote, normal human population. And I'm afraid that normal human
20 population is without risk factors -- without susceptibility factors.

21 I'm teaching a genomics course right now, and one of the
22 issues is what is normal? It's projected that by 2025, four years from now, one-
23 third of all Americans will have diabetes. Do we therefore say the normal

1 human population we have to assume is diabetic? And these are real
2 considerations?

3 **DR. KENNETH PORTIER:** Thank you. Ruthann
4 Rudel?

5 **MS. RUTHANN RUDEL:** Hi, I was going to just add
6 one quick point which is that, as I -- in general, I think of the 10X uncertainty
7 factor for human variability being there at least partly, if not all, to account for
8 variability that we don't know about. So it concerns me to sort of use it up for
9 variability that we do know about and especially if it's variability that's actually
10 quite common in the population. So I would be supportive of us coming up with
11 a recommendation for how the EPA risk evaluation can account more explicitly
12 for some of these variabilities.

13 **DR. KENNETH PORTIER:** Thank you. Dr. Kissel?

14 **DR. JOHN KISSEL:** So I wanted to add a little
15 comment on the bodyweight business. My understanding from long ago -- and
16 since I'm not a toxicologist, I don't deal with this all the time. But the 70-
17 kilogram historical number was actually a lifetime average bodyweight and not
18 your existing current bodyweight. Now, risk assessments can involve laborers
19 who are bigger over just their working period. But I think something that gets
20 lost is that that 70-kilogram number was not necessarily a current bodyweight.

21 And I would also point out that if you divide by a bigger
22 number -- if you make the bodyweight bigger, than the dose -- the lifetime
23 average dose goes down, and you actually then predict lower risk, not higher
24 risk, in the normal calculation. So I think those considerations just got ignored.

1 **DR. KENNETH PORTIER:** Yeah. John, in the
2 bodyweight work I did, it was interesting to note that while the upper range of
3 bodyweights has been going up, the lower range of bodyweights has stayed
4 pretty consistent. So the lightest among our populations have stayed light. And
5 actually the fraction in that light group has not changed that much. It's the
6 normal people have gotten heavy. The lighter people have stayed light. Dr.
7 Bruckner? Dr. Bruckner, you're muted in Webex. John, you're not muted. Dr.
8 Gilbert?

9 **DR. KATHLEEN GILBERT:** Well, just getting back to
10 Dr. Barone's question about what our recommendation is going to be here, so
11 I've been hearing all these really great comments and trying to figure that out.
12 So I'm going to ask whether this is a correct interpretation. So maybe a two-part
13 recommendation, one in which we ask a modeler to take into account the
14 different susceptibilities that may be associated with all those different factors.
15 And some of those may be generic, and some of those may be specific for the
16 chemicals, things like Dr. Willhite's mentioning of the Sparrow paper and things
17 about obesity and all those things -- and come up with a range of potentially
18 increased susceptibility people might have to this particular chemical.

19 And then I really liked Ruthann Rudel's suggestion about
20 then using data to try and estimate what percentage of the population may fall
21 into this increased susceptibility. And I don't know how hard this is to do in a
22 modeling point of view, and I don't know whether this increased risk should be
23 calculated individual factors or as a cumulative effect. But I keep hearing this
24 whole idea of modeling, of trying to come up with a better number to actually

1 estimate how much increased susceptibility may occur to a particular chemical.

2 Is that what everyone else is saying?

3 **DR. KENNETH PORTIER:** Dr. Gilbert, this is Ken
4 Portier. Let me kind of turn it around and say, to me, one of the actionable
5 things is that in the past discussion it needs to start by being clear what's covered
6 under the current -- or what EPA assumes is covered under the current values
7 that they're proposing, including the 10X factor. So does that include a normal
8 distribution of body weights among workers, or does it include the theoretical
9 normal lifetime body weight estimate? Is it assumed to include workers who
10 may be alcoholic?

11 I heard what Ruthann said, and I think it's very clear. If
12 we're assuming that what the 10X is covering is the unknowns, you have to
13 know, well, what of the knowns are covered in that estimate. We've discussed a
14 lot of health status, lifestyle, and genetic factors that we know will impact the
15 probability of that health effect due to exposure.

16 The question we have to discuss in PESS is which of those known factors which
17 are identified are covered and which ones aren't. And if they aren't covered,
18 then Dr. Grant's suggestion that we develop and impose uncertainty factors for
19 known but not covered kind of makes sense.

20 To me, that's kind of the discussion -- the PESS discussion being three parts:
21 what do we know are the important health status, lifestyle, and genetic factors?
22 Which are covered in the standard estimates with the 10X uncertainty? Which
23 are not, and how is EPA planning to look at it? And then what's left is we just
24 don't know. If what's left was assumed to be covered in that tenfold --

1 **DR. KATHLEEN GILBERT:** Ken, I'm sorry. I can't
2 hear you.

3 **DR. KENNETH PORTIER:** What was that?

4 **MS. TAMUE GIBSON:** Dr. Portier, you sound like
5 you're on an island far, far away. I think he's resetting his audio. Hold one
6 second.

7 **DR. KENNETH PORTIER:** I'm sorry, Tamue, was that
8 you?

9 **MS. TAMUE GIBSON:** Yes.

10 **DR. KENNETH PORTIER:** Tamue, I'm back.

11 **MS. TAMUE GIBSON:** Okay. Great.

12 **DR. KENNETH PORTIER:** I apologize. My
13 microphone is Bluetooth, and it shuts off when it feels like it. And it doesn't tell
14 me. So where was I when you lost me?

15 **MS. TAMUE GIBSON:** Let's see. Lifetime bodyweight
16 estimates.

17 **DR. KENNETH PORTIER:** Well, I was saying our
18 recommendation could be that the PESS discussion be done in three parts. What
19 factors do we know impact? And then what of those factors are covered in the
20 standard estimate with the 10X placed in? What factors do we know that are not
21 covered or we don't think are covered? And then Dr. Grant's suggestion of
22 developing additional uncertainty multipliers to account for those. And then
23 what's left is those PESS individuals that we haven't covered we don't know
24 about. Those are the factors we don't know about that's supposed to be covered

1 in the 10X. I think Ruthann made a very good point about that. Dr. Willhite, I
2 see your hand up.

3 **DR. CALVIN WILLHITE:** Yes, sir. I was intrigued by
4 the conversation about diabetics. Now, and I'm also intrigued by your
5 suggestion of using the PBPK models to find out which parameters are
6 important. Now mind you, I'm not advocating for the Spearow paper et al or the
7 27X. I point that out only as an item of information.

8 However, there's a lot of -- what do I want to say --
9 genomic type data that's in there. But whether that range of those different
10 parameters has anything to do with actually how PERC is handled or risk, I don't
11 know. But I can imagine if we're talking about alcoholics -- and Dr. Apte can
12 help me with this, maybe -- let's assume that my liver is damaged or that I've
13 already had so much carbon tetrachloride I'm just barely alive.

14 I might be in kind of a situation where I was less
15 susceptible because my liver won't be able to process the parent PERC molecule,
16 and I might not generate as many reactive metabolites. In fact, I might even
17 blow off more of a parent compound in my exhaled air. I'm not sure about it,
18 but I think your suggestion of going to the PBPK model, trying to put in these
19 different parameters, and seeing if the spread is larger than the 10. Thank you.

20 **DR. KENNETH PORTIER:** Dr. Bruckner, I saw your
21 hand fly up.

22 **DR. JAMES BRUCKNER:** Right. I was just going to
23 agree with Calvin. That's exactly the case. If you have decreased liver blood
24 flow, perhaps you have increased fibrous tissue, you have decrease in

1 hepatocytes. You're going to have decrease metabolism. So that would tend to
2 be protective against any metabolite. So you'll have a decrease in metabolism
3 either by decreasing blood flow or deliver of the chemical to the liver or decrease
4 in metabolic activation within the liver. So it could be protective, or it could
5 have no effect. So it's not necessarily a bad thing from that perspective.

6 **DR. KENNETH PORTIER:** Dr. Johnson?

7 **DR. MARK JOHNSON:** Yeah. In regard to the
8 previous comment before varying PBPK parameters, many won't like this
9 comment. But there are ways to do this. I've seen it done where you do
10 probability bounds. You use bodyweight. You use any exposure parameters, the
11 means and maxes. If you know what the proper distribution is you can kind of
12 do a Monte Carlo with all those distributions. Takes a lot of computer time, but
13 you can actually get distributions of exposure. And there we would actually
14 have risk estimates.

15 We would then have a probability of adverse effect. We
16 don't have probabilities here. We have risk quotients or margin of exposure. So
17 I just throw it out there as a consideration. I don't know if the EPA wants to go
18 through all that work because it is a lot of work, but there are tools to do it.

19 **DR. KENNETH PORTIER:** Yeah. This is Ken Portier.
20 I was trying to hold my tongue and not say it wouldn't be Monte Carlo. But Dr.
21 Apte's been patient, and then Dr. Daniels. Dr. Apte?

22 **DR. UDAYAN APTE:** Okay. So just a couple of
23 comments regarding what Dr. Willhite and Bruckner brought up and the
24 considerations here also from the bodyweight standpoint that was made. So the

1 scenarios that Drs. Willhite and Bruckner have said, yes, in those cases, where
2 somebody who has a decompensated liver where there is hardly any hepatocytes
3 left and you have major issues going on where if you have PERC there will be a
4 competitive issue with something else. That's possible, especially with alcohol.
5 The scenario I can see is where, with alcohol, PERC can compete for 2E1 and
6 things like that.

7 However, having said that, that issue essentially ignores a
8 lot of other things. The issue ignores things like ongoing inflammation, which
9 can be exacerbated by PERC itself or its metabolites. And yes, metabolites
10 might be an issue there but PERC itself. And that could actually make situations
11 worse rather than either not affecting or making them better. So the competition
12 with existing disease actually holds only in certain situations where you're
13 assuming that the person who's getting exposed essentially has very little liver
14 left to do anything. In that case, the person's already so sick that it doesn't
15 probably matter.

16 Now, the real issue associated here is not so much of the
17 existing liver disease, but it is about having more bodyfat, which will actually
18 store PERC as a parent compound because it will dissolve in fat. And the
19 bodyweight issue, again, that was brought in earlier saying that if you divide the
20 dose by bodyweight that will reduce it, yes, that's technically probably true. But
21 the issue really is what is that bodyweight made up of.

22 So a man is at 300 pounds and full muscle like an NFL
23 player versus somebody who's 300 pounds and more like towards my
24 constitution, more fat -- the latter person is going to have an ability to store

1 PERC after exposure to the same dose than the earlier person which was more
2 muscle. So that's where the thing is. So people with larger BMI, which is
3 essentially considered the fat content, will actually have possibly more body
4 burden of PERC because they keep storing more and more of this and then
5 releasing it. And on the top of that -- so that's one thing.

6 The other thing, I want to go back to the 2E1 issue as well
7 as the computation issue that Dr. Willhite had brought up. In the majority of
8 these cases where -- with nonalcoholic fatty liver disease and alcoholic fatty liver
9 disease as well, we actually see induction in SIP 2E1 levels. We also see
10 hepatocytes that are highly oxidatively active. So anything that increases those
11 mechanisms are -- it's probably going to make things worse and not really make
12 them necessarily better. Or it's less likely to have no effect. So that's the two
13 points I wanted to make.

14 **DR. KENNETH PORTIER:** I'm sorry. I want to bring
15 this conversation to close here, but I see Dr. Daniels, Dr. Bruckner, and Dr.
16 Willhite have hands up. We'll take those three, and then I'll turn back to Dr.
17 Gilbert to finish things up. Dr. Daniels?

18 **DR. MICHAEL DANIELS:** Yeah. Just a quick
19 comment back to the Monte Carlo thing I think that Dr. Johnson brought up and
20 harkening back to kind of one of my comments earlier about using Monte Carlo
21 related to the global and the local sensitivity analysis. The thing with a lot of
22 these Monte Carlo simulations or sensitivity analysis, they give you probabilities
23 that are kind of potentially very powerful but doing them without taking into

1 account correlation between the parameters. So they're usually this distributions
2 -- they just sample all the parameters independently.

3 So you can get kind of things that are basically much
4 wider than they should be or narrower than they should be or shifted from where
5 they should be just because, like when one parameter's high, these other two
6 parameters are most likely to be high. But when you sample it, you could have
7 that one high and the other two at like their lowest values. So you just have to, I
8 think, use a little bit of kind of caution with kind of doing the Monte Carlo stuff
9 properly. And it's, as I said before and as mentioned, I think, a couple of times,
10 it's very hard to kind of get at those correlations. It's hard enough to kind of get
11 reasonable values for the parameters. So that was all I was going to say.

12 Thanks.

13 **DR. KENNETH PORTIER:** Dr. Bruckner?

14 **DR. JAMES BRUCKNER:** Hi. I was going to point out
15 that alcohol's usually a concern with other solvents or other volatile organic
16 compounds like trichlorethylene because you usually think of an alcoholic or
17 someone who drinks quite a lot of alcohol as being induced or having higher
18 levels of SIP 2E1. And by analogy, that's being, I think, extrapolated to
19 Perchloroethylene. But with Perchloroethylene, 2E1 doesn't appear to be the
20 P450 isotope that's involved, so I'm not sure we can make that jump. So if that
21 makes sense, I think that we can't just base our thinking on carbon tetrachloride
22 or trichloroethylene or other solvents since 2E1 doesn't appear to be significantly
23 involved with metabolism of Perchloroethylene.

1 Another thing you might think about is, if a person has a
2 considerable body burden of alcohol, if the alcohol and the PERC were
3 metabolized by the same compound, the inducer -- that is the alcohol -- would
4 actually be a competitive inhibitor of the metabolism of the solvent. So there are
5 a number of other considerations. It's not a real simple phenomenon or situation.
6 So I just wanted to bring that clarity if that helps.

7 **DR. KENNETH PORTIER:** Thank you, Dr. Bruckner.
8 Dr. Willhite put his hand down. I wanted to make a final comment. The reason
9 I hadn't gone to Monte Carlo was exactly what Dr. Daniels was saying that -- I
10 don't want to go there. But I was thinking more in terms of what I'd call
11 targeted normal scenarios that incorporate some of these extrinsic factors.

12 So I don't think -- it's a matter of running the model for
13 some of these situations, taking into account what we know about this particular
14 chemical and how it potentially would interact in the body and running that
15 through the model. So I'm not thinking 1,000 runs. I'm thinking 10 runs to kind
16 of set some bounds and give us some confidence that our estimate incorporates
17 some of these extrinsic factors for conditions of -- health conditions and other
18 conditions of individuals in the worker population. Dr. Gilbert, you got all that
19 right?

20 **DR. KATHLEEN GILBERT:** Yeah. Every word. It's
21 a fairly complicated discussion, but I think that you, Ken, did a really good job
22 articulating what we can perhaps write up as an actual recommendation. So I
23 will work with you to do that.

1 **MS. RUTHANN RUDEL:** This is Ruthann. Can I make
2 one really quick --

3 **DR. KENNETH PORTIER:** Sure, Ruthann.

4 **MS. RUTHANN RUDEL:** -- one really quick follow up
5 about what Dr. Bruckner just said? So I think I heard him say that SIP 2E1 is not
6 an important -- is not important metabolism of PERC. But searching the risk
7 evaluation, it seems to be featured, at least in the section on oxidative
8 metabolism. And I haven't gotten farther than that. So it just surprised me
9 because I thought people had been talking a lot about SIP 2E1 this whole week.
10 So maybe I misheard.

11 **DR. JAMES BRUCKNER:** No, that's correct. There
12 are a number of other P450 isozymes which appear to be more important. And I
13 can provide references to those papers.

14 **DR. KENNETH PORTIER:** Yeah. And I will work
15 with Dr. Gilbert. I was going to say I apologize to the Committee for this long
16 discussion on PESS. But I think in the past we've kind of shortchanged our
17 PESS discussion under some of the chemicals. And with this chemical, it brings
18 up a lot of these issues that we've struggled with before. But we have so much
19 information at least we have a nice PBPK model that we can work from and
20 work against it. It kind of has helped us begin to focus about what we can do
21 and can't do in the PESS discussion.

22 In regard to Dr. Barone's question, we will consider this
23 from what can you practically do framework. That's why I keep bringing it back
24 to occupational workers and consumers, looking at it from that point of view.

1 And I've also been thinking about the PESS issue from the point of view of the
2 people who are going to read this risk assessment and implement it in risk
3 management. And part of the PESS discussion is to kind of raise the awareness
4 of those risk managers as to when they see some of these uncovered PESS
5 subpopulations, how do they identify a situation where they may be PESS
6 subpopulations that would not be covered by the standard safety factors that we
7 establish here?

8 I have exactly 1:00. We're scheduled to break from 1:00
9 to 1:45 for lunch. Why don't we go ahead and break at this point, and we will
10 return at 1:45 to take on Question 6.6 and all of Question 7.

11 **MS. TAMUE GIBSON:** Thank you.

12 **[BREAK FOR LUNCH]**

13 **DR. KENNETH PORTIER:** Let's reconvene, please. I
14 have 1:45 Eastern Time. Just as a sound check, Tamue, can you hear me?

15 **MS. TAMUE GIBSON:** I can, yes.

16 **DR. KENNETH PORTIER:** Great. Tamue, I just sent
17 you a figure that I'd like you to pass on to Dr. Matten so that I can look at it. I
18 think we'll come back to at the end of 6.6 -- I mean 6.7. It has to do with the
19 discussion on 6.6, but it's a diagram I'd like to include in the minutes that'll help
20 in our discussion for 6.6. At this point, any additional comments on 6.6 that you
21 may have thought of over lunch?

22 **MS. TAMUE GIBSON:** We need to do the roll call.

23 **DR. KENNETH PORTIER:** If they're not major, please
24 --

1 **MS. TAMUE GIBSON:** The roll call.

2 **DR. KENNETH PORTIER:** Oh, that's right. We have
3 to -- the last of the roll calls, yes. Thank you.

4 **MS. TAMUE GIBSON:** You're welcome.

5
6 **DR. KENNETH PORTIER:** That's why there's two of
7 us here. Okay. I'd like to call the roll. I see a number of people haven't quite
8 gotten back yet from lunch. Dr. Barton?

9 **DR. CHARLES BARTON:** Here.

10 **DR. KENNETH PORTIER:** I don't see his phone.
11 Okay. Good.

12 **DR. CHARLES BARTON:** I'm here.

13 **DR. KENNETH PORTIER:** Got it. Thank you. Dr.
14 Bennett?

15 **DR. STEVEN BENNETT:** I am here.

16 **DR. KENNETH PORTIER:** Thank you. Dr. Blystone?

17 **DR. SHERI BLYSTONE:** I am here.

18 **DR. KENNETH PORTIER:** Dr. Bruckner?

19 **DR. JAMES BRUCKNER:** Here.

20 **DR. KENNETH PORTIER:** Dr. Cory-Slechta?

21 **DR. DEBORAH CORY-SLECHTA:** I'm here.

22 **DR. KENNETH PORTIER:** Dr. Davies?

23 **DR. HOLLY DAVIES:** I'm here.

24 **DR. KENNETH PORTIER:** Dr. Doucette?

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DR. WILLIAM DOUCETTE: Virtually present once again.

DR. KENNETH PORTIER: Dr. Gilbert?

DR. KATHLEEN GILBERT: I'm here.

DR. KENNETH PORTIER: Dr. Johnson?

DR. MARK JOHNSON: Buenas tardes.

DR. KENNETH PORTIER: Dr. Kaufman?

MR. ALAN KAUFMAN: I am here.

MS. TAMUE GIBSON: All right.

DR. KENNETH PORTIER: Dr. Kissel?

DR. JOHN KISSEL: Here.

DR. KENNETH PORTIER: Dr. Rowlands?

DR. CRAIG ROWLANDS: I'm here.

DR. KENNETH PORTIER: Ruthann Rudel?

MS. RUTHANN RUDEL: Yup. I'm here. I'm here.

Thanks.

DR. KENNETH PORTIER: Thank you. Dr. Schlenk?

DR. DANIEL SCHLENK: Buongiorno.

DR. KENNETH PORTIER: Dr. Apte?

DR. UDAYAN APTE: Yes, I'm here.

DR. KENNETH PORTIER: I can see that the Committee is kind of looking forward to completing this discussion. Dr. Cobb?

DR. GEORGE COBB: I'm here.

DR. KENNETH PORTIER: Dr. Daniels?

1 **DR. MICHAEL DANIELS:** I'm here.

2 **DR. KENNETH PORTIER:** Dr. Grant?

3 **DR. STEPHEN GRANT:** Bonjour.

4 **DR. KENNETH PORTIER:** Dr. Hossain?

5 **DR. MUHAMMAD HOSSAIN:** I am here.

6 **DR. KENNETH PORTIER:** Dr. Lash? Dr. Lash? Dr.

7 Lin?

8 **DR. ZHOUMENG LIN:** Hi, I'm here.

9 **DR. KENNETH PORTIER:** Dr. Meliker? I don't think
10 he's joining us 'til 2:00, right?

11 **MS. TAMUE GIBSON:** Yes, yes.

12 **DR. KENNETH PORTIER:** At 2:00, yes?

13 **MS. TAMUE GIBSON:** Yes.

14 **DR. KENNETH PORTIER:** Dr. Roby?

15 **DR. KATHERINE ROBY:** Here.

16 **DR. KENNETH PORTIER:** Dr. Vorhees?

17 **DR. CHARLES VORHEES:** Still here.

18 **DR. KENNETH PORTIER:** Dr. Willhite? It looks like
19 we've lost Calvin. Dr. Pennell?

20 **DR. MICHAEL PENNELL:** Present.

21 **DR. KENNETH PORTIER:** Thank you. Well, we still
22 have our quorum, and we'll move forward.

23 **DR. HENRY ANDERSON:** Ken?

24 **DR. KENNETH PORTIER:** Yeah.

1 **DR. HENRY ANDERSON:** It's Henry Anderson. I got
2 done early, so I'll be back on this afternoon.

3 **MS. TAMUE GIBSON:** All right.

4 **DR. KENNETH PORTIER:** Very good. I thought I
5 saw Dr. Anderson's name, and then I just kind of glanced over it. Great. Thank
6 you for joining us, Dr. Anderson. At this point, we're going to move on to
7 Question 6.7. If we could have that read into the docket, Dr. Lee?

8

9 **CHARGE QUESTION 6 (6.7)**

10

11 **DR. MARI LEE:** Can you just advance the slide for me?

12 EPA risk characterization of human health risk from inhalation exposure to
13 workers includes estimates of risk for respirator use. These estimates are
14 calculated by multiplying the high end and central tendency MOE or extra
15 cancer risk estimates without respirator use by the respirator assigned protection
16 factors, or APFs, of 10, 25, and 50 air-supplied respirators. EPA did not assume
17 occupational nonusers, or ONUs, or consumers used personal protective
18 equipment in the risk estimation process.

19 Question 6.7, please comment on whether EPA has
20 adequately, clearly, and appropriately presented the reasoning, approach,
21 assumptions, and uncertainties for risk characterization to workers using air-
22 supplied respirators and to ONUs and consumers who would not be expected to
23 use PPE.

1 **DR. KENNETH PORTIER:** Okay. The PPE
2 discussion. Dr. Kissel, you have the lead.

3 **DR. JOHN KISSEL:** Okay. So first, I think that there's
4 a problem with the question, which we should have caught in the pre-meeting.
5 The question says -- well, it's asking for the difference for workers using air-
6 supplied respirators. I think that should be air-purifying respirators because
7 that's the more common case. In fact, I'm not sure that air-supplied respirators
8 are assumed for any case.

9 **DR. KENNETH PORTIER:** Let's ask Dr. Lee. Is that
10 clear? Is that correct? This may have been copied from the TCE or the NC --

11 **DR. MARI LEE:** I'm trying to see if anyone knows.
12 Unfortunately, I'm not as familiar with PPE. I'm wondering if the 50 -- the APF
13 of 50 is for an air-supplied respirator but the 10 and 25 are air-purified. Does
14 anyone else from EPA that's on -- can you answer that?

15 **DR. KENNETH PORTIER:** Dr. Barone?

16 **DR. STANLEY BARONE:** Yeah. This is Stan Barone.
17 I believe that's correct. An APF of 50 and 100 and 1,000 are air-supplied, not
18 air-purified.

19 **DR. JOHN KISSEL:** Well, the relevant table is 216 on
20 page 132 of the DRE. And air-purifying respirators are 5, 10, or 50. And the
21 supplied air respirators go generally above that, including up to 1,000. The
22 distinction, I think, doesn't really matter. It's just the posing of the question
23 because ultimately the correction factors are only 5, 10, or 50. And we're not
24 using the thousand-fold figures. And the 50 is ambidextrous, so the way the

1 question is posed it suggests that the 5, 10, 25 kind of factors are not relevant to
2 the question, which I think they are.

3 **DR. STANLEY BARONE:** So to clarify, it is relevant to
4 the question -- the 10, 25, and 50. I think the intention -- and this may have been
5 incorrect. We'll double check -- that the 50 was the air-supplied. The 10 and the
6 25 are purified.

7 **DR. JOHN KISSEL:** Okay. That's not the question.
8 That's the preface to the question. In the question, it only says air-supplied
9 respirators.

10 **DR. STANLEY BARONE:** Okay. So now I follow
11 what you're saying. I was up above. Thank you.

12 **DR. JOHN KISSEL:** Okay. So in any case, this is well-
13 trod ground, and we've wrangled over the PPE use quite a bit through the prior
14 reviews. And I don't think there's anything new in this document with respect to
15 greater characterization of PPE use and efficacy. So all of the prior discussions
16 are still relevant and can be cited.

17 The background here, there are some general issues. One
18 is where PPE fall in our APF controls, and the implication is that PPE is a first
19 choice rather than engineering controls or other measures, which is
20 philosophically offense to at least some of the members of the Committee. And
21 that's trod ground.

22 I will reiterate that the efficacy of PPE depends upon
23 appropriately selected and readily available routinely replaced PPE, which
24 occurs some of the time in the real world but certainly not routinely. And it also

1 depends upon trained and conscientious workers, which is also an issue in the
2 real world. So basically, we don't have good empirical population-based data,
3 which would imply a distribution of actual efficacy as implemented in the
4 workplace, rather than in vitro.

5 So there's a very large amount of uncertainty about how
6 effective PPE actually is. And while it's undoubtably very effective for some
7 individuals in short term uses, how effective it is for a broader range of
8 individuals over chronic exposures is not at all clear. Like lots of other things
9 we do in regulatory science, we're making some pretty crude approximations
10 here, which are not entirely satisfactory to the members of the Committee.

11 You know, you can -- one of the things that's done with
12 PPE is to test it in challenges in vitro, and those are valuable tests. You want to
13 know, for starters, whether the material is, under ideal conditions, likely to be
14 efficacious. But putting a fabric material into a diffusion cell and then putting a
15 static load on it is kind of an initial condition. It's a necessary but insufficient
16 test of the material. And you certainly wouldn't want to use for PPE something
17 that would fail one of those in vitro tests.

18 But when you get out into the real world, human behavior
19 can defeat the PPE, and those in vitro tests are just not adequate to tell the whole
20 story. And multiple members, I think, can testify that safety cultures vary pretty
21 widely, both within and across industries out there. And many of us can tell
22 stories of people wearing respirators as necklaces or putting their feet in can
23 crushers and doing other things that are just completely inappropriate, which

1 lead to injury and exposure. So that's the background, and people can to their
2 satisfaction reiterate or expand upon all those points.

3 With respect to this particular document, I think there's
4 general support for the reporting of the worker MOEs or risks both with and
5 without PPE, given the cautionary views about the PPE. Getting both numbers
6 is appropriate and appreciated by the Committee. With respect to the
7 nonworkers, there's general consensus that a presumption of no PPE use is also
8 appropriate. At least one member feels that it's fine to discuss benefits --
9 potential benefits to ONUs and consumers if they do use PPE, but it shouldn't be
10 the default assumption.

11 And then finally, one member suggested the tabulation of
12 air concentrations representing 10 to the minus four, 10 to the minus five, 10 to
13 the minus six risk levels -- so we're talking about carcinogens here -- be
14 tabulated for workers, ONUs and consumers. The consumer thing implies that
15 you would be doing chronic consumer exposures, which are not actually in the
16 document at the moment. That member can speak for himself, but I believe that
17 that's just a risk communication kind of request that has to do with the fact that,
18 for this particular compound, there's lots of numbers out there, such as the air
19 concentrations in apartments above dry cleaners. And translation of the meaning
20 of those concentrations to something that lay people or people that are just
21 maybe technical but not completely immersed in this topic can more easily
22 interpret would be valuable.

23 So what I've done here is try to summarize what people
24 said. I got written responses from everybody, which is good. Some of the

1 responses, I think, were on topics that were not particularly on point for this
2 question. But if the members that I'm not giving a very brief summary of want
3 to see to that, they're now free to do so.

4 **DR. KENNETH PORTIER:** Thank you, Dr. Kissel. I'll
5 go through the associates. Dr. Grant, anything to add?

6 **DR. STEPHEN GRANT:** In general, my comments
7 were well summarized. The only comment that I would add is that during these
8 evaluation responses we've been reminded many times that EPA is not interested
9 in mitigation. I find it inconsistent with that, that we are including in the
10 evaluation of the chemical an assumed mitigation technique. That's it.

11 **DR. KENNETH PORTIER:** Dr. Hossain?

12 **DR. MUHAMMAD HOSSAIN:** Dr. Kissel very nicely
13 presented the comments and the recommendations. The only one concern, but I
14 think I will too agree that presenting a process and methods for the risk
15 characterization in the area seems to be very logical and scientific. But in some
16 portions on some of the general assumptions, for example, the lab (inaudible)
17 usually have the respiratory protection program. But the concern is about the
18 harm about the small commercial facilities such as dry cleaning.

19 So I think this worker in this setting is likely -- not likely
20 to have a respiratory protection program and they are not using. So this may be a
21 potential uncertainty for those people -- how we can evaluate the risk for them.

22 Another thing is that (inaudible) that user respirator on the
23 imaging controls and (inaudible) permissible exposure limit on their own. If the
24 presence of a lower (inaudible) respirator, but it does not mean that workers used

1 PPE effectively and currently. So that is the main uncertainty in these facilities
2 for workers. That's all.

3 **DR. KENNETH PORTIER:** Thank you, Dr. Hossain.
4 Dr. Lash?

5 **DR. LAWRENCE LASH:** Yes, I'm here. For some
6 reason I had it in my mind that our restart time was 2:00. But I'm here. So I
7 missed a little bit of the initial discussion, but it sounds like most of my points
8 were made. I didn't have lot.

9 I remember from earlier chemical review meetings that
10 there was a lot of discussions about PPEs. And I was always in favor of
11 presenting it both ways. I think the uncertainty, of course, is if people actually
12 obey the law in the workplace and use the PPEs. But I think it's appropriate to
13 calculate all the MOEs and so on both with and without.

14 And I think the only key question is the assumption that
15 consumers wouldn't use it or that they shouldn't use it. And I think I made a
16 note, either here or elsewhere, that it might be appropriate at least to discuss the
17 potential impact of using it when they are identified for consumers and
18 bystanders -- the cases where there are identified unreasonable risks. That was
19 it.

20 **DR. KENNETH PORTIER:** Thanks, Dr. Lash. Dr.
21 Roby?

22 **DR. KATHERINE ROBY:** No, my comments were
23 already included. I have nothing else to add. Thanks.

1 **DR. KENNETH PORTIER:** Thank you. Dr. Willhite?

2 I don't know if Dr. Willhite joined us. Yes, he's here. Calvin?

3 **DR. CALVIN WILLHITE:** Yes, sir. It signed me on as
4 a participant, and that's why they couldn't see me. But I've been listening.
5 Now, it's repaired itself. Thank you.

6 **DR. KENNETH PORTIER:** Did you have any
7 additional comments on Question 6.7?

8 **DR. CALVIN WILLHITE:** None.

9 **DR. KENNETH PORTIER:** Thank you. Dr. Anderson?

10 **DR. HENRY ANDERSON:** I have one thing that I think
11 would be helpful. In the discussion in the document, a reference was made to the
12 NIOSH 2001 survey, which really was a very large survey -- but there really
13 isn't any description of how the reference is relevant here. It's a very, very long
14 document. There's lots of information. Which of the tables and where does
15 EPA feel support this?

16 You can go from the start where basically they did well
17 over 600,000 establishments, and only 10 percent of private industry workplaces
18 reported using respirators. On the other hand, that really isn't particularly
19 relevant because there's a lot of workplaces where it wouldn't be appropriate.
20 So it would be helpful if EPA could describe that study, since they appear to rely
21 on it in some way, and then say which table or what characterization they're
22 using that would be -- they consider to be relevant, particularly the various
23 workplaces here.

1 Manufacturing certainly would sort of fit in there, but I
2 had a hard time going through all the tables to find some information on
3 respirator usage that would be relevant to the various circumstances we're
4 talking about. If it's there, it'd be helpful if EPA would put that into the
5 document rather than just say there's been a survey done. But it's kind of the so
6 what? What did the survey find?

7 **DR. KENNETH PORTIER:** Thank you, Dr. Anderson.
8 Anyone else want to comment on PPE issues? Dr. Blystone?

9 **DR. SHERI BLYSTONE:** Yeah. As usual, I have to say
10 something, right? So I was just going to support what Dr. Lash was saying. I
11 am also a proponent of it being appropriate to provide the information both with
12 and without PPE because there are certainly industries -- and I'm speaking
13 specifically of the manufacturers of this chemical where I think PPE use would
14 be proper and appropriate and a good system to ensure its proper use.

15 **DR. KENNETH PORTIER:** Sheri, I tend to agree with
16 you, too. I keep thinking of who's reading this document. And it's going to be
17 the people who move forward to risk management and risk mitigation. And at
18 least this gives some idea that if they push a certain mitigation, they have an
19 expectation of a certain reduction in risk. Any additional comments? Dr.
20 Anderson, your hand is still up? Additional comment?

21 **DR. HENRY ANDERSON:** No, I could just add to that
22 on the manufacturing side, at least, one of the plant's data that was submitted,
23 they had no detectable levels. So it's unclear to me why you would provide air-
24 supplied respirators in a manufacturing facility where they have totally

1 controlled their exposures. So certainly they would use them for like the sort-
2 term tests that are done where somebody is actually breaking a pipe or repairing
3 something. That's pretty standard in industry to use respirators. But once you
4 finish that task, you go on to do your regular job, and it may not involve needing
5 a respirator.

6 So I would say the assumption to be, if there's sufficient
7 exposure, I would assume that the likelihood of respirators being used in all of
8 these circumstances would be greater than if there's been an evaluation and the
9 exposures are low. The respirator program is expensive. So if you characterize
10 that you don't have much exposure, there really isn't any incentive to give your
11 workers an additional -- or the workers to put with the hassle of a respirator
12 program and get rid of their air -- face hair and all those kinds of things if it
13 really isn't necessary.

14 So I would just put in the caveat that one assumes -- or
15 you could assume that companies that know they have exposures that could be
16 significant, they are more likely to be the ones with the staff that would be using
17 the respirators.

18 **DR. KENNETH PORTIER:** Dr. Blystone, your hand's
19 still up?

20 **DR. SHERI BLYSTONE:** I actually put it back up just
21 to respond to Dr. Anderson. That is my point is that, certainly on the
22 manufacturing side, I think it's more likely than not that they have a good
23 industrial hygiene program that includes respirators if necessary. Oftentimes,
24 you may have PPE that -- PPE is the last line of defense, so you might be

1 wearing PPE even if exposure -- even if monitoring data says that there's no
2 exposure in case there's some failure of some other safety system. So my point
3 is simply that those manufacturers would most likely have a robust industrial
4 hygiene program that includes the use of PPE when required.

5 **DR. KENNETH PORTIER:** I'm going to turn back to
6 Dr. Kissel. Any final comments? I'm assuming you captured most of this.

7 **DR. JOHN KISSEL:** I think I got it. So we're good.

8 **DR. KENNETH PORTIER:** Thank you. I'll turn to
9 EPA. Any clarifying questions or comments on the panel discussion?

10 **DR. STANLEY BARONE:** No, I don't think so, Dr.
11 Portier. This is Dr. Barone.

12 **DR. KENNETH PORTIER:** That's a heck of a lot less
13 discussion than we had four chemicals ago. That's for sure. I want to ask
14 Tamue whether that image that I had submitted is available to be put up?

15 **MS. TAMUE GIBSON:** Dr. Portier?

16 **DR. KENNETH PORTIER:** Yeah.

17 **MS. TAMUE GIBSON:** They are in the process of
18 loading that figure. So can you give them a couple of seconds?

19 **DR. KENNETH PORTIER:** Thank you. And I
20 apologize --

21 **MS. TAMUE GIBSON:** Yes. Uh-oh.

22 **DR. KENNETH PORTIER:** It looks like it got loaded
23 sideways. There we go. Just for the Committee, at lunch, thinking about our
24 discussion on 6.6 and how we kind of circled a couple of times, I got to thinking

1 about how PESS fits in with all of this. So if you think of exposure in one
2 dimension and susceptibility in another, part of our conversation had to do with
3 how a lot of this overlaps and that one of the issues that I personally would like
4 to see in the PESS discussion is some -- identifying those PESS that are not
5 within the OU, ONU circle because we'd be kind of assuming that those are the
6 ones that are covered by the risk analysis. It's the ones that are outside there, the
7 ones that are not covered as a consumer user in the consumer risk and not
8 covered in the worker group -- that part that's not overlapped.

9 And I just want to use this as just a way to kind of
10 illustrate that those individuals are on the higher susceptible side. They may or
11 may not be higher exposed, but they are exposed. They're not in the unexposed.
12 They may be consumers, users, or both, a small overlap there. So I'm going to
13 open it up if anybody wanted to kind of comment on how I could improve that
14 diagram because I'd like to include that in our discussion on 6.6. Dr. Grant?

15 **DR. STEPHEN GRANT:** Yeah. I'm a little concerned
16 about this because most of your PESS population is now outside of the worker
17 and consumer population. They then become the general population. And
18 they'll just be dropped from discussion because it's not part of the charge to this
19 Committee. Again, I think we talked a little bit earlier about perhaps a healthy
20 worker effect where you had to have some level of health in order to get up and
21 go to work.

22 I'm not sure the opioid crisis would support that. But I
23 think if there are potentially exposed subpopulations that are not in the worker or
24 consumer population, I don't think that's what we're considering. I think we

1 need to make sure that we're looking at subpopulations which might be not
2 blocked from working or would inadvertently be accepted into the working
3 population because their susceptibility wasn't known until they were challenged
4 with the agent.

5 **DR. KENNETH PORTIER:** Okay. I stand corrected.
6 You're absolutely right because the ones outside the green box and the yellow
7 box are in the general population and are not covered under TSCA. Can you
8 suggest improvements to this? I guess I don't want to continue this discussion
9 too much more. But if you've got a suggested improvement, send it to me and
10 I'll modify the diagram. Dr. Anderson?

11 **DR. HENRY ANDERSON:** Yeah. The suggestion I
12 would have is maybe have separate circles for OUs or ONUs. When we talk to
13 the susceptible population, if in fact you're going to assume they have to be able
14 to wear a respirator, you'll eliminate a fair number of these individuals who have
15 respiratory problems. If you have to wear a respirator continuously, it's pretty
16 tough to be an asthmatic or somebody with COPD. So those susceptible
17 populations will be less prevalent in the OUs who are supposedly wearing
18 respirators, which would not be in the ONU group. So I think there is a
19 difference between the OUs and the ONUs, the prevalence of susceptible
20 populations in them.

21 **DR. KENNETH PORTIER:** Thank you. That's a good
22 point. Dr. Kissel?

23 **DR. JOHN KISSEL:** So two points. One is that if we
24 are going to recommend that occupational bystanders be included, they're not on

1 the figure. And I hope we will be recommending that occupational bystanders
2 are included. And the other comment is that the X axis is misspelled -- the X
3 axis label is misspelled.

4 **DR. KENNETH PORTIER:** Yeah. Yeah. I caught that
5 too late. I will put in occupational bystanders. I'm not quite sure where they fit,
6 though. Do occupational bystanders look like consumers? What is their
7 exposure? Is it on the low side? I guess it kind of -- yeah. If you can give me
8 some idea of where that box goes, I'll be happy to put it on their, John.

9 **DR. JOHN KISSEL:** Okay. I'd have to look at the
10 numbers a little bit. But I think that given that the occupational bystander
11 exposures could be chronic instead of -- or likely are chronic rather than
12 episodic, I think their exposures would be oftentimes bigger than the consumer
13 exposures.

14 **DR. KENNETH PORTIER:** Thank you. And the other
15 thing I wanted to point out is that the size of the box does not represent their size
16 in the population. I put a big PESS group because that's the focus of our
17 discussion, but I don't think they're as big as the OUs and ONUs. But I don't
18 know, and that's part of one of the issues. Dr. Barone, you wanted to comment?

19 **DR. STANLEY BARONE:** Yes, I'd like a clarification
20 of what occupational bystanders are because, at least in our discussions within
21 the Agency, we have occupational nonusers who we consider bystanders to the
22 actual users. If we're talking -- if Dr. Kissel is talking about apartment dwellers
23 or folks who are living or working next door that are not the users, than that's
24 part of what we consider general population.

1 **DR. JOHN KISSEL:** Those are the people that I'm
2 talking about, plus potentially the take-home pathway folks. So if you have a
3 worker who is taking their daily exposure home to their family and then
4 exhaling, that's probably actually a bigger deal than somebody periodically --
5 because it happens every day -- than somebody periodically taking home dry
6 cleaning and hanging it in their closet. I would guess that the air concentrations
7 in those consumer houses are much lower than in families of people that are
8 actually active workers.

9 **DR. KENNETH PORTIER:** And John, I think my
10 thinking here is that, while to a certain extent I agree with Dr. Barone that those
11 are people who are in the general population -- but our concern is their exposure
12 is occupationally linked. And it's suspected of being much higher than non-
13 consumers in the general population. So they fit somewhere in between the
14 fairly low-level population exposure and the higher-level consumer -- direct
15 consumer user and the occupational workers that we talked about here. So that's
16 why you wanted to include it. And I've made a note.

17 **DR. JOHN KISSEL:** And the temporality is quite
18 important. For a child resident above a -- a preschool child resident in an
19 apartment above a dry cleaner, you're talking about seven days a week, 24 hours
20 a day exposure. And the consumers are not getting that kind of exposure.

21 **DR. KENNETH PORTIER:** Yeah. And we promise to
22 define that occupational bystander in an earlier question. Okay. Let's go ahead
23 and move on to Question 7 at this point. Thank you for putting this slide up.
24 We'll go back to our questions. And Dr. Lee if you'll read in all of Question 7.

CHARGE QUESTION 7 (7.1)

DR. MARI LEE: Question 7, content and organization, EPA's final rule, *Procedures for Chemical Risk Evaluation under the Amended Toxic Substances Control Act*, stipulates that processes by which EPA is to complete risk evaluations under the Frank R. Lautenberg Chemical Safety for the 21st Century Act. It is important that the information presented in the risk evaluation and accompanying documents are clear and concise and describe the process in a scientifically credible manner. Peer reviewers' critical recommendations should pertain to the usefulness of the technical information as presented in documents for the intended users and the public.

Question 7.1, please comment on the overall quality and relevance of the resources used in this draft risk evaluation. Describe data sources or models that could improve the risk evaluation. 7.2, please comment on the overall content, organization, and presentation of the draft risk evaluation for Perchloroethylene. 7.3, please provide suggestions for improving the clarity of the information presented in the document.

DR. KENNETH PORTIER: Thank you. Ruthann Rudel has the lead on Question 7.1. Ruthann?

MS. RUTHANN RUDEL: Thank you. I have some comments from other discussants, so I'm going to try to represent them, as well as mine. And then anyone can chime in who wishes to.

1 The overall sense is that the evaluation uses many of the
2 standard resources that one would expect. These include previous risk and/or
3 hazard assessments from federal, state, and international agencies and previous
4 EPA assessments, such as the IRIS documents and ATSDR, NTP, California
5 EPA, IARC, and the European Union. The peer review literature, including both
6 key studies used in a previous assessments and those published more recently,
7 are also stated to be used.

8 One commenter said that although the evaluation
9 discusses the issues of quality and relevance in selecting studies, the criteria used
10 to determine these are not that clear. And further comment on this problem will
11 be, I think, presented in the context of Question 7.3. Another important source
12 of data for the draft risk evaluation includes all the occupational exposure
13 scenarios and environmental exposure information collected across the U.S.

14 As with the peer review literature, the evaluation explains
15 that the EPA conducts a systematic review and grades the data as being
16 unacceptable or acceptable with low-, medium-, or high-quality. And there's
17 repeated reference made to this throughout the document regarding exposure
18 information but also for risk estimations and mode of action studies. While there
19 is reference made to standard EPA policy, there's no description in this
20 evaluation of what specific properties are included in the ratings listed above.
21 And this was brought up in 5.6, too. So at some point, we should decide where
22 in the report that will go.

23 It was also pointed out that there were alternative dermal
24 models -- dermal exposure models that were discussed in the context of Question

1 4.9, and the literature that EPA selected for evaluation of dermal exposure and
2 absorption excludes some papers that may be relevant. And I think that may also
3 have been discussed, and this raises questions about the selection criteria for
4 those papers.

5 Several reviewers appreciate the efforts to compare
6 monitoring and modeled air concentrations and suggested that EPA extend this
7 by using OSHA enforcement data to -- as exposure concentrations, as we've
8 discussed previously. Section 2.3.4.3 presents biomonitoring data for the general
9 population, for example, from NHANES, and air levels for the general
10 population. And that was helpful, but it wasn't clear how these data were used in
11 the assessment.

12 A couple suggested uses would be to provide information
13 about background exposures that need to be added to the exposures calculated
14 for these conditions of use. This would be essential if EPA's intention is to keep
15 worker ONU and consumer exposures below health-based benchmarks. The
16 data might also be helpful for validating consumer exposure models and maybe
17 for worker exposures, too. For example, NHANES might be able to be used to
18 compare biomonitored levels and back calculate intakes for using the PBPK
19 model for people whose work is in dry cleaning.

20 I know there are some occupational data that are collected
21 as part of NHANES. I'm not sure if they would permit this level of granularity.
22 But there are so many people exposed to PERC at work and not at work -- but
23 even at work. And so this risk evaluation really matters, and it's going to affect
24 exposure and health for lots of people.

1 It was pointed out also that it's important to pay careful
2 attention to the no unreasonable risk determination, so those are the scenarios
3 that the evaluation determines don't face any unreasonable risk -- that those are
4 serious decision because they remove those uses from any future risk
5 management and preempts state action as well. And there are many, especially
6 for the occupational nonuser -- there are many uses that are determined in this
7 risk evaluation as not posing any unreasonable risk. And because this is so
8 important, uncertainties should be more robustly quantified, and the assessment
9 should shift to bringing more scenarios into a risk management. In the risk
10 management phase, additional data can be collected to reduce uncertainty and to
11 target risk management more effectively.

12 The target cancer risks of 10 to the minus four for workers
13 are pretty high. It's not certainly de minimus. And there's been an opportunity
14 for public feedback about that decision.

15 Margin of exposure benchmarks, I think, don't account for
16 uncertainties adequately, for example. And we had extensive conversation about
17 that. And they don't consider that the workers have other exposures, also, in air,
18 water, and consumer use. And it's been suggested to leave room in the risk
19 bucket for these other exposures and also co-exposures to chemicals with similar
20 properties. Several members suggested that chronic exposure to consumers
21 should also be evaluated.

22 And a couple last points about background exposures and
23 co-exposures that many need to be considered cumulatively and in aggregate in
24 terms of some additional data. From the California Water Board data for the

1 state of California, detects of PERC in drinking water systems in California are
2 quite common. It looks like 15 percent in surface supplies and 23 percent of
3 groundwater supplies have PERC detected. And the most common co-
4 contaminant is TCE. 13 percent of all the supplies have both -- or the testing
5 sites, I should say.

6 And co-exposure to other contaminants with similar
7 exposure patterns and modes of toxicity should be discussed. For example, you
8 could present the correlation in TCE and PCE, maybe some others in air toxics
9 and drinking water data. I mentioned USGS 2006 data previously. The most
10 common pair of compounds detected in drinking water sources is TCE and PCE.

11 And then a final point, in terms of thinking about how to
12 reduce population risks from PERC exposure, looking upstream from the
13 scenarios we focused on and reducing use in consumer and commercial products
14 would be an effective strategy. From that USGS 2006 study, the most -- the key
15 associations between where there were drinking water wells with PERC detects
16 are areas with lots of septic systems and urban land. And I think this is an
17 important consideration because these are non-point sources that are likely most
18 effectively controlled upstream by TSCA versus at the end of the pipe by local
19 boards of health. And so I think readers of the document might appreciate some
20 of this information being included as framing to understand the context of the
21 exercise. That's what I have.

22 **DR. KENNETH PORTIER:** Thank you. Dr. Kissel, do
23 you want to add?

1 **DR. JOHN KISSEL:** I would just -- as a matter of
2 clarification with respect to the dermal literature, there's two types of dermal
3 literature that come into play here. The 4.9 stuff was about consumer --
4 available consumer methodologies, which EPA explicitly asked for. In Question
5 6.4, what I was talking about was the literature that would inform consideration
6 of skin damage, which is excluded entirely from the document. So two different
7 topics which I will expand upon in the written comments.

8 **DR. KENNETH PORTIER:** Thank you. Dr. Lash?

9 **DR. LAWRENCE LASH:** Yeah. My comments were
10 captured, and I made a notation about further comments in Charge Question 7.3.
11 So we could leave it for that, probably. But I think everything was captured
12 otherwise.

13 **DR. KENNETH PORTIER:** Great. Any additional
14 comments? Okay. I'll turn to EPA. Any clarifying questions or comments?

15 **DR. STANLEY BARONE:** I don't think so, Dr. Portier.
16 This is Stan Barone.

17 **DR. KENNETH PORTIER:** Thank you. We'll move
18 on to Question 2, commenting on overall content organization and presentation
19 in the DRE for PERC. Dr. Lash?

20

21 **CHARGE QUESTION 7 (7.2)**

22

23 **DR. LAWRENCE LASH:** Yes, hi. Okay. So I have a
24 lot on this one, as you can imagine. So I think universally there were -- with

1 regard to organization, there were kind of two types of comments. One was the
2 acknowledgement that there is kind of a standard structure to these evaluations --
3 that it seems to -- that this document seems to follow.

4 But it was noted, though, by several Committee members
5 that the way it's presented is very complex. And you've got the 636-page
6 document and then 16 or so supplementary files. And in the next charge
7 question, there are specific recommendations for potentially how to deal with
8 that.

9 And there was also acknowledgement, I think, of the need
10 for the EPA to address certain concerns and to include all conceivable uses and
11 possible exposure pathways and conditions. But it was basically concluded that
12 it makes the document quite cumbersome and at times unwieldy. And the other
13 kind of issue that was raised was that the ability, I think, to use the document
14 efficiently or to find specific information was not always easy.

15 So let's see. I'm trying to paraphrase more than read
16 because I have like five pages here. So I won't do that. So let's see. Okay.

17 So in terms of the environmental sections, there's
18 significant difficulties were encountered when comparing risk characterization
19 tables for environmental assessments in Section 4, with risk determination tables
20 than in Section 5. And there was also a bio monitoring discussion in the
21 environmental section that should probably be moved to the human health
22 section following PBPK data. And there also were identified some discrepancies
23 between metabolites measured in human media and those that were discussed in
24 the metabolism and PBPK sections.

1 So in addition, there was complexities noted in the
2 supplemental file on data quality evaluation of environmental releases and
3 occupational exposure. And an observation was made that this file contained
4 valuable individual study information and that would allow the reader to see the
5 characteristics of many of the publications that were graded and, most
6 importantly, those rejected by the systematic review criteria. But it was -- the
7 Committee member concluded that they found the file to be not very useable --
8 or actually the term was "largely unusable" because it prevented really -- the way
9 it was organized quick searches to be done. And this goes -- and I'll discuss this
10 more in Question 7.3 in terms of recommendations.

11 And I've said this elsewhere, I believe, as well that cross-
12 listing would be helpful. Then it was also noted that the bibliography from the
13 systematic review is challenging to use as well. And another Committee
14 member also suggested that the exposure, hazard, and risk characterization for
15 each part be put together rather than having them rotating in a manner -- so that
16 it would be presented more in a manner similar to how the EPA presented their
17 overview the first day of this meeting. And I'll discuss that a little more in the
18 next set.

19 As far as content -- so it noted that the work presents --
20 before this evaluation began in December of 2016, and the concern here is that
21 some of the main documents on which the EPA based its work are now six or
22 more years old, some even close to 10 years old, such as an environmental health
23 perspective review published by Guyton et al and a National Research Council
24 publication from 10 years ago. So there was a concern noted that essentially the

1 current document repeats those same results. And it says while the current
2 manuscript does -- or document does include cancer potency calculations,
3 ecological factors and discussions of measured and modeled workplace
4 consumer exposures that were not in previous publications, there seems to be --
5 the basic science discussion, really the underlying discussion MOAs and all has
6 not really been updated since the previous EPA IRIS publication, which is now,
7 as noted, is more than six years old.

8 So most of the problematic occupational health exposure
9 issues are the same or similar to ones identified and discussed in previous
10 reviews. So this one Committee member noted that there, I guess, are sort of
11 recurring themes or concerns. And similarly in the most recent TCE evaluation,
12 noting concerns about the systematic review process. And I think more
13 explanation on that would be helpful.

14 There were notes about concerns about personal protective
15 equipment, PPE use and application of protection factors, lack of description or
16 comparative use of data available from OSHA inspection database or data from
17 international programs similar to OSHA -- also a concern about not considering
18 aggregate exposure of inhalation and dermal exposures and not considering
19 community drinking water and air exposures because they are addressed by other
20 EPA regulations. And I understand -- I know we've had discussion on this that
21 TSCA tries to differentiate between -- or to specify really what its goal is as
22 opposed to other components of the EPA. Let's see. Okay.

23 So there are more comments on, for example, regulatory
24 history and assessment history that's in the introduction. And it was observed

1 that this section really doesn't provide sufficient information because it basically
2 just shows the -- states the reference and doesn't really get any summary of what
3 that regulation was. And readers were referred to Appendix A.

4 There are a number of specific comments, such as the
5 absence of consideration of bladder cancer, which we talked about earlier.
6 Comments about the literature search and how that was done. And although
7 there is a supplemental document that's provided on the literature search from
8 2017 that shows the strategy, it was commented that the information was not
9 clearly described there. So you really couldn't tell exactly what search terms
10 were used and the yields from all of that.

11 Also a comment made about criteria for evaluating
12 confidence in studies and that the criterion are not always clear as to what
13 constitutes a low, medium, or high level of confidence. And let's see. I have a
14 number of other specific comments and then maybe -- which are all in the text
15 that I'll submit. But maybe I'll just go then to the recommendations, which kind
16 of encapsulate everything. And there are only five of them, so it's not too bad.

17 So the first one is -- and this -- we further expound on this
18 in the next charge question, which actually specifically asked for suggestions or
19 recommendations. But the first one is here that the evaluations should be
20 reorganized for better comprehension and ease of finding specific information.

21 There were multiple proposals. They ranged from one Committee member
22 suggested breaking it up into several separate documents, whereas another
23 suggested reorganizing to be more similar to the introduction that -- the
24 PowerPoint that we were presented on Tuesday.

1 The second one is that the EPA should make sure that
2 metabolites that are measured in humans are adequately discussed in the sections
3 on metabolism and PBPK. Then third recommendation that the EPA should
4 update the TSCA systematic review process to incorporate recommendations
5 from the SACC on this and other draft risk evaluations and notes that the review
6 is in progress by the National Academies of Sciences. An alternative suggestion
7 that other existing systematic review methods could be adapted for use under
8 TSCA. And a couple of suggestions were made, including a navigation guide
9 and method developed by the National Toxicology Program Office of Health
10 Assessment and Translation.

11 The next to last one, the fourth is that the criteria used by
12 the EPA to evaluate datasets as either unacceptable or acceptable with low,
13 medium, or high-quality need better explanation. And reference to other Agency
14 reports I think is insufficient here. And as I mentioned earlier, I think that's
15 because, to me, this is such an overriding -- or underlying thing for the entire
16 document that it's better if it's better explained.

17 And then finally, the fifth one is the conclusions of the
18 levels of confidence should match the discussion of uncertainties and data
19 deficiencies. And this is because there are cases where it seemed like
20 uncertainties would be noted or admitted or that, for example, when modeling
21 data were used because actual measured data were not available -- and the
22 evaluation would then note that this is likely to over- or underestimate the actual
23 exposure. But then the confidence level is -- in the conclusion is described as

1 being medium or high, so it doesn't seem to match. So that's what I had. I kind
2 of paraphrased some of it, so others may want to elaborate.

3 **DR. KENNETH PORTIER:** Thank you, Dr. Lash. Dr.
4 Davies?

5 **DR. HOLLY DAVIES:** Hi. I think that Dr. Lash did a
6 good job of summarizing everything, so I don't have anything to add right now.

7 **DR. KENNETH PORTIER:** Thank you. Dr. Schlenk?

8 **DR. DANIEL SCHLENK:** Ditto on my part. Larry
9 covered everything I submitted.

10 **DR. KENNETH PORTIER:** Good. Dr. Cobb?

11 **DR. GEORGE COBB:** Am I here? Can you guys hear
12 me?

13 **DR. KENNETH PORTIER:** Yes, yes, you are. We can
14 hear you. Yes, I can hear you.

15 **DR. GEORGE COBB:** Okay. So this is just a point to
16 keep us from going around in circles on the writing part. There was a mention
17 that there was biomonitoring discussion in some of the earlier questions. That
18 was probably things that I brought up in Question 2.2. There are probably other
19 areas.

20 The intent there was environmental biomonitoring, not
21 human biomonitoring. I've clarified that in the language in Question 2.2 as this
22 discussion was going on. But Ken, I don't want you to get pulled in 20 different
23 directions when we're doing that. I'm just trying to put environmental
24 biomonitoring where I meant that not to be human health.

1 **DR. KENNETH PORTIER:** Dr. Lash?

2 **DR. LAWRENCE LASH:** Yeah. So I'm looking at that
3 comment, and it does say biomonitoring discussion in the environmental section.
4 Are you saying it should be just deleted from here because it's discussed
5 elsewhere at this point or that it needs cross-referencing? Because the comment
6 actually reads that the biomonitoring discussion in the environmental section
7 should be moved to the human health section following PBPK data, since there
8 were discrepancies measured between metabolites measured in human media
9 than those discussed. So what I'm thinking, now that I think about the language
10 more -- what it's saying doesn't quite make sense maybe or maybe that there
11 should be cross-referencing of this discussions to allow or to resolve or explain
12 discrepancies between -- in the PBPK data, something like that.

13 **DR. GEORGE COBB:** Larry, what I think is there's
14 possibilities that there's dual meanings for biomonitoring in different sections.
15 I'm going through all of the write ups I have and searching for biomonitoring
16 and trying to see where the intent was environmental biomonitoring or get from
17 the discussants whether they meant environmental or human biomonitoring just
18 to clarify that. There's probably a lot of crosstalk there, but I would hesitate to
19 move all the mentions of biomonitoring to the human health section until we get
20 some clarification on that.

21 **DR. LAWRENCE LASH:** I mean, usually, I don't
22 usually see biomonitoring as the term used. We talk about biomarkers. But I've
23 never seen it really phrased as biomonitoring because to me that sounds more
24 like a term where you're monitoring the environment as opposed to, say,

1 measuring urinary metabolites or blood levels of things. So I think maybe this
2 little paragraph needs rewording that it's not so much that it should be moved,
3 but that the discussion needs to be maybe mentioned and cross-referencing to
4 explain some of the metabolites that are discussed in the human section.

5 **DR. GEORGE COBB:** Yeah. That sounds right.

6 **DR. LAWRENCE LASH:** Yeah. I'll work on that.

7 Okay.

8 **DR. KENNETH PORTIER:** I think Dr. Schlenk wants
9 to kind of comment in there. Dan?

10 **DR. DANIEL SCHLENK:** Yeah. That was my
11 comments. The biomonitoring data is 2.3.4.3, and I think if you just put those
12 parentheses around -- because that whole section is nothing but human health
13 biomonitoring. There's no environmental biomonitoring that's going on there.
14 That's human health biomonitoring data.

15 The term can be used either way. That's not the issue.
16 It's the fact that you have human health biomonitoring data in the environmental
17 fate and transport section. And I would think that that biomonitoring data for
18 human health -- and everything in that section only deals with human health.
19 There's nothing there that has any biota issues whatsoever except for human
20 health. I would think you'd want that in the human health section. That's all
21 I'm saying.

22 **DR. LAWRENCE LASH:** Can you say it again? 2.4. --

23 **DR. DANIEL SCHLENK:** 2.3.4.3.

24 **DR. LAWRENCE LASH:** 2.3.4.3. Okay.

1 **DR. DANIEL SCHLENK:** Line 2497.

2 **DR. LAWRENCE LASH:** So it's just basically that
3 there's a subset of the biomonitoring discussion in the environmental section that
4 relates to human health. And that's what --

5 **DR. DANIEL SCHLENK:** Exactly. It's all NHANES
6 data. It's basically all the NHANES data that's present there that they got from
7 NHANES data. And even the targeted metabolites that they used have a
8 different acronym than the ones that were actually presented in the metabolism
9 section as well. So there's a disconnect there, as well. It's almost like two
10 different groups did that. In terms of clarity, I think you'd want all your
11 NHANES type data in the human health section.

12 **DR. LAWRENCE LASH:** Yeah. I would agree. Now it
13 makes more sense than before.

14 **MS. RUTHANN RUDEL:** And this is Ruthann. That's
15 the same section that I just highlighted in 7.1 as being this is interesting, but how
16 did it get used? It wasn't clear at all how EPA used it in the evaluation to
17 support it being there.

18 **DR. DANIEL SCHLENK:** I agree. I think it's great
19 data. Again, this question is sort of examining flow. And it just kind of came
20 out of nowhere. It's like, oh, wow. Here's human health biomonitoring data
21 when we talked about water discharge. And it just seems to me it would fit
22 better in the human health section. That's all.

23 **DR. KENNETH PORTIER:** Dr. Davies?

1 **DR. HOLLY DAVIES:** I also had thought it was odd to
2 find the biomonitoring data in with the environmental fate and transport and
3 estimates of exposure. It seemed to be showing the general population exposure
4 with the biomonitoring, which is something not included in this draft risk
5 evaluation. So I was sure what the point was and why it was here.

6 **DR. KENNETH PORTIER:** Dr. Barone has his hand
7 up, so I'm assuming he's going to tell us why. Stan?

8 **DR. STANLEY BARONE:** Actually, I appreciate the
9 suggestions on the monitoring data. I think the Committee has identified
10 something we've recently changed in the scope of our format -- our format of
11 our scope, excuse me, for the next 20. I also think there were comments made --
12 I want to get some clarification about cross-referencing that Dr. Lash made and
13 the bibliography -- challenges with the bibliography. If you could elaborate
14 more, it would help us understand what the problem is and the possible solution.

15 **DR. LAWRENCE LASH:** So the way the charge
16 questions are constructed, we actually have more -- even though there's some
17 recommendations here, there are more specific recommendations in the next one,
18 7.3. But I've kind of made this comment in various places that, in general, I
19 think with having some data -- I think our comment was made that there's
20 actually little real data described in the document, that where there are data it's in
21 the supplementary files, some of which are quite long. And specific referencing
22 to those -- and also the fact -- I also made a comment or noted that I think, kind
23 of out of necessity, there is repetition because you're talking about the
24 environmental, the exposures, then hazards and the risk considerations and then

1 risk conclusions -- that it would be helpful to make statements referring back to
2 specifically where this was discussed previously in the 600-plus page document
3 in another context. The references, I don't have a lot on that. I don't recall a lot
4 more. Let me see.

5 **DR. STANLEY BARONE:** So I ask because we have
6 tried to cross-reference and hyperlink a lot throughout the document. And I was
7 wondering if there were specific suggestions that we could do more or, if
8 something wasn't working, please call that to our attention. With regard to the
9 bibliography, we've HERO-ized the bibliography so that you know what the title
10 and abstract is throughout the document and the bibliography -- what the actual
11 document is. You can go to that. So if there's something else there, it would be
12 helpful to know.

13 **DR. LAWRENCE LASH:** Yeah. I forget who -- I'd
14 have to look back who had submitted the comment on the bibliography which
15 lists on-topic and off-topic determinations. They said they found that
16 challenging to use. So I don't know that we address that in 7.3 directly, but
17 that's something that we could elaborate on specifically. Yeah.

18 **DR. STANLEY BARONE:** Thank you.

19 **DR. LAWRENCE LASH:** Yeah.

20 **DR. KENNETH PORTIER:** Okay. We've got a lot of
21 hands up. Dr. Anderson's been waiting. Henry?

22 **DR. HENRY ANDERSON:** Yeah. I was just going to
23 say on the bibliography it could be that I just don't have the proper software or
24 haven't paid for the fancier programs. But you can't do a word search on the

1 bibliography. So for instance, I went into it to try to look for “worker” or
2 “manufacturing” or various words to see which of the documents in the
3 bibliography -- especially in those that were deemed to be off target -- may have
4 contained some information that could have been useful to understanding things.
5 And that really couldn’t be done. Now, maybe if I had the program to convert it
6 to a Word document so I could do a word search or have Adobe -- the one where
7 you have to pay for it, that might have changed that.

8 The other thing that I found -- and I would just, again -- if
9 the document was really only intended for the use by panelists, that’s fine. But
10 when I first went into it, I guess I just was working on the document that was
11 sent to us as an attachment to an email. And most of the references, especially to
12 individual papers, were not valid, or you were given an error message of the
13 number that’s referenced is not in the HERO database. And it turns out you have
14 to first sign into -- log in to HERO in order to be able to make the document
15 work.

16 So I don’t know how -- if it seemed to be the general
17 public who might have wanted to do similar review or would assume the public
18 commenters probably didn’t have access like we did to HERO. So that, I think,
19 going forward -- if it’s going to be useful to -- I think in terms of my students. If
20 they can’t actually look at the underlying data, they get very upset. So that’s just
21 one thing to think about as you go into being a final document.

22 It was fine for us because, once you figured out how you
23 can actually make HERO work, other than -- every one of the EPA references
24 came up fine in HERO and some of the letters and other things. But then others

1 didn't, so that was sort of problematic. And given the short timeframe we had to
2 try to sort all this out, it was a challenge.

3 **DR. KENNETH PORTIER:** Thank you, Henry. Dr.
4 Davies?

5 **DR. HOLLY DAVIES:** I also wanted to remember or
6 mention something that we mentioned earlier, which is how hard it was to search
7 through the data quality evaluation supplemental files because we couldn't do
8 word searches. And they weren't in alphabetical order or some other order that
9 we could figure out. So that's another comment for future documents.

10 **DR. KENNETH PORTIER:** Thank you. Dr. Kissel?

11 **DR. JOHN KISSEL:** So I commented firmly on the
12 bibliography earlier, and the bibliography that I'm talking about is the
13 bibliography which is listed as a supplement to the scoping document. And I
14 don't know if there's another bibliography than that. The bibliography for the
15 scoping document is organized by topic area, so a given reference may appear
16 multiple times in the document as being either on or off topic, under exposure,
17 for instance, or engineering or fate. And it would be easier to use.

18 So when I started search on authors to try to find things, I
19 could do that. It's just a PDF, so searching on word strings was fine. But I
20 would have to sort through every topic area to see whether the document was
21 listed as on topic or off topic. That was the -- if the articles could somehow just
22 be presented in alphabetical order, with then columns to the right which indicate
23 what they were considered on topic for or off topic for or not evaluated for, that
24 would be an easier string of references to get your hands around.

1 **DR. KENNETH PORTIER:** Thank you, Dr. Kissel.
2 Anybody else want to -- anyone else on the Committee want to comment? Some
3 good discussion. I'll turn to Dr. Lash. Did you catch all of this?

4 **DR. LAWRENCE LASH:** Yes. I think I get better the
5 gist of the comment. So what I basically got is that the organization of the
6 bibliography to the scoping document -- how it's organized, it's by topic. And
7 within each one, citations are designated as on or off topic. So they may be on
8 topic for one and off for another. So it makes it confusing in that respect. And
9 some reorganization would be helpful for that. Yeah. And I'll work on the text.

10 **DR. KENNETH PORTIER:** And given that moving
11 forward I think EPA's going to skip the scoping document and go directly to --
12 not the scoping, the -- senior moment here.

13 **DR. STANLEY BARONE:** Dr. Portier, this is Stan
14 Barone.

15 **DR. KENNETH PORTIER:** Problem formulation
16 document.

17 **DR. STANLEY BARONE:** Yes. We're skipping the
18 problem formulation. We have a draft scope and a final scope.

19 **DR. KENNETH PORTIER:** So the bibliography will be
20 for the DRE?

21 **DR. STANLEY BARONE:** The bibliography -- there's
22 actually now literature trees in the scopes, which we didn't have in the previous
23 scopes. We have more technology and more facility in our draft scopes and what

1 will be in our final scopes than what we had in the problem formulation and the
2 scopes in the previous ten.

3 **DR. KENNETH PORTIER:** Thank you for that
4 clarification. I just couldn't come up with problem formulation. While I have
5 you here, any additional comments from EPA or clarifying questions? I think
6 EPA got it.

7 **DR. STANLEY BARONE:** Not at this time.

8 **DR. KENNETH PORTIER:** Let's go ahead and move
9 on to -- let's go ahead and move on to Question 7.3 on suggestions for
10 improvements. Dr. Lash?

11
12 **CHARGE QUESTION 7 (7.3)**

13 **DR. LAWRENCE LASH:** Right. So this one is
14 basically a continuation of 7.2, and it's designed to make specific
15 recommendations. So I'll go through -- we have actually about 16 or so, and I'll
16 try and paraphrase where appropriate. But the first one is that the Committee
17 recommends more consistent and methodical cross-referencing of key discussion
18 topics to be done throughout the document.

19
20 Second is Committee recommends more specific
21 information regarding literature searches, including the specific search terms that
22 were used. Because I had made a comment about depending upon what you look
23 up or depending upon who's doing the work, some people refer to the compound
24 as Perchloroethylene, others as PERC, also tetrachloroethylene or

1 tetrachloroethene. And so sometimes all the citations will not show up with a
2 given term. And it just wasn't clear what these terms -- what terms were
3 specifically used. And I looked through the supplement, as I noted, and that
4 wasn't clear.

5 The next one is that the Committee recommends the
6 evaluation provides specific definitions of what makes a dataset of low, medium,
7 or high quality, and understanding of this is critical for the entire evaluation.
8 And the Committee suggests addition of a summary table in the introduction
9 section that defines these quality terms. And I think one of the Committee
10 members noted that this may be difficult simply because the different classes of
11 studies are so different. But I guess my think is that there are some general
12 characteristics that might be able to be described, such as reproducibility and
13 following certain standards, either industry standards or good laboratory practice
14 and so on.

15 Then fourth is the Committee recommends that the table
16 summarizing the assessment history of PCE, which is Table 1-3, be enhanced to
17 be more useful and informative. So I mentioned this briefly in 7.2, so the table
18 as currently presented simply has two columns: one listing the authorizing
19 agency and one providing the citation. So suggestion says a third column should
20 be added on the right that summarizes the key recommendations or conclusions.
21 And that could probably be done very briefly.

22 Then recommendation five, the Committee recommends
23 that conclusions of overall confidence align with stated limitation where clear
24 and more detailed rational for the conclusion be provided. And this is in

1 reference to some cases where it seemed like, while uncertainties or potential
2 under- or overestimations of exposure, for example, are noted, then it seems like
3 the conclusion of the overall confidence in the risk estimation doesn't seem to
4 match those stated uncertainties or over or underestimations. Six is the
5 Committee recommends that assumptions described by the EPA for PPE use
6 need more explanation and justification. That's one that's come up before and
7 we discussed already.

8 Seventh is there was a suggestion that the EPA consider
9 graphics wherever possible to improve reproducibility. And I have in the
10 comments that'll be submitted for the report an example of a pie chart that very
11 clearly illustrates PCE uses as a percent of production volume, as an example.
12 Then next, number eight, the Committee recommends addition of a detailed
13 index to help readers find material on specific topic. It was noted that there's no
14 index in the volume. So for example, if you wanted to just look for something
15 on glutathione conjugates or material mentioned on bystander exposures or
16 something, an index would be helpful as a starting point.

17 Another recommendation, number nine, is to address the
18 problem of the unwieldy nature of the large volume. One Committee member
19 suggested dividing it into at least three or possibly even four or five separate
20 volumes. And I have detailed specifics on what those could comprise. But as I
21 said, there was other suggestions that the reorganization according to instead
22 how the introduction slides that were presented on Tuesday might be effective as
23 well in clarifying the presentation.

1 Number 10 is Committee members suggested or
2 recommended that the Agency provide potential actions for its regional offices to
3 adopt as a result of this evaluation because it was noted that the potential actions
4 that the Agency could recommend were not noted here. And there's a couple of
5 suggestions made. Number 11 is the Committee recommends that the risk
6 estimation tables, such as 4-108, include exposure concentrations that are being
7 compared with the HECs and UFs to produce the MOEs. That's a lot of
8 abbreviations, huh? And as presented, it was noted that one has to dig into
9 exposure section to find them. So having them listed in the table, as well, for
10 these risk estimation tables would be helpful.

11 Number 12 is the Committee recommends that the EPA
12 simply use a hazard index approach in the risk characterization. A comment was
13 made that the presentation of calculated MOEs in relation to target MOEs, which
14 is referred to as benchmarks, may be confusing to some because the terminology
15 is used differently by other stakeholders. And it might be easier to understand if
16 the target acceptable air concentrations, the RFC, were compared directly with
17 expected exposure concentrations as is done in others.

18 Sort of a related recommendation is that the Committee
19 recommends that the EPA use more standard terminology that is more readily
20 understandable. And this is kind of related because, for example, it's noted that
21 the term "benchmark" usually refers to an alternative to NOAEL and LOAEL.
22 Here, the EPA is using the term to mean something different. And there's a little
23 elaboration on that.

1 The 14th recommendation is the Committee recommends
2 the EPA take a more holistic approach to evaluation of the data beyond what is
3 done in the assessment of study quality and use as much of the data as possible
4 to support derivation of ecotoxicological benchmarks. And it's noted that there
5 are cases where data are not used but they could be used. And number 15 is the
6 Committee endorses the use of a species sensitivity distribution approach. It's
7 noted that when insufficient data of appropriate quality and relevance are not
8 available, it is recommended that the EPA can provide refined data according to
9 toxic endpoint in a scatter diagram relative to exposure. And this approach
10 would make selection of the point of departure for ecotoxicity more transparent
11 and potentially resolve concerns regarding biases in specific critical study
12 selection.

13 And then the last formal recommendation is that it's also
14 recommended that the EPA consider corroborative evidence and pay particular
15 attention to data outside the reasonable range of other similar data where issues
16 of false positives, methodological or other attributes may explain large
17 discrepancies. And there were a number of also specific comments or
18 corrections regarding some terminology, use of scientific notation, and also I was
19 forward two tables that are recommended to be used or examples where you
20 could summarize -- the document could better summarize the literature used in
21 establishing weight of evidence for environmental hazard as one example and
22 then a second table for use in establishing weight of evidence for human health
23 hazard. So that is what I have.

1 **DR. KENNETH PORTIER:** Larry, this is Ken Portier.

2 Can you go back to number 10, which sounded to me like more of a risk
3 management task rather than a risk assessment task?

4 **DR. LAWRENCE LASH:** Mm-hmm. Yeah. So

5 number 10 was that the Committee recommends that the Agency provide
6 potential actions for its regional offices to adopt as a result of its evaluation.

7 And then text under there that I didn't really go through in detail -- but it said,

8 "Actions the Agency could recommend may include, but not be limited to,

9 recommending EPA regional offices adopt a nationwide consistent preliminary
10 remedial goal for air borne PCE or a revision of the current PEL."

11 **DR. KENNETH PORTIER:** And again, to me, that
12 sounds a risk mitigation recommendation, which is not really under the purview
13 of this Committee.

14 **DR. LAWRENCE LASH:** Sure.

15 **DR. KENNETH PORTIER:** We can keep it in there.

16 I'm just warning the Committee it's probably a non-starter.

17 **DR. LAWRENCE LASH:** Sure. Well, I know we've
18 encountered that, and I've always -- I think the documents that I've read -- these
19 TSCA documents, do, I think, do a nice job of explaining in the introduction the
20 focus and purpose of TSCA. But it's kind of hard, I guess, when you're coming
21 up with conclusions, I think, about hazards that you always think of the next
22 step. Well, if you identify a hazard, what can be done about it? Or if you
23 identify a specific value that sort of delineates where unacceptable risk begins,

1 then you want to have an action from that -- lead from that. So yeah. But I
2 understand your -- in terms of the specific purposes. Yeah.

3 **DR. KENNETH PORTIER:** So let's go to the associate
4 discussants. Dr. Johnson, anything to add?

5 **DR. MARK JOHNSON:** Yeah. Just a little bit to what
6 Larry brought up. I think any time -- I kind of brought this up earlier -- you use
7 the critical study approach, you open yourself up to controversy or disagreement,
8 I guess. But spatially displaying toxicity information, you're trying to use as
9 much information as possible I think helps resolve that. It provides greater
10 transparency. That's why we're an advocate of the species sensitivity
11 distribution approach, even if you can't use it. Just displaying the information in
12 a spatial context helps sell the use of that critical study.

13 And even for human health evaluation, I would say the
14 same applies. Certainly, you can't -- you don't want to use a species sensitivity
15 distribution. It wouldn't work. But spatially showing that information using
16 other information that maybe you excluded because the data quality reasons to
17 help support or corroborate the number you have all would help. And that's all I
18 wanted to add. Thanks.

19 **DR. KENNETH PORTIER:** Thank you. Dr. Kissel?

20 **DR. JOHN KISSEL:** Yeah. I had a couple of
21 comments, and I'm not sure whether I heard them in the summary or not. With
22 respect to figures, in particular, I think that the two mass balance figures, which
23 are 1-1 and 2-1, are inadequate, at least inadequate and maybe misleading

1 because they don't really show a very good picture of what's going on. So that's
2 -- there's definitely a clarity problem there.

3 The second thing was the -- and we already had this
4 discussion, so I don't need to really go into it. But the derivation of the dermal
5 slope factor is mysterious. So that lacks clarity. And the third point, which we
6 just got an email on, is the question of file access.

7 So I requested that the file 19, which is the spreadsheet for
8 calculation of consumer dermal, be unhidden so we could see it. And we just got
9 an email to the effect that there isn't actually anything in the hidden columns,
10 that those are just placeholders, and they will be filled in at some future data.
11 Well, that's okay, assuming that future data is not very far in the future because -
12 -

13 **DR. MARI LEE:** Sorry. This is Mari Lee with EPA. I
14 can clarify that. It's not that they're going to be filled in the future. They were -
15 - this is the spreadsheet that's used for all of the ten chemicals, and some of the
16 chemicals had different endpoints than PERC. So I hid the columns for which
17 we didn't have data.

18 So I can send you -- I'm going to send you an unlocked
19 version. For clarity to be able to see the results more clearly, I hid things such as
20 adult receptors because that was null. And I hid things such as liver chronic
21 POD value because that wasn't used. So it's columns that weren't used, not be
22 used. But I will send you an unlocked or an extended version of the spreadsheet.

23 **DR. JOHN KISSEL:** Okay. Well, that's still more
24 confusing to me. What I'm looking for is just the numbers that you're using for

1 exposure factors. And I don't -- for a given consumer use, there has to be some
2 duration, some volume or mass of material that -- and some amount of skin that's
3 in contact, and I don't know where that is.

4 **DR. MARI LEE:** I think you're confusing the risk
5 calculator -- this is Mari Lee again -- the risk calculator with the exposure values.
6 So the risk calculator is taking the already calculated exposure values, applying
7 the POD, and calculating the MOE from that. So this spreadsheet does not do
8 the full exposure calculations. It only has the exposure values put into it to
9 calculate the final risk.

10 The exposure values and all of the inputs -- if you look in
11 the exposure section, I believe it's Table 2-64 and the immediately following
12 table has the duration of use, the mass used, the weight fractions. Those are also
13 repeated under each condition of use for each individual section within the risk
14 evaluation. And then the supplemental consumer file -- and let me make sure I
15 can find the number for that. Let me see if I can find a number. The
16 supplemental consumer file has the full list of all inputs, all values, for all
17 iterations that you can look at.

18 **DR. JOHN KISSEL:** Okay. I'll look. I didn't see those
19 the first time through.

20 **DR. MARI LEE:** Yup. Let me just find real quickly --
21 the supplemental file you want is going to be file number 20, the supplemental
22 information on consumer exposure. It has embedded spreadsheets with all of the
23 inputs. And then, as I mentioned -- and let me just, again, make sure I have the

1 right number. In the draft risk evaluation, Section 2.4.2, Tables 2-64 and 2-65
2 list the input parameters that were varied.

3 And again, you'll see those input parameters listed in each
4 section of the POU. So for example, 2.4.2.3.1.1 -- I know that's a mouthful --
5 aerosol cleaners for motors, you can see under duration percentile the number of
6 minutes used for each of the different scenarios, weight fraction percentages in
7 parentheses, and mass use percentile is in parentheses in grams. So the key
8 parameters that were varied are listed directly under each condition of use.

9 **DR. JOHN KISSEL:** Okay. I was looking for a -- and I
10 should be able -- if the information's there, I should be able to reproduce it. But
11 what I was looking for was an actual calculation that I could just run through and
12 check.

13 **DR. MARI LEE:** Yes, I'm sorry. You would have to
14 use CEM Version 2.1 on the specified consumer models, which are listed in 2-64
15 and 2-65 to do those calculations. And there's also a user's guide with the CEM
16 2.1 version that lists the full calculation that were used to model the inhalation
17 and dermal exposures.

18 **DR. JOHN KISSEL:** Okay. Well, it would be -- I guess
19 then my final comment is it would be nice if there was actually a spreadsheet in
20 which all of what you just said is incorporated so we can follow it from point A
21 to point B instead of having to reconstruct.

22 **DR. MARI LEE:** Okay. I think maybe the clarification
23 is that, just like EPI Suite or EFAST, CEM is a standalone published, publicly
24 available model.

1 **DR. JOHN KISSEL:** Well, I've been in the CEM
2 guidance quite a bit, and the gross equations are there, if we don't have the
3 numbering problem, which is -- specifying which model is which number has
4 been a problem also. But ultimately, somebody has done those calculations in a
5 spreadsheet, and it would be easier to see it -- instead of saying "Here's three
6 inputs and here's a model in a different document, you can go look at that model
7 and you can plug these in. And you can get that result," it would be nice to just
8 give us a spreadsheet which does the calculation, and then we could check it.

9 **DR. MARI LEE:** Sure. Thank you for your comment. I
10 do think it will help if you look at the supplemental file with the embedded
11 spreadsheets.

12 **DR. JOHN KISSEL:** Okay. Well --

13 **DR. KENNETH PORTIER:** Dr. Barone -- I think --
14 John, I think Dr. Barone wanted to clarify something. Stan?

15 **DR. JOHN KISSEL:** Okay. Fine.

16 **DR. STANLEY BARONE:** Actually, it was on another
17 point. I think Mari addressed Dr. Kissel's comment about the supplemental files.
18 I'm glad she was able to pull those up. We have a lot of supplemental files. We
19 acknowledge there are 20 different supplemental files with embedded
20 spreadsheets.

21 Again, this is a challenge because we're trying to show all
22 of our calculations. We can't do that in the body of the document. It makes it
23 very unwieldy, particularly when we have 70 different conditions of use, as we
24 do in tetrachloroethylene. Mari also pointed to the risk calculator, which is also

1 in the supplement and also will allow you to see what risks are by varying
2 different input parameters, exposure conditions versus PPE and so on and look at
3 central tendency versus high end. So we also hope that that provides some
4 transparency.

5 I did want to underscore a couple of points for
6 clarification. I was glad you brought up the issue about actions and
7 recommendations for regional offices. I want to make it clear so everybody
8 understands that the risk evaluation and the identification of unreasonable risk in
9 the final risk evaluation will trigger those other actions. So risk management
10 will start once we have finalized the risk evaluation and identified unreasonable
11 risk. And in that process is where we propose -- and it's a process -- a rule
12 making process where we propose different options for consideration, take
13 public comment, and so on. So that is, again, under TSCA required in a two-
14 and-a-half-year timeframe.

15 I wanted to get some clarification because, in a couple of
16 the comments from Dr. Lash, it sounded confusing, at least to me, whether the
17 comments were referring to study quality or strength of the evidence. The
18 comments about study quality and putting a table of study quality considerations
19 into the introduction -- those are in the Appendix for each discipline. We have
20 the study quality considerations for each type of study for different disciplines.
21 And I want to make sure folks understand that.

22 What we don't have as well documented in our framework
23 now is the considerations for strength of the evidence and the weight of evidence
24 considerations. So that is in a narrative, and it's not tabulated in our assessment.

1 The issue of corroborative evidence is part of our weight of the scientific
2 evidence narrative. And if you have specific suggestions of where we could
3 improve our narrative on weight of the scientific evidence, please include that in
4 your specific comments.

5 **DR. KENNETH PORTIER:** Thank you. I want to go
6 back to Dr. Kissel to see if we finished your conversation. John?

7 **DR. JOHN KISSEL:** I've just been trying to page
8 through the supplement number 20. And there's an odd table in it, which I just
9 lost -- so I'm not sure where it is. But it's a table with Excel images in each of
10 the cells in the table. And I don't know if those were supposed to -- I'm not sure
11 if that's what embedded Excel files mean. Okay. It's on page 22 of the
12 supplemental document number 20. And within the cells, there would appear to
13 be icons that are Excel cells, but they're dead to me. If those are the embedded
14 things that I'm supposed to be able to have access to, I don't have access to
15 them.

16 **DR. MARI LEE:** This is Dr. Lee, again.

17 **DR. KENNETH PORTIER:** I agree. I see that.

18 **DR. MARI LEE:** I'll look at that. It might be a problem
19 with converting to PDF. I will make sure to find out if we can get those -- the
20 access.

21 **DR. JOHN KISSEL:** Okay. So I think one thing that
22 this whole discussion highlights is something that Larry said: the cross-
23 referencing. So this is obviously an enormous endeavor, and you've got stuff

1 stuffed all over. But just more arrows pointing to places, more hyperlinks would
2 be helpful.

3 **DR. KENNETH PORTIER:** This is Ken Portier. You
4 know, John, I just envisioned a roadmap. It's almost like you need a roadmap.
5 Well, if you want to look at the dermal parameters for this scenario, you need to
6 take this road and go over here in this document and click on that icon and a
7 spreadsheet opens up. And following the road without a roadmap or a GPS
8 system is kind of difficult here. I understand. Dr. Lash?

9 **DR. LAWRENCE LASH:** Yes, thanks. So my
10 comment also about cross-referencing or explaining the data quality -- so the
11 reason why I've said that a few times is that I kind of take the position that this
12 document should be understandable on its own, and that where specific points --
13 so for example, if you look at Section 1, the introduction, it starts on like page
14 38. And then it goes into more detail with regard to physical properties, uses,
15 and regulatory history, scope, and systematic review. So it's not -- the whole
16 section is probably about 23 pages long, something like that, which is fine. So I
17 guess what I would have liked to see is a statement saying that the criteria to
18 determine the data quality -- and actually what makes good data. I think there
19 are certain general principles that -- and if that's explained in a supplement, then
20 it should be specifically referred to.

21 But I don't see anywhere -- there are statements, for
22 example, in Section 1.5.2, it says -- let's see. It says like, "During the data
23 evaluation stage, the EPA assesses the quality of the methods." But it never says
24 what that -- the term "quality" is never defined. So that's what I kind of mean by

1 -- and it doesn't have to be very long because I know we want to -- obviously,
2 there's no desire to make this document any longer. But I think some brief
3 statements saying the criteria for assessing quality are defined and discussed here
4 and then a link to it or a reference to it, that kind of stuff is what I meant.

5 **DR. KENNETH PORTIER:** Thank you. Tamue, are
6 there slides of those two tables able to be brought up? So Larry mentioned two
7 tables that I submitted to him to talk about weight of evidence. And so you're
8 seeing one right now.

9 **MS. TAMUE GIBSON:** Yes. Mm-hmm.

10 **DR. KENNETH PORTIER:** So to me, missing from the
11 discussion -- on the weight of evidence discussion for both environmental and
12 human health hazard is a summary of the literature that's been extracted and
13 examined. And I've been thinking about this in terms of weight of evidence and
14 trying to understand first why weight of evidence is presented like it is in the
15 DRE and then what can be done to improve that discussion. The cancer
16 guidelines, for example, notes that "The weight of evidence narrative should
17 highlight the quality and quantity of the data, as well as other aspects."

18 And I realize it's the quantity of the data that kind of gets
19 missed, as well as the quality. So thinking about this yesterday evening and this
20 morning, I kind of thought about how EPA might be able to summarize the
21 literature, say, related to environmental hazard and the weight of evidence -- at
22 least as an introduction in the weight of evidence. So the first line on the left, it
23 says, "Total." Under "Total" that's the total number of studies that you've

1 looked at. And I think -- my guess is that number is 30 for environmental
2 hazard.

3 But then I want to know, well, how many of these were
4 fish studies? How many talked about aquatic invertebrates? How many talked
5 about algae under acute exposures, same thing under chronic exposures? And
6 then going down, breaking it out, how many were rated high, medium, low, or
7 unacceptable? How many had high or low relevance? How many looked at
8 death? How many looked at immobility? How many looked at reduced growth?
9 And then how many of these articles, say fish, aquatic exposure articles were
10 used to quantify hazard? And I think the answer there is two.

11 So I can tell there's a total of 20, and there's a total of two
12 fish studies that were used to qualify hazard. But I cannot recreate the rest of
13 this table. And I think from what Dr. Barone was saying in the next generation
14 the bibliography database is going to be organized -- that you'll be able to find
15 these categories. But what I'm suggesting is that a summary in the weight of --
16 to start the weight of evidence discussion might help people to understand the
17 effort and the quantity of available information that goes into this hazard
18 discussion.

19 In the next slide I did a similar thing for human health.
20 The problem there is you've got cancer and noncancer endpoints. And then
21 you've got different aspects of noncancer, different aspects of cancer that are
22 looked at. And then you've got high, medium, low, unacceptable quality and
23 relevance because it's quality and relevance that are the two factors that kind of
24 come into the weight of evidence discussion.

1 And so it's just -- it's a fairly simple thing. I think it's
2 something that could be easily done, but I think it gives you a quick snapshot of
3 the literature. And I noticed I misspelled summary -- a snapshot of the literature
4 or the quantity of information and also a feeling for the quality of the
5 information that went into establishing, say, the human health hazard point of
6 departure. So that was that particular comment. And I'll include cleaned up
7 versions of this in the minutes report. I've got a lot of hands up. I think,
8 Ruthann, you were next.

9 **MS. RUTHANN RUDEL:** Hi, Ken and everybody. I
10 just have three quick points. The first one related to these data quality
11 evaluations and counting studies, it's always very helpful to have a systematic
12 evaluation of data quality of studies and consistent criteria. The biggest
13 challenge to keep in mind, though, that's not address when you do that is these
14 kinds of -- they don't evaluate whether the study design was matched well to the
15 underlying exposure effect relationship. And if it isn't, you can have a high-
16 quality study that didn't see the effects because it didn't measure the right
17 endpoint or whatever. And so that's -- I've known that to be a bigger problem or
18 a big problem, and it's not addressed by these kind of ratings. But those ratings
19 still can be helpful.

20 Back onto recommendations in 7.3, my recommendation
21 is for EPA to present air concentrations that this evaluation concludes are
22 acceptable in workplaces and in homes and to compare them -- or at least allow
23 others to compare them easily with common numbers from the literature,
24 including, for example, the IRIS inhalation reference concentration. So this

1 would add interpretability and utility to this document, which is obviously the
2 result of a substantial amount of effort. For example, it could facilitate
3 interpretation of current and future workplace and residential air measurements.
4 Somebody goes into a workplace and does a measurement, and it would be nice
5 if they could come into this document and compare it with some numbers and
6 get a sense of where they are in these risk -- how it compares with what EPA
7 designated as reasonable and unreasonable risks. Along these lines, Table 4-108
8 and the rest of the risk estimation tables -- it would be helpful if the exposure
9 concentrations that are being compared with the HECs and UFs to produce the
10 MOEs could be included in these tables.

11 And then I just have one editorial comment, for the Sonya
12 Sax exposure study that's noted in the DRE in Tables 2-62 and line 4830, I'm
13 asking or recommending that you remove "inner city" as a descriptor of that
14 exposure setting. The meaning of that is unclear, and I'm not sure the relevance.
15 I know that the study authors described their study community that way, but it's
16 not really useful to describe -- to use those words to describe the setting. So I
17 would recommend removing that. Thank you.

18 **DR. KENNETH PORTIER:** Thank you. Dr. Johnson?

19 **DR. MARK JOHNSON:** Thanks. Ken, I like your table.

20 I think that's a great first start. Just a couple points I want to bring up. What's
21 kind of missing there is dose, and that's why I'm a big advocate of scatter
22 diagrams because that gives me much more confidence in that corroborative
23 sense that Dr. Barone mentioned earlier. If I see a scatter diagram and I see this

1 is where we drew our line, that gives me a sense of where the data lie and that
2 we're all in this kind of same ballpark.

3 The other thing, too, is for some of these aquatic receptors
4 -- I think George brought this up earlier, and I think he's spot on -- is that quality
5 may be a moving target. Some of these older data, especially if they're data rich
6 may be based on nominal. It may be static versus flow through designs.

7 So I don't have an answer to that right now. I think
8 certainly you could call ones with analytical chemistry, with flow through
9 designs as high quality. No doubt there. I guess maybe medium quality would
10 be assigned for ones that are maybe nominal or static renew or static. And then
11 you could consider using medium quality data, as well as high quality data when
12 you look at those diagrams. And you could carry those quality ratings with you
13 into the scatter diagram also, maybe with superscripts, for example.

14 **DR. KENNETH PORTIER:** I'm just looking for first
15 steps on a lot of this stuff. Let's see. I see that Ruthann still has her hand up.
16 Lawrence has his hand up. Dr. Kissel has his hand up. I'll start from the top.
17 Yeah. Okay. Dr. Kissel's got his down. Lawrence has got his down, and
18 Ruthann dropped her hand. Anyone else want to comment on this? Dr.
19 Hossain?

20 **DR. MUHAMMAD HOSSAIN:** Hello?

21 **DR. KENNETH PORTIER:** Yup. You're live.

22 **DR. MUHAMMAD HOSSAIN:** Okay. So I have one
23 comment regarding the summary Tables 3-7 and 3-8. Here they presented
24 noncancer hazard from acute and chronic exposure scenarios. When I was

1 looking at the table, I saw that there is some data from human exposure for acute
2 scenarios, but they presented only the implementation from one study. I think
3 there are several other noncancer endpoints are in the document, so they need to
4 be included in this summary table.

5 And the Table 3-8, here they presented from chronic
6 exposure scenarios. And I saw that they presented from human and animal data
7 here for kidney, liver, developmental, liver toxicity, but I don't see the animal
8 data for neurotoxicity endpoint. I think it would be better to add animal data for
9 neurotoxicity and endpoint in this table for better presentation and to include all
10 the information.

11 **DR. KENNETH PORTIER:** Thank you. I missed that.
12 I guess that's neurological, kidney, liver, developmental, reproductive. Yeah.
13 This table is just meant to give them the idea. They're going to make this table
14 work for each risk assessment, but I was just trying to say the starting point for
15 the discussion on weight of evidence because one of the things I've noticed in
16 the literature is someone -- sometimes they'll say, "While there were 20
17 noncancer neurological studies, only two of which had relevance to this
18 chemical, and they were of high quality." Well, that's two out of 20. That like a
19 10 percent -- it's a little bit of a kind of a measure of how extensive is the
20 literature base here. I don't know. I'm still trying to think of some of this stuff
21 working around these issues. Dr. Rowlands?

22 **DR. CRAIG ROWLANDS:** So I also really like this.
23 It's always helpful to have a summary table you can look at across all the
24 evidence in one spot if possible. I also would echo what Dr. Johnson said. Dose

1 point of departure benchmark would be very nice to see here so you can compare
2 those.

3 And then the total number of studies is important, but also
4 you need to see the total number supporting and the total number not supporting
5 the outcome because there are studies that are negative. In fact, the literature, as
6 we know, is very bias towards positive. It's hard to get a paper published that's
7 negative. So we really need to understand the body of literature in terms of
8 supporting the data, supporting the effect and dose -- or studies that don't
9 support that effect if we happen to get our hands on that are published. And that
10 was it.

11 **DR. KENNETH PORTIER:** Thank you. That's an
12 excellent concept, and I'm sorry I didn't think about that before. But that is
13 good. For the human health one, I definitely have another column of support,
14 plus or minus. Is it supportive or not supportive?

15 And that's important in the epidemiological studies,
16 especially, where we were talking about the meta-analysis and the fact that half
17 of them find the effect and the other half don't find the effect. And at least in the
18 epidemiology literature, they do publish negative results regularly, unlike like
19 you're saying. In many of the animal studies, you don't get the negative results.
20 Okay. We can remove these slides and go back to the question. Any additional
21 comments on Question 7.3? Dr. Lash, good discussion. Any final comments
22 from the lead?

23 **DR. LAWRENCE LASH:** I think we've covered a lot.
24 A couple of the suggestions I think are -- I thought it was very interesting the

1 comment that was made about the action statements and that's kind of part of the
2 process at a later stage than what this is at. But I guess even though we try to
3 keep the specific purpose of a TSCA hazard assessment -- risk assessment in
4 mind, I think you sort of naturally think about what comes next. So I suppose
5 rather than propose specific actions based on the findings that some statement
6 could be added, a broad statement about where this goes and how it would
7 progress towards actions would be helpful for readers.

8 **DR. KENNETH PORTIER:** Yeah. I think the hardest
9 part for scientists to do is to, like you said, kind of give up that discussion section
10 in the research article to someone else. And that's what we're doing here.
11 We're analyzing the methods and the results, and we're making sure the results
12 look good. But we don't have a hand in the discussion session. We have to turn
13 that back over to EPA's risk management -- risk mitigation people to really talk
14 about the implications of this work and what the next practical intervention
15 step's made to be. And it's taken me years to come to terms with that, Larry.

16 **DR. LAWRENCE LASH:** I think the introduction does
17 a reasonably good job of putting the TSCA program in focus and in context. But
18 I think because the document -- the evaluation is so long, that by the time you get
19 to the end you've forgotten those points maybe, or you don't really appreciate
20 them. Yeah. Good point.

21 **DR. KENNETH PORTIER:** Okay. I'll turn to EPA.
22 Any clarifying questions or comments on Question 7.3?

23 **DR. STANLEY BARONE:** Not at this time. I don't
24 think we have any more clarification.

1 **DR. KENNETH PORTIER:** Thank you. This brings us
2 to the end of the questions that EPA has posed before the panel and this part of
3 our discussion. We're a little bit over our allocated time, but I think I'm
4 prepared to close the public meeting at this point. I ask the panel to stay on the
5 call for a few minutes. We'll have an administrative, organizational meeting
6 where we'll discuss final disposition -- or creation of our minutes report. But at
7 this point, I turn it back over to the DFO, Tamue Gibson, for final comments.

8 **MS. TAMUE GIBSON:** Okay. Great. Thank you, Dr.
9 Portier. This is Tamue Gibson, and as DFO, I want to thank the SACC peer
10 reviewers and the public for listening online. From what I've heard, we had
11 many members of the public listening, and I want to thank you all for your
12 virtual attendance online. This week's TSCA SACC meeting is the second
13 online meeting for the SACC committee, and it is the second of our peer review
14 team in the EPA Office of Science Coordination and Policy. So let me add a
15 very special emphasis note at this point of gratitude and thank you.

16 I also want to make a special recognition of the OPPT
17 team for being online in an efficient and responsive way for providing your
18 interactions with the SACC peer reviewers. I can say that things went quite
19 smoothly in this regard. And I finally want to say that I would like to state that
20 the peer reviewers deserve our many thank yous for your work and robust
21 deliberations and contributions that will certainly lead to the recommendations
22 and advice to the Agency as to how the evaluation of Perchloroethylene can be
23 refined.

1 So this concludes the peer review activities for today, and
2 this concludes the SACC meeting for the peer review of EPA's draft risk
3 evaluation for Perchloroethylene. This day's session is now adjourned and thank
4 you all once again. Have a great day.

5 **[MEETING ADJOURNED]**