

U.S. ENVIRONMENTAL PROTECTION AGENCY (EPA)

TOXIC SUBSTANCES CONTROL ACT (TSCA)

SCIENTIFIC ADVISORY COMMITTEE on CHEMICALS

(SACC)

OPEN VIRTUAL MEETING

DRAFT RISK EVALUATION FOR Trichloroethylene

(TCE)

DOCKET NUMBER: EPA-HQ-OPPT-2019-0500

(Trichloroethylene)

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

Meeting Location: Phone and Webcast

March 24-27, 2020

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OPENING OF MEETING

DR. TODD PETERSON: Thank you. This is Todd Peterson. I am the designated federal officer for the U.S. EPA Toxic Substance Control Act, the Science Advisory Committee on Chemicals. That is the TSCA SACC. I want to thank Dr. Portier for agreeing to serve as the chair of the SACC for this meeting. I also want to thank the members of the committee, the ad hoc peer reviewers, and the public for attending this important meeting.

We appreciate the time and effort the peer reviewers have put in for this meeting. Their time and effort is vital to good deliberation, and we know that you have busy schedules. So we really appreciate your effort in this regard. In addition, I want to thank EPA's Office of Pollution prevention and Toxics and my colleagues on the TSCA SACC staff for their hard work in preparing for this important review of EPA's Draft Risk Evaluation for Trichloroethylene. As an added note, Tamue Gibson is my colleague and co-DFO, plus Steve Knott, our Executive Secretary and Senior DFO, are on the line this week and will serve as backups to my role as DFO.

1 Today through Friday, the SACC peer
2 review will focus on Trichloroethylene. And this is,
3 obviously, a virtual meeting, meaning that audio is
4 provided by telephone or over the computer and that
5 graphics are presented by the WebEx online internet
6 platform. For any reason, if the WebEx platform or
7 audio transmissions encounter any technical
8 difficulties, you will be able to find additional
9 information at our website. And it's a rather long
10 URL, but I will read through it carefully and do it by
11 words first and then maybe go back and do some
12 spelling.

13 So you would access H-T-T-P-S, colon,
14 forward slash, forward slash, W-W-W-.E-P-A-.G-O-V,
15 forward slash -- and it's -- I'll go spell this in a
16 minute, but it's TSCA, hyphen, peer, hyphen, review,
17 forward slash, peer, hyphen, review, hyphen, draft,
18 hyphen, risk, hyphen, evaluation, hyphen,
19 trichloroethylene, hyphen, T-C-E. So again, a little
20 slower, www.epa.gov/T-S-C-A, hyphen, P-E-E-R, hyphen,
21 R-E-V-I-E-W, forward slash, P-E-E-R, hyphen, R-E-V-I-
22 E-W, hyphen, D-R-A-F-T, hyphen, R-I-S-K, hyphen, E-V-
23 A-L-U-A-T-I-O-N, hyphen, T-R-I-C-H-L-O-R-O-E-T-H-Y-L-
24 E-N-E, hyphen, T-C-E.

1 Now, I will repeat this again. I
2 realize that people are logging onto the system as I
3 give my opening remarks. And it is an internet
4 platform. It's been a very busy time out there with
5 people across the nation logging on for college
6 courses or telework. So if there's any kind of
7 wrinkle in the system and we have a problem, this is
8 the go-to page to get additional information.

9 The function of the SACC committee and
10 composition, the TSCA SACC is a federal advisory
11 committee that provides independent, scientific peer
12 review and advice to the EPA on chemical related
13 issues, government issues regarding the impact of
14 proposed regulatory actions on human health and the
15 environment. Okay. The TSCA SACC only provides
16 advice and recommendations to EPA. The decisions
17 making and implementation authority remains with the
18 Agency.

19 For the present meeting, there are 12
20 ad hoc peer reviewers and 17 of the 19 established
21 SACC members that are contributing to the peer review
22 for trichloroethylene. As the DFO, designated federal
23 officer, for this meeting, I serve as the liaison
24 between the TSCA SACC and the Agency. I am also

1 responsible for ensuring provisions of the Federal
2 Advisory Committee ACT, FACA, are met. TSCA SACC
3 meetings are subject to all FACA requirements (Drop
4 out in audio).

5 **DR. KENNETH PORTIER:** Todd, you've gone
6 mute. Please check your mute button. This is Ken
7 Portier.

8 **DR. TODD PETERSON:** Oh, I don't know
9 why it went mute. Where was I? Ken?

10 **DR. KENNETH PORTIER:** You were
11 reviewing the FACA roles.

12 **DR. TODD PETERSON:** So the TSCA SACC is
13 a federal advisory committee -- was I there? Okay.

14 **DR. KENNETH PORTIER:** Yes.

15 **DR. TODD PETERSON:** All right. Sorry,
16 everyone. A little communications hiccup. The TSCA
17 SACC is a federal advisory committee that provides
18 independent, scientific peer review and advice to the
19 EPA on chemical related issues regarding impact of
20 proposed regulatory actions on human health and the
21 environment. The TSCA SACC only provides advice and
22 recommendations to EPA. The decision making and
23 implementation authority remains with the Agency.

1 For the present meeting, there are 11
2 ad hoc peer reviewers and 17 of the 19 established
3 SACC members that are contributing to the peer review
4 of trichloroethylene. As DFO, designated federal
5 officer, for this meeting, I serve as the liaison
6 between the TSCA SACC and the Agency. I'm also
7 responsible for ensuring provisions of the Federal
8 Advisory Committee Act are met. TSCA SACC meetings
9 are subject to all FACA requirements. These include
10 open meetings, timely public notice of meetings, and
11 document availability.

12 So just note that the documents for
13 this meeting are located at the public docket. You
14 access that by the internet at this URL: W-W-W. R-E-G-
15 U-L-A-T-I-O-N-S. G-O-V. That's www.regulations.gov.
16 And the docket ID to directly access these documents
17 is E-P-A, hyphen, H-Q, hyphen, O-P-P-T, hyphen, 2019-
18 0500. And that's also listed on the agenda.

19 As a designated federal official for
20 this meeting, a critical responsibility is to work
21 with appropriate Agency officials to ensure that all
22 appropriate ethics regulations are satisfied. In that
23 capacity, committee members received training on
24 provisions of the federal conflict of interest laws.

1 In addition, each participant has filed a standard
2 government financial disclosure report. Our deputy
3 ethics official for the Office of Science Coordination
4 and Policy, and in consultation with the Office of
5 General Counsel, have reviewed these reports to ensure
6 ethics requirements are met.

7 For the next four days, we will have a
8 full agenda, and meeting times are approximate. Thus,
9 we may not keep to exact times as noted due to the
10 committee discussions and public comments. We strive
11 to ensure adequate time for Agency presentations,
12 public comments, and committee deliberations. And
13 I'll just add a note that we're going to be rather
14 methodical and make sure we go a step at a time to
15 make sure we work through the agenda and don't miss
16 anything, even with this virtual format for the
17 meeting. We may take a little extra time at various
18 points in the meeting to help with coordination and
19 thus work step by step through the agenda.

20 An added note for SACC peer reviewers,
21 remember to bring your discussion to the virtual
22 conference table so that whatever is verbalized during
23 the meeting can go into the meeting minutes and final
24 report. And if you have a temptation to use the chat

1 for a sidebar discussion, whatever you talk about
2 through email or chat, make sure that you bring those
3 points to the entire committee's attention at the
4 virtual conference table. For presenters, committee
5 members, and public commenters, please identify
6 yourselves when you're asked to speak or initiating
7 speaking and do that directly into the telephone.

8 This meeting is being webcasted and
9 transcribed and recorded. And, if at all possible,
10 please refrain from using speakerphones. One added
11 note, we highly recommend the use of a landline for
12 those who are speaking as a committee member, oral
13 commenter, or Agency spokesperson. Copies of all EPA
14 presentation materials and written public comments
15 will be available in the docket. And I just gave you
16 the regulations.gov address for that. Copies of
17 presentation materials submitted this week by public
18 commenters will be available in the public docket
19 within the next week.

20 Members of the committee are encouraged
21 to fully consider all written or oral public comments
22 submitted for this meeting. For members of the public
23 that have not pre-registered for oral comments, you
24 may still notify us with your desire to make a public

1 comment. And the agenda's rather full, but, however,
2 if we can move through the proceedings and time
3 allows, we may be able to add additional comments.
4 Again, these are for five minutes or less. As
5 mentioned previously, there is a public docket for
6 this meeting. Background materials, questions posed
7 to the committee by the Agency, and other supplemental
8 documents, related meeting agenda and materials are
9 all there.

10 For members of the press, EPA media
11 relations staff are available to answer your questions
12 that directly relate to this meeting. We have a new
13 contact. I'm going to spell the individual's name.
14 Ken Labbe, it's K-E-N. Last name is L-A-B-B-E. He
15 can be reached at email, which is [L-A-B-B-E.K-E-N@E-P-](mailto:L-A-B-B-E.K-E-N@E-P-A.G-O-V)
16 [A.G-O-V](mailto:L-A-B-B-E.K-E-N@E-P-A.G-O-V). And his phone number is 202-740-3770.
17 Again, that's 202-740-3770.

18 At the conclusion of the meeting, the
19 TSCA SACC will prepare a report as a response to
20 questions posed by the Agency, background materials,
21 presentation, and public comments. This final report
22 also serves as the meeting minutes. We anticipate
23 final report and meeting minutes will be completed in
24 approximately 60 days after this meeting.

1 Again, I started with -- I'm going to
2 repeat myself. I know people are still dialing on.
3 This is a virtual meeting, meaning that audio is
4 provided by telephone or over computer. And the
5 graphics are presented by WebEx online internet
6 platform. If for any reason the WebEx platform or
7 audio transmission encounters any technical
8 difficulties, you will be able to find additional
9 information to refer to at our website. And it's a
10 very long URL. And I'm just going to speak it by
11 words. Again, <https://www.epa.gov/> -- and it's TSCA-
12 peer-review/peer-review-draft-risk-evaluation-
13 trichloroethylene-tce.

14 Again, in closing my remarks for now --
15 again, I wish to thank the committee for your
16 participation. And I now turn the meeting over to our
17 chair, Dr. Portier.

18
19 **INTRODUCTION AND IDENTIFICATION OF PANEL MEMBERS**

20
21 **DR. KENNETH PORTIER:** Hello to the
22 panel, the committee, and good morning to the
23 committee and good morning to the public out there.
24 As Todd mentioned, we have 17 of 19 TCE SACC committee

1 members here and a number of ad hocs. And at this
2 point, we're going to go in -- we're going to proceed
3 to introduce all of the members of the committee,
4 starting with Dr. Anderson. Would you please unmute
5 and tell everyone who you are? Dr. Anderson, you're
6 not unmuted. I think we may have lost him. Let's go
7 on to Dr. Bennett.

8 **UNIDENTIFIED MALE:** Yeah. I was going
9 to say it's a little confusing. You have to unmute on
10 the screen and on your phone.

11 **DR. KENNETH PORTIER:** Let's move on to
12 Dr. Bennett. I don't see Dr. Anderson on the panelist
13 list. He may have dropped off. Dr. Bennett?

14 **DR. STEVEN BENNETT:** Good morning. I'm
15 Steve Bennett. Hopefully you can hear me.

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

17 **DR. STEVEN BENNETT:** Okay. Good. I
18 wanted to get that confirmation after Dr. Anderson.
19 I'm with the Household and Commercial Products
20 Association. I'm a chemist by training, and I will
21 bring expertise on consumer use and exposure to the
22 discussion.

23 **DR. KENNETH PORTIER:** Thank you. Dr.
24 Barton?

1 **DR. CHARLES BARTON:** Hello. My name is
2 Chuck Barton. I'm an independent consultant in
3 toxicology. And my expertise is in toxicology and
4 risk assessment. Thank you.

5 **DR. KENNETH PORTIER:** Thank you. Dr.
6 Blystone?

7 **DR. SHERI BLYSTONE:** Good morning.
8 Sheri Blystone. I am a chemist by training, as well,
9 working as a product safety and compliance
10 professional in the chemical industry, currently with
11 SNF Holding Company.

12 **DR. KENNETH PORTIER:** Dr. Bruckner? I
13 see Dr. Bruckner is on the presentation, but his phone
14 icon's not there. So he may not be fully dialed in at
15 this point. Dr. Cory-Slechta?

16 **DR. DEBORAH CORY-SLECHTA:** I'm Deborah
17 Cory-Slechta from the University of Rochester Medical
18 Center. My areas of expertise, in particular, are
19 neurotoxicology, both developmental neurotoxicology
20 and neurodegenerative disease.

21 **DR. KENNETH PORTIER:** Dr. Davies?

22 **DR. HOLLY DAVIES:** Good morning. This
23 is Holly Davies. I'm a toxicologist at the Washington

1 State Department of Health. And my background is in
2 developmental genetics.

3 **DR. KENNETH PORTIER:** Thank you. Dr.
4 Doucette?

5 **DR. WILLIAM DOUCETTE:** Yeah. Good
6 morning. This is Bill Doucette. I'm an environmental
7 fate chemist and professor at Utah State University.

8 **DR. KENNETH PORTIER:** Dr. Jimenez-
9 Gonzalez?

10 **DR. CONCEPCION JIMENEZ-GONZALEZ:**
11 Hello. Good morning. I am Conception Jimenez-
12 Gonzalez. I am an adjunct professor at North Carolina
13 State University. I lead environmental health,
14 safety, and sustainability support for R&D in
15 GlaxoSmith Kline. I am a chemical engineer by
16 training. And my specialty is environmental
17 engineering and risk assessment.

18 **DR. KENNETH PORTIER:** Thank you. Dr.
19 Gilbert?

20 **DR. KATHLEEN GILBERT:** Good morning.
21 This is Kate Gilbert. I'm a retired med school
22 professor, and my expertise is immunotoxicology.

23 **DR. KENNETH PORTIER:** Dr. Johnson?

1 **DR. MARK JOHNSON:** Good morning. It's
2 Mark Johnson. I'm Director for Toxicology at the
3 Army's Public Health Center. And my background's
4 environmental tox and risk assessment.

5 **DR. KENNETH PORTIER:** Thank you. Dr.
6 Kaufman?

7 **MR. ALAN KAUFMAN:** Hi. Can you hear
8 me?

9 **DR. KENNETH PORTIER:** Yes.

10 **MR. ALAN KAUFMAN:** Hello? Okay. Hi,
11 this is Al Kaufman. I'm currently Senior Vice
12 President Technical Affairs for the Toy Association.
13 Biologist and organic chemist by training, and my
14 expertise is in downstream uses of chemicals and
15 exposure -- consumer exposure, particularly with
16 regard to children. Thank you.

17 **DR. KENNETH PORTIER:** Thank you. Dr.
18 Kissel?

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

24 **DR. KENNETH PORTIER:** Dr. Rowlands?

1 **DR. CRAIG ROWLANDS:** Good morning. I'm
2 Craig Rowlands. I'm a toxicologist with Underwriters
3 Laboratories corporate research and development. And
4 my background is in mammalian toxicology and risk
5 assessment.

6 **DR. KENNETH PORTIER:** Dr. Schlenk?

7 **DR. DANIEL SCHLENK:** Hello. This is
8 Dan Schlenk. I'm a professor of aquatic ecotoxicology
9 in the Department of Environmental Sciences at the
10 University of California, Riverside.

11 **DR. KENNETH PORTIER:** Let's go back to
12 Dr. Anderson. I still see you muted Dr. Anderson.
13 And Dr. Bruckner's not signed in. That's the regular
14 committee, and now for the ad hocs. Dr. Apte?

15 **DR. UDAYAN APTE:** Hello. Can you hear
16 me?

17 **DR. KENNETH PORTIER:** Yes.

18 **DR. UDAYAN APTE:** Hi, my name is Udayan
19 Apte. I'm Associate Professor of Toxicology at
20 University of Kansas Medical Center. I'm a
21 toxicologist by training, and my research is focused
22 mainly on liver cancer, liver toxicity, liver
23 hypertrophy.

24 **DR. KENNETH PORTIER:** Dr. Cobb?

1 **DR. GEORGE COBB:** Hi. This is George
2 Cobb. I am a professor of environmental science at
3 Baylor University in the Department of Environmental
4 Science. And my training is in environmental and
5 analytical chemistry.

6 **DR. KENNETH PORTIER:** Thank you. Dr.
7 Hossain?

8 **DR. MUHAMMAD HOSSAIN:** Hi, I'm Muhammad
9 Hossain from Florida International University. My
10 training is in veterinarian and neurotoxicologic, and
11 I have advanced training in molecular neuroscience. I
12 have been working in the field of neurotoxicology and
13 investigating effects of environmental chemical.

14 **DR. KENNETH PORTIER:** Dr. Hossain, your
15 connection is pretty weak, and you break up. You may
16 want to consider switching to a landline or cellphone.
17 Dr. Jenkins?

18 **MS. ALLISON JENKINS:** Good morning.
19 This is Allison Jenkins. I'm a toxicologist and risk
20 assessor at the Texas Commission on Environmental
21 Quality.

22 **DR. KENNETH PORTIER:** Dr. Lash?

23 **DR. LAWRENCE LASH:** Hi, this is Larry
24 Lash. I'm a professor and associate chair in

1 pharmacology at Wayne State University in Detroit.

2 And I've worked on and off on trichloroethylene for
3 about 35 years or so, mostly focusing on metabolism
4 and mechanisms of renal toxicity, primarily the
5 glutathione dependent toxic mechanisms.

6 **DR. KENNETH PORTIER:** Thank you. Dr.
7 Morandi?

8 **DR. MARIA MORANDI:** Hi. My name is
9 Maria Morandi, and I am retired from the University of
10 Texas and the University of Montana. And my areas of
11 interest and expertise are exposure assessment and
12 industrial hygiene.

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

14 **DR. JOHN MORRIS:** Hi, this is John
15 Morris. I'm an emeritus professor at the University
16 of Connecticut. And my expertise is inhalation
17 toxicology and PBPK modelling.

18 **DR. KENNETH PORTIER:** Dr. Pessah?

19 **DR. ISAAC PESSAH:** Hi. Good morning.
20 Isaac Pessah, University of California, Davis. My
21 focus is as a research toxicology -- neurotoxicologist
22 in molecular and cellular mechanisms.

23 **DR. KENNETH PORTIER:** Dr. Rosol?

1 **DR. THOMAS ROSOL:** Hi, this is Tom
2 Rosol. I'm a veterinary and toxicologist pathologist.
3 And I am the professor and chair of biomedical
4 sciences at the Heritage College of Osteopathic
5 Medicine in Ohio.

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

7 **DR. CHARLES VORHEES:** Hi, I'm a
8 professor of pediatric neurology at the University of
9 Cincinnati and Cincinnati Children's Hospital. And my
10 areas are neuroscience and neurotoxicology.

11 **DR. KENNETH PORTIER:** Dr. Zu?

12 **DR. TODD PETERSON:** Hi, Dr. Portier.
13 For various reasons, Dr. Zu is not going to be on the
14 line this week.

15 **DR. KENNETH PORTIER:** Oh, okay.

16 **DR. TODD PETERSON:** Yeah. Sorry about
17 that. I need to make a couple corrections. This is
18 Todd Peterson. Okay. I think we've gone the full
19 list.

20 **DR. KENNETH PORTIER:** I need to go back
21 to Dr. Anderson to see if we can get him on.

22 **DR. SHARLENE MATTEN:** Dr. Portier, when
23 you're ready, Alex Dunn, our assistant administrator
24 is waiting for you to call upon her. Thanks.

1 **DR. KENNETH PORTIER:** Yup. I just
2 wanted to check to see if Dr. Bruckner was able to get
3 on. I see you Dr. Bruckner. You're just -- there we
4 go, unmuted. James? We're still having some
5 technical difficulties because I see he's unmuted, but
6 I don't hear him and the same thing with Dr. Anderson.
7 They're here but not connected.

8 So at this point, we're going to move
9 on with the agenda. This morning's focus is on
10 viewing and discussing the TCE draft risk assessment.
11 But first, we have a couple of comments from EPA
12 administrators. And I think at this point Mark
13 Hartman -- Mr. Hartman with EPA, you have a few
14 comments, followed by Administrator Alex Dunn --
15 Assistant Administrator Alex Dunn. Mr. Hartman?

16
17 **INTRODUCTION AND WELCOME**

18
19 **MR. MARK HARTMAN:** Thanks, Dr. Portier.
20 This is Mark Hartman. I'm a deputy director with the
21 Office of Pollution Prevention and Toxics. Good
22 morning. First, I'd like to thank the members of the
23 committee and all of our interested stakeholders who
24 are taking the time to participate in this important

1 meeting, especially considering this being such a
2 challenging time. The peer review process is a
3 critical step in the TSCA chemical risk evaluation
4 process, and EPA looks forward to the proceedings this
5 week on TCE.

6 I also want to express deep gratitude
7 to the TCE team in the Office of Pollution Prevention
8 and Toxics for their work and dedication to mission in
9 crafting the draft risk evaluation. It is a
10 significant accomplishment that reflects a great deal
11 of effort and thought. Drs. Keith Jacobs and Heidi
12 Bethel will be representing the team during our
13 presentations this morning. Now, I'd like to take the
14 opportunity to introduce to you Alex Dunn, the
15 assistant administrator for the Office of Chemical
16 Safety and Pollution Prevention, who will provide
17 introductory remarks.

18
19 **WELCOME AND INTRODUCTORY COMMENTS**

20
21 **MS. ALEXANDRA DUNN:** Thank you, Mark.
22 I hope you can all hear me.

23 **DR. KENNETH PORTIER:** Yes.

1 **MS. ALEXANDRA DUNN:** All right. Dr.
2 Portier, thank you so much for chairing this meeting
3 and thank you to all members of the panel for moving
4 with us in a direction that I don't think any of us
5 could have expected this morning. Due to the COVID-
6 19, we did move the meeting to a virtual only format.
7 Many of you were not able to travel. And, of course,
8 there are requirements for all of us to slow the
9 spread of the virus and to increase our social
10 distancing.

11 I can tell you that this is not
12 something that comes to us easily. There's a great
13 value of being face to face, but I think in these
14 extraordinary times we are demonstrating that we can
15 be nimble and that we can be effective. We know that
16 there's significant public interest in the review of
17 TCE. And for that reason, we accommodated the
18 schedule to include additional public comment time,
19 longer than the typical time that we have included in
20 past meetings.

21 And I think you also know -- thank you
22 to our West Coast members. I know it's only 7:00
23 something out there, but we did move to a later start
24 and shorter days for the benefit of all of our health.

1 Get up, walk around while you're listening. I've been
2 challenging myself to get my steps in while I'm
3 working from home. It is definitely a challenge, but
4 we want you all to stay healthy and engaged. And we
5 thank you for your flexibility. Perhaps when this is
6 all over, we will look back and realize we have
7 technology to help us in new ways that we hadn't
8 thought of before. But I know that we will all agree
9 that nothing replaces a face to face meeting and the
10 relationships that can be built that way, although our
11 teenagers might challenge us otherwise.

12 I want to tell you thank you so much
13 for the incredible amount of time that you put into
14 the previous seven draft risk evaluations. Today is a
15 really important moment. We are moving into the
16 eighth of the first ten reviews, and it's really
17 something to be proud off in terms of the amount of
18 work and the commitment that you have all made to this
19 effort. Your efforts are making a real and lasting
20 difference. We are listening to you. Your reports
21 and recommendations are the invaluable scientific
22 building blocks that are forming the foundation of our
23 risk evaluations going forward.

1 And when we complete our tenth review,
2 we will be working with you to look at ways to
3 streamline and focus how to use the SACC expertise in
4 a more effective way and how to accomplish the
5 committed peer review and public transparency of 22
6 more chemicals as we go forward. But I do want to say
7 we, again, are listening to you.

8 As an example of that, about a month
9 ago we issued the first ever TSCA Section IV test
10 order on PV29 to the two manufacturers. We asked them
11 to develop some solubility data and also inhalation
12 data. That was a direct result of us reviewing your
13 report and listening to you as you met and using a new
14 authority under TSCA. So do not think that you are
15 not making a difference in our work. You really are.

16 We ask you to do your best to provide
17 your feedback to us on TCE. And then we will proceed
18 with the final two chemicals, perchloroethylene and
19 asbestos. And we are committed to completing the
20 public review of these documents this spring. We want
21 to reflect, as I noted, on the future of the SACC. We
22 just -- if it hasn't published already, it will
23 publish very soon -- a call for new members of the
24 SACC. Some of your terms are expiring. And some of

1 you have run your race with us, or will have by the
2 time you finish ten, of ten chemicals.

3 But we do hope that we can rely on you
4 to encourage other professionals that you know to
5 raise their hand for this incredible public service to
6 the nation and to our nation's chemical evaluation
7 program. We are looking forward to keeping the SACC
8 robust and full of tremendous experts as we have with
9 us today. And it is not in my talking points, but I
10 don't think there's anything that prevents you all
11 from a second tour with us. But I'll let our experts
12 from our federal advisory committee give you the final
13 answer on whether you can come back for a second tour
14 of duty. We certainly would welcome any of you, if
15 it's possible. And we just want to thank you for
16 making peer review real and robust, transparent, and
17 thoughtful.

18 So I want to commend all of you and
19 also the EPA staff. As Mr. Hartman noted, they have
20 worked very, very hard to adapt to a new presentation
21 style. They're very proud of their work. They are
22 ready to walk you through it and to answer your
23 questions. And we look forward to robust dialogue as
24 we go forward. Dr. Portier, I'm going to return the

1 floor to you. But again, please accept our most
2 sincere thanks for your time during this challenging
3 moment for the country. And we appreciate it. Thank
4 you, Dr. Portier.

5 **DR. KENNETH PORTIER:** Thank you,
6 Administrator Dunn. At this point, we're going to
7 move on with the EPA presentation. But before, I want
8 to introduce Dr. Stephen Grant who I left off my call
9 list, who's an ad hoc member on the committee. Dr.
10 Grant, would you please introduce yourself?

11 **DR. STEPHEN GRANT:** This is Stephen
12 Grant. I'm a professor of public health at Nova
13 Southeastern University in Fort Lauderdale. I was
14 trained as a geneticist. Most of my research has been
15 based on human biodosimetry and biomonitoring.

16 **DR. KENNETH PORTIER:** Thank you. And
17 again, I'm sorry I left you off the list. At this
18 point, I'm going to turn the mic over to Dr. Keith
19 Jacobs with EPA/OPPT who is going to lead the
20 technical presentation on the draft risk evaluation.
21 For viewers, you should now see a slide set in WebEx
22 that accompanies this presentation. Dr. Jacobs?

23 **DR. KEITH JACOBS:** Can everyone hear me
24 clearly?

1 DR. KENNETH PORTIER: Yes, we can hear
2 you.

3
4 OPPT TECHNICAL PRESENTATION - OVERVIEW OF RISK
5 EVALUATION
6

7 DR. KEITH JACOBS: Okay. Thank you.
8 Good morning to the Scientific Advisory Committee on
9 Chemicals, public commenters, and stakeholders. My
10 name is Keith Jacobs, and I am the primary team lead
11 for the TCE team. Rehan Choudhary and Heidi Bethel
12 are co-team leads for this assessment. Our management
13 lead is Nhan Nguyen. We are fortunate to be part of a
14 very dedicated and talented team, whose names are
15 listed (audio drops out.)

16 DR. TODD PETERSON: Did we lose Keith?

17 DR. KEITH JACOBS: Sorry. The WebEx
18 system seems to like auto-muting people. I will start
19 again with this slide.

20 DR. KENNETH PORTIER: Yeah. We can
21 hear you now. Thank you.

22 DR. KEITH JACOBS: Slide two is an
23 overview of the presentation. We will begin with
24 general background and history on TCE, followed by an

1 overview of its physical-chemical properties, and the
2 scope of the evaluation. We will then move into an
3 overview of the technical assessment, beginning with
4 environmental fate and transport and moving into the
5 environmental risk assessment and, finally, the human
6 health risk assessment. The TCE risk evaluation had a
7 deeper focus on the human health assessment. However,
8 the presentation first covers the environmental
9 assessment, in accordance with the layout of the
10 document and the charge questions.

11 This is Slide 3. EPA first published a
12 risk assessment in 2014 for a subset of uses with high
13 potential for exposure and identified both cancer and
14 noncancer risks. Following enactment of amended TSCA
15 in June 2016, EPA decided to evaluate a broader range
16 of conditions of use, including a reanalysis of the
17 original uses. The 2020 draft risk evaluation
18 includes application of the TSCA systematic review
19 process and updated information, assessment of all
20 identified conditions of use, evaluation of risk to
21 environmental receptors, and evaluation of
22 occupational and consumer risks from both inhalation
23 and dermal exposure.

1 In the 2018 problem formulation, EPA
2 identified potential exposure pathways for the general
3 population. However, these are covered under other
4 environmental statutes, and exposures are managed
5 accordingly. Therefore, EPA did not evaluate hazards
6 or exposure to the general population in this risk
7 assessment.

8 Slide 4 summarizes the physical-
9 chemical properties of TCE. The general structure of
10 the chemical is presented on the left, and the few
11 basic physical-chemical properties are provided on the
12 right. TCE is a liquid at room temperature with a
13 boiling point of about 39.7 degrees Celsius and a high
14 vapor pressure. The vapor pressure provides an
15 indication of the relative tendency of the substance
16 to volatilize, which in turn indicates a concern for
17 potential inhalation exposure pathways.

18 The diagram here in Slide 5 depicts
19 each stage of the TCE lifecycle and associated
20 conditions of use as reported in the 2016 chemical
21 data reporting, or CDR. Almost 172 million pounds of
22 TCE were manufactured or imported into the U.S. in
23 2015, with 83.6 percent used as an intermediate in
24 refrigerant manufacturing and the rest used as a

1 degreasing solvent, as well as other applications. We
2 are now on Slide 6. This slide presents examples of
3 some occupational conditions of use, or COUs, and
4 corresponding occupational exposure scenarios, or OES.
5 EPA grouped similar conditions of use into single OES
6 and assessed releases and exposures based on data for
7 the applicable OES.

8 Slide 7, this slide shows examples of
9 consumer COUs. The consumer exposure assessment
10 recategorized COUs compared to the problem formulation
11 in order to improve clarity. Additionally, several
12 COUs were split into additional subcategories based on
13 different forms of a product, e.g. aerosol versus
14 liquid. We are on Slide 8. The TCE risk evaluation
15 assessed various different receptors and populations.
16 For ecological receptors, EPA performed a quantitative
17 assessment for aquatic species. For human health, EPA
18 performed distinct assessments for occupational and
19 consumer exposure scenarios.

20 Occupational populations include
21 workers and occupational nonusers, or ONUs. And among
22 these receptor categories, EPA also provided estimates
23 for the PESS group, women of reproductive age.
24 Workers are employees who directly handle TCE. And

1 ONUs do not directly handle TCE but perform work in an
2 area where TCE is present. EPA assessed both
3 inhalation and dermal exposure to workers and
4 inhalation exposure to ONUs.

5 The consumer assessment covered both
6 users and bystanders and included consideration of
7 different life stages, including children. Consumer
8 users are direct users of a TCE containing product,
9 while bystanders are incidentally exposed within the
10 same residence where TCE is being used. Inhalation
11 and dermal exposure was assessed for users, and only
12 inhalation exposure was assessed for bystanders.

13 Beginning here on Slide 9 we now
14 introduce the environmental fate and transport aspect
15 of the risk evaluation. This information is describe
16 in Section 2.1 of the draft risk evaluation and is
17 related to Charge Question 1. Slide 10 describes the
18 fate and transport approach for the draft risk
19 evaluation. EPA evaluated and extracted fate and
20 transport data from 52 studies. Some characteristics
21 were estimated with EPI Suite, a set of predictive
22 models for physical-chemical and fate and transport
23 characteristics. EPI Suite was reviewed by EPA's

1 Science Advisory Board in 2007, and individual models
2 have been peer-reviewed in numerous articles.

3 Slide 11 provides a summary of various
4 environmental fate and transport properties of TCE.
5 These properties provide an indication of the
6 partition of TCE in environmental media. For
7 instance, the Henry's Law Constant, which is the ratio
8 of vapor pressure to water solubility, indicates that
9 TCE likely partitions to air at the air-water
10 interface of an environmental system. In direct
11 photolysis is between one and 11 days, so long-range
12 transport is possible. TCE's soil and sediment
13 organic carbon partition coefficient, or KOC,
14 indicates that partitioning to soil and sediment will
15 be low. TCE is not bioaccumulative based on its
16 estimated bioconcentration factor and data from
17 bioaccumulation studies. TCE's estimated soil and
18 sediment KOC indicates that partitioning to soil and
19 sediment will be low.

20 Now on Slide 12, TCE is expected to be
21 present in the aqueous fraction in pore water of
22 biosolids or sediments. Based on low equilibrium
23 partitioning in soil and sediments, e.g. log KOC, and
24 potentially rapid anaerobic biodegradation,

1 concentrations in sediments are expected to be lower
2 than those in overlying surface water. Concentrations
3 of TCE and biosolids are expected to be similar to or
4 less than concentrations in wastewater treatment plant
5 effluents. If release to land via biosolids, TCE is
6 expected to volatilize to air or migrate to ground
7 water based on low log KOC, high water solubility,
8 high vapor pressure, and high Henry's Law Constant.

9 We're now on Slide 13. Based on
10 physical-chemical properties and environmental fate
11 characteristics, overall, TCE has low bioaccumulation
12 potential. TCE is not likely to absorb to biosolid,
13 sediments, and soil. TCE is expected to rapidly
14 volatilize from surface water and soil. And TCE may
15 undergo slow aerobic biodegradation or fast anaerobic
16 biodegradation in soil, sediment, and water.

17 I would now like to describe the
18 environmental risk assessment, starting with the
19 releases and exposures. This information is described
20 in Section 2.2 and Appendix E of the draft risk
21 evaluation and relates to Charge Question 2. I am now
22 on Slide 14, moving on to Slide 15.

23 The manufacturing, processing, use, and
24 disposal of TCE can result in releases to the

1 environment. As previously discussed, EPA categorized
2 the conditions of use into occupational exposure
3 scenarios. For each occupational exposure scenario, a
4 daily water release was estimated based on annual
5 releases, release days, and the number of facilities.
6 EPA used the 2016 Toxic Release Inventory, or TRI, and
7 2016 Discharge Monitoring Report, or DMR, data to
8 provide a basis for estimating releases. Where
9 releases are expected by TRI and DMR data were not
10 available, releases were estimated using data from
11 other sources, such as, but not limited to,
12 literature, relevant emissions scenario documents, or
13 ESDs, generic scenarios, or GS, and relevant effluent
14 limitation guidelines, ELG.

15 Slide 16, to characterize environmental
16 exposure to aquatic species, EPA conducted modelling
17 and considered environmental monitoring data. EPA
18 modeled near facility concentrations of TCE in surface
19 water using EPA's EFAST model, with releases based on
20 the occupational exposure environmental release
21 assessment. A wastewater treatment removal rate of 81
22 percent was applied in modelling when appropriate to
23 release volumes characterized as offsite transfers or
24 indirect releases, while no wastewater removal was

1 applied for direct discharge volumes, which were based
2 on post-treatment release estimates. Direct
3 discharges were modeled, assuming 20 days of release,
4 as well as a higher frequency of release scenario
5 informed by the occupational exposure scenarios.

6 Indirect discharges were only modeled
7 with the higher number of release days. Site specific
8 receiving waterbody stream flows were used where
9 possible. Otherwise, sector specific average stream
10 flows were applied. Modeled surface water
11 concentrations reflecting low-flow conditions were
12 compared with ecological concentrations of concern for
13 the purposes of risk characterization. EPA also
14 examined surface water concentrations from monitoring
15 data obtained through systematic review. These data
16 were sourced from the water quality portal, as well as
17 from literature.

18 Beginning now at Slide 17, I will
19 describe the hazards and risk characterization
20 associated with the environmental assessment of TCE.
21 This is discussed in Section 3.1 and Appendix H of the
22 draft risk evaluation and relates to Charge Question
23 3. This diagram on Slide 18 presents the
24 environmental exposure pathways and receptors

1 quantitatively assessed in this risk evaluation.
2 Available TRI and DMR release information indicated
3 that aquatic releases are expected for TCE. As a
4 result, EPA carried out a quantitative assessment
5 comparing available environmental hazard data for
6 aquatic species and estimated aquatic exposure
7 concentrations. EPA determined that no further
8 quantitative analysis was necessary for exposure
9 pathways to terrestrial and sediment dwelling aquatic
10 species based on a qualitative consideration of the
11 physical-chemical and environmental fate
12 characteristics, as well as the conditions of use for
13 TCE, which indicate limited presence in terrestrial
14 environments and aquatic sediments.

15 Here on Slide 19 is an overview of the
16 environmental hazard data available for TCE's
17 environmental risk assessment. During the systematic
18 review process, 25 acceptable environmental hazard
19 studies were identified on fish, amphibians, aquatic
20 invertebrates, and algae. Algae were assessed
21 separately from other aquatic organisms because
22 durations normally considered acute for other species,
23 for example, 96 hours, can encompass several
24 generations of algae.

1 Of the acute hazard data, aquatic
2 invertebrates are the most sensitive aquatic species.
3 And for chronic hazard data, fish are the most
4 sensitive. For algae, there was a wide range of
5 toxicity values not easily characterized by a single
6 toxicity value from a single species. Therefore, EPA
7 took two approaches for integrating the algae data.
8 EPA calculated a geometric mean of a no effect
9 concentration, or NOEC, and a lowest effect
10 concentration, or LOEC, for one of the most sensitive
11 species of algae in the data. EPA also used a species
12 sensitivity distribution to calculate a hazardous
13 value for five percent of algae species or an HC05
14 using EC50s from nine algae species available in the
15 data.

16 Here on Slide 20 I will outline the
17 approach EPA used to calculate the environmental
18 hazard to aquatic species. EPA calculated hazard
19 thresholds known as concentrations of concern, or
20 COCs. After weighing the scientific evidence and
21 selecting the appropriate toxicity values from the
22 integrated data, EPA applied an assessment factor, or
23 AF, according to EPA methods to calculate acute,
24 chronic, and algae COCs. The application of AFs

1 provides a lower bound effect level and accounts for
2 differences in intraspecies variability.

3 For fish and aquatic invertebrates, the
4 acute endpoint values are divided by an AF of five.
5 For chronic and fish -- sorry, for chronic and algae
6 COCs, an AF of ten is used. EPA calculated an acute
7 COC, a chronic COC, and two algae COCs, one based on
8 the geometric mean of the NOEC and LOEC and the other
9 based on the HC05.

10 This section discusses the
11 environmental risk characterization for TCE, discussed
12 in Section 4.1 of the document and related to Charge
13 Question 6. We are on Slide 21, moving to Slide 22.
14 Environmental risks were estimated by calculating a
15 risk quotient, or RQ, which is the estimated
16 environmental concentration divided by the effect
17 level thresholds for the taxa of interest. An RQ
18 equal to one indicates that the exposures are the same
19 as the concentration that causes effects.

20 If the RQ exceeds one, the exposure is
21 greater than the effect concentration, and there is
22 potential for risk presumed. If the RQ did not exceed
23 one, the exposure is less than the effect
24 concentration, and there is no risk presumed. To

1 estimate risk to aquatic organisms near facilities,
2 EPA calculated RQs by dividing the surface water
3 concentrations estimated using EFAST by the
4 appropriate COC.

5 Slide 23, for risk estimate near
6 facilities releasing TCE based on available data for
7 aquatic species, one of 64 open-top vapor degreasing
8 facilities had an RQ greater than one and also had a
9 chronic RQ greater than one with surface water
10 concentrations exceeding a chronic COC for 20 days or
11 more. For facilities that process TCE as a reactant,
12 no facilities had acute RQs greater than one, but one
13 of 443 facilities had a chronic RQ greater than one
14 with surface water concentrations exceeding the
15 chronic fish COCs for 20 days or more. For algae, 15
16 facilities had an algae RQ greater than one and 20
17 days or more of exceedances using the COC of three
18 PPB. However, no facilities had an RQ greater than
19 one using HC05 of 52,000 PPB, indicating that as a
20 taxonomic group 95 percent of algae species are
21 protected.

22 Slide 24, to estimate risk to aquatic
23 organisms in ambient water, EPA also calculated RQs by
24 dividing monitored data from water quality parvo and

1 from the published literature by the COC. Acute and
2 chronic RQs range from zero to 0.02. Because the RQs
3 are less than one, risk to aquatic organisms, like
4 fish and aquatic invertebrates, were not identified in
5 ambient water. Therefore, the risks identified for
6 the two facilities mentioned in the previous slide are
7 likely localized to surface water near the facility.
8 Algae risk was identified in ambient water for the
9 most sensitive species but not for the taxonomic group
10 as a whole, with RQs as high as 5.77 using the COC of
11 three PPB and RQs of zero using the COC of 52,000 PPB
12 based on the HC05.

13 Now on Slide 25, qualitative
14 consideration of the COUs, physical-chemical
15 properties and environmental fate properties of TCE
16 indicate that risks are not expected for sediment
17 dwelling or terrestrial organisms. Based on its
18 volatility, water solubility, and log KOW, TCE will
19 largely be present in terrestrial environmental
20 compartments as a vapor and will not absorb to
21 sediment in aquatic environments. TCE is expected to
22 be in the sediment pore water rather than absorbed to
23 the organic matter. Concentrations of TCE are

1 expected to be lower in pore water than concentrations
2 in the water column.

3 EPA did not include the emission
4 pathways to ambient air from commercial and industrial
5 stationary sources or associated inhalation exposure
6 of terrestrial species because stationary source
7 releases of TCE to ambient air are adequately assessed
8 and any risks effectively managed under the
9 jurisdiction of the Clean Air Act. Additionally, TCE
10 is not expected to bioaccumulate. And the high
11 volatility from water means that exposure to
12 terrestrial species through oral routes is negligible.
13 As a result, no quantitative analysis of risk to
14 terrestrial receptors or sediment dwelling aquatic
15 invertebrates was carried out as part of this
16 evaluation as risks from these exposure pathways are
17 not expected.

18 The next slide, Slide 26, outlines
19 several of the uncertainties discussed in the document
20 that relate to the environmental risk conclusions.
21 For the hazard data used, the algae data encompassed a
22 wide range of toxicity values not easily characterized
23 by a single toxicity value from a single study.
24 Therefore, as previously mentioned, EPA calculated two

1 COCs for algae, one based on geometric mean of a NOEC
2 and LOEC from one species and the other based on HC05
3 from nine different species of algae.

4 For the exposure data used, the
5 environmental exposure data could be over- or
6 underestimating exposure to aquatic organisms. For
7 example, E-FAST results used to estimate surface water
8 concentrations near facilities used TRI and DMR data
9 as inputs. Neither dataset includes every industrial
10 release in the country, so some releases to surface
11 water may not be captures. On the other hand, TCE is
12 a volatile chemical, and E-FAST does not account for
13 volatilization. The monitor data used to estimate
14 ambient water concentrations is limited temporarily
15 and geographically, and measured samples are
16 predominantly not in watersheds of known TCE releases.

17 We are on Slide 27. To summarize,
18 quantitative assessments of reasonably available
19 environmental hazard data indicate that EPA found risk
20 to aquatic organisms like fish and aquatic
21 invertebrates in the environment near two facilities
22 that release TCE to surface water. One out of 64
23 open-top paper degreasing facilities had risk, and one
24 out of 443 facilities that process TCE as a reactant

1 had risks. No risks to these aquatic organisms were
2 identified in ambient water. Therefore, the risks
3 identified for the two facilities are likely localized
4 to surface water near the facility.

5 Slide 28, I will now transition into a
6 discussion of human health, including the exposures,
7 hazards, and risk characterization. I will begin the
8 discussion of human health with occupational exposure.
9 This information can be found in Section 2.4.1 and
10 relates to Charge Questions 4.1 through 4.6. Slide
11 29, EPA had several objectives in developing the
12 occupational inhalation and dermal exposure
13 assessment. Those objectives included evaluating and
14 grouping similar worker activities and occupational
15 exposures, determining the distinction between workers
16 and occupational nonusers, and ultimately providing
17 the inhalation and dermal estimates for workers and
18 occupational nonusers where possible.

19 Slide 30 describes the assessment of
20 inhalation exposure. As part of the assessment, EPA
21 provides a central tendency and the high-end exposure
22 values based on reasonably available data. For each
23 OES, EPA also calculated the average daily
24 concentration, or ADC, and the lifetime average daily

1 concentration, LADC. Slide 31, to assess inhalation
2 exposure for workers and occupational nonusers, EPA
3 used both monitoring data and modeling approaches.
4 Where monitoring data are available, EPA used personal
5 breathing zone data for eight-hour and 12-hour TWA
6 exposures, directly applicable scenarios. Two sources
7 of monitoring data came from NIOSH, OSHA, open
8 literature and submitted public comments. All of the
9 data were evaluated through the systematic review
10 process. Where EPA had information to construct a
11 model, exposure modeling was performed to supplement
12 monitoring data.

13 To estimate inhalation exposures for
14 ONUs, EPA considered ONU specific personal monitoring
15 data and modeled far-field air concentrations. In the
16 absence of these estimates for ONUs, EPA provided
17 worker central tendency exposure values as surrogates
18 for ONU exposures. Where EPA had information to
19 construct a model, exposure modeling was performed to
20 supplement monitoring data. To estimate inhalation
21 exposures for ONUs, EPA considered ONU specific
22 personal monitoring data, modeled far-field air
23 concentrations, and area monitoring data. In the
24 absence of these estimates for ONUs, EPA assumed ONU

1 exposures could be estimated using worker PBC central
2 tendency values.

3 This table on Slide 32 provides a
4 summary of each of the 18 occupational exposure
5 scenarios, OES, indicating whether monitoring data was
6 reasonably available and whether the data was used to
7 estimate inhalation exposures for workers and ONUs.
8 The table also indicates whether EPA used modeling to
9 estimate inhalation and dermal exposures for workers
10 and ONUs. Dermal exposure for ONUs was not evaluated
11 because these employees are not expected to be in
12 direct contact with TCE.

13 We're now on Slide 33. For several
14 OES, EPA used the two-zone probabilistic modeling
15 approach to assess inhalation exposure. In this
16 modeling approach, TCE emissions occur in the near-
17 field zone. Workers are assumed to spend their time
18 in the near field when handling TCE. Occupational
19 nonusers are assumed to spend their time in the far-
20 field zone. Air exchange occurs between the near-
21 field and the far-field. Model input parameters such
22 as far-field size, worker activity pattern, TCE use
23 rate, and environmental parameters were defined using
24 reasonably available data from literature. EPA

1 performed a *Monte Carlo* simulation to capture
2 variability within the modeled scenario.

3 Slide 34 provides an example comparison
4 of modeled estimates with monitoring data. For the
5 few scenarios where modeling and monitoring data were
6 available, there were typically reasonably good
7 agreement between the modeling and monitoring exposure
8 values for workers. In these examples, the estimates
9 using both approaches are within a factor of five.
10 The worker modeled value shown here are from the
11 corresponding near-field/far-field probabilistic model
12 for batch open top vapor degreasing, along with spot
13 cleaning and wipe cleaning. HE represents high-end,
14 and CT is central tendency.

15 Slide 35 provides an example of the two
16 zone near-field/far-field model used for batch open-
17 top vapor degreasing to develop exposure estimates for
18 both workers in the near-field zone and for
19 occupational nonusers who are exposed to TCE in the
20 far-field zone. Slide 36, there are uncertainties and
21 limitations in the inhalation monitoring data and
22 modeling approaches. For the monitoring data, these
23 limitations include occasionally limited number of
24 data points for certain OES or job categories and the

1 representativeness of the data, along with accurate
2 identification and distinction of the worker and the
3 ONU. For the modeling approaches, those limitations
4 include any inherent variability and uncertainty in
5 the end parameters and impacts that may have on the
6 representativeness of the modeling result.

7 Slide 37, to assess dermal exposure,
8 EPA used the dermal exposure to volatile liquids model
9 to calculate the dermal retained dose for both
10 nonoccluded and occluded scenarios. The equation
11 modifies the EPA two-hand dermal exposure to liquids
12 model by incorporating a fraction absorbed, or FABS,
13 parameters to account for the evaporation of volatile
14 chemicals. The steady state FABS for TCE is estimated
15 to be 0.08 in industrial facilities with higher indoor
16 wind flows or 0.13 in commercial facilities with lower
17 indoor wind speeds based on the theoretical framework
18 provided by Kasting and Miller in 2006. This means
19 that approximately eight or 13 percent of the applied
20 doses absorbed through the skin following exposure
21 from industrial and commercial settings respectively.

22 Here on Slide 38 is an example of how
23 the dermal exposures through the occupational exposure
24 scenarios were groups or binned based on

1 characteristics that are known to effect dermal
2 exposure. This slide presents example dermal exposure
3 estimates for Bin 1, which covers large scale
4 industrial uses that typically occur in mostly closed
5 systems. For these uses, dermal exposure is likely
6 limited to chemical loading and unloading activities,
7 e.g. connecting hoses.

8 **DR. KENNETH PORTIER:** We're getting
9 feedback from someone.

10 **DR. KEITH JACOBS:** Yes. If you are
11 dialed into this event, please mute your lines.

12 **DR. TODD PETERSON:** James Bruckner
13 needs to be muted.

14 **DR. KEITH JACOBS:** Slide 39, as with
15 the inhalation exposure assessment approaches, there
16 were some uncertainties and limitations with the
17 occupational dermal exposure assessment. Those
18 limitations include using a fixed fractional
19 absorption approach to quantify dermal dose. In
20 reality, dermal absorption may depend on skin loading
21 conditions. Additionally, the model also assumes a
22 single exposure event per day and does not address
23 variability in exposure duration and frequency.
24 Further, there is limited information on glove type

1 and glove use for most conditions of use. Therefore,
2 the actual exposure reduction from glove protection is
3 uncertain.

4 The following slides cover the consumer
5 exposure approach methodology and uncertainties.

6 Consumer exposures are described in Section 2.3.2 and
7 Appendix D of the draft risk evaluation and relate to
8 Charge Questions 4.7 to 4.10. We are currently on
9 Slide 40, moving on to Slide 41. A total of 25
10 consumer conditions of use are evaluated in the draft
11 risk evaluation. EPA used CEM Version 2.1 to evaluate
12 inhalation and dermal exposure routes. The
13 availability of TCE in consumer products was
14 determined primarily through the development of EPA's
15 2017 market and use report and preliminary information
16 on manufacturing, processing, distribution use and
17 disposal for TCE.

18 We're on Slide 42. Inhalation and
19 dermal exposures are evaluated for acute consumer
20 exposure scenarios, i.e. those resulting from short
21 term or daily exposures. In general, typical
22 frequencies of product use were considered to be too
23 low to generate chronic risk concerns for consumer.
24 Based on physical-chemical properties of TCE, oral

1 exposure is not expected. Exposures were assessed for
2 users or consumers, as well as for bystanders in the
3 home. Users are the receptors using a product
4 containing TCE within a residence in an identified
5 room of use, while bystanders are receptors within the
6 residence where a product containing TCE is used that
7 are incidentally exposed to the product.

8 Slide 43, as described on the previous
9 slide, inhalation and dermal exposures were estimated
10 through the modeling of acute exposure scenarios. Key
11 parameters for exposure modeling include use duration,
12 amount of mass of product used, weight fraction of TCE
13 in product used, room of use, air exchange rate, and
14 zone two volume. Three of these inputs, duration,
15 mass, and weight fraction, that describe product use
16 and user behavior patterns were varied to capture a
17 range of exposures by combining low-end, central
18 tendency, and high-end inputs for the key parameters
19 listed on the slide. This resulted in a maximum of 27
20 modeling combinations for inhalation scenarios and
21 nine modeling combinations for dermal scenarios.
22 Results were presented for a range of modeling
23 combinations reflected by three exposure scenarios:
24 high, moderate, or low intensity use.

1 We're now on Slide 44. Manufacturer
2 developed consumer product safety datasheets, or SDSs,
3 were used to obtain the TCE weight fraction input, as
4 well as product density information. The Westat
5 survey is a comprehensive national survey of consumer
6 use patterns and was used to parametrize other key
7 modeling inputs, such as duration of use, mass of
8 product used, and room of use. The survey includes
9 responses from thousands of American households on
10 consumer behavior patterns and product
11 characteristics.

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

Slide 45, inhalation exposures were evaluated for all 25 consumer conditions of use. Receptors are product users, which include adult and children ages 11 and older, and bystanders, which can include any age group. CEM predicts indoor air concentrations by implementing a deterministic mass balance calculation. The model uses a two-zone representation of a house, with Zone 1 representing the room of use and Zone 2 being the remainder of the house. The arrows depict airflows between each zone and the outdoors, as well as the airflows between the two zones.

Modeled air concentrations for users reflect time spent in Zone 1 during chronic use, while modeled air concentrations for bystanders reflect time spent in Zone 2 during product use. Both receptors moved throughout the house following prescribed activity patterns for the rest of the day. The CEM emission models used for TCE products include E1, or emission from a product applied to a surface indoors incremental source model, and E3, or emission from a product sprayed model. E1 was applied for all liquid formulations, and it assumes a constant application rate and emission rate that declines exponentially

1 over time. E3 was applied for aerosol formulations
2 and assumes overspray and subsequent volatilization
3 from the target surface.

4 This is Slide 46. Dermal exposures
5 were evaluated for 12 consumer conditions of use or
6 product users, which include adults and children age
7 11 and older. The exposures to bystanders were not
8 evaluated, as generally only users are expected to
9 have contact with liquid TCE. Based on the physical
10 and chemical properties of TCE and predictions
11 surrounding the level of volatilization and absorption
12 expected, dermal modeling focused on the relevant
13 conditions of use is more likely to involve dermal
14 contact with impeded evaporation or in scenarios where
15 TCE may not readily volatilize from the skin surface
16 due to a factor such as a product soaked rag held
17 against the hand.

18 The P_DER2b, or dermal dose from
19 product applied to skin, permeability model within
20 CEM2.1 was selected as the most appropriate model for
21 these exposure conditions. The model estimates dermal
22 flux based on the permeability coefficient, or Kp, and
23 assumes a constant supply of chemical throughout the
24 exposure duration. The Kp used, 0.19 centimeter per

1 hour, is a measured value from Poet et al. 2000. This
2 falls between the range of predicted Kp values, with
3 0.01197 centimeter per hour predicted in the NIOSH
4 skin notation profile for TCE and 0.028 centimeter per
5 hour predicted within CEM2.1.

6 This is Slide 47. CEM developers
7 conducted a detailed sensitivity analysis, as
8 described in Appendix C of the CEM user guide and
9 summarized in Appendix D of the draft risk evaluation.
10 As explained in approach slides, EPA varied three
11 input parameters, weight fraction, duration, and mass,
12 to capture a range of exposure estimates. These
13 parameters are reflective of consumer products and
14 consumer behavior patterns, two of which are highly
15 sensitive in inhalation modeling, mass used and weight
16 fraction. Other highly sensitive inputs for CEM's
17 inhalation models include zone volumes and air
18 exchange rates, which were held constant at central
19 tendency inputs.

20 We're now on Slide 48. The overall
21 modeling approach was deterministic but captured a
22 range of exposure estimates by varying key parameters.
23 Since a probabilistic approach was not employed and
24 all inputs were not varied, there remains uncertainty

1 regarding the full range of possible exposures.
2 Appropriate monitoring data were not identified for
3 use in validating modeling results. EPA made best
4 efforts to cross Westat survey data to TCE consumer
5 conditions of use. However, certain associations were
6 weaker than others and are discussed in the risk
7 evaluation. In examining Westat for appropriateness,
8 EPA considered reasonableness of the reported
9 durations and masses used and compared primary
10 formulation type, i.e. liquid versus aerosol.

11 In dermal modeling, there were two main
12 sources of uncertainty: assumption surrounding the
13 likelihood and duration of dermal contact involving
14 impeded evaporation and the use of a measured aqueous
15 KP to estimate dermal flux in the permeability model.
16 Dermal exposures may be overestimated for some
17 scenarios, particularly those using higher-end use
18 durations. Measured emission rates from TCE
19 containing products were not identified for use in
20 modeling. Therefore, emission rates were estimated
21 within CEM.

22 As to the strengths of EPA's modeling
23 approach, CEM2.1 is a peer reviewed and publicly
24 available exposure model. It also employs well-

1 establish central tendency default values for
2 sensitive parameters, such as building and room
3 volumes, the interzonal ventilation rate, and air
4 exchange rates. The modeling inputs that EPA selected
5 to vary, mass use, duration, and weight fraction, are
6 based on high quality survey data cross a range of
7 values. Given the uncertainties, limitations, and
8 strengths of the approach, there was overall moderate
9 to high confidence in the consumer inhalation exposure
10 estimates and low to moderate confidence in the dermal
11 exposure estimates.

12 Now, on Slide 49 begins the discussion
13 of human health hazard, which is described in Section
14 3.2 of the risk evaluation, along with several
15 appendices, and relates to Charge Question 5. Here on
16 Slide 50 is a breakdown of TCE's toxicokinetics,
17 covering absorption, distribution, metabolism and
18 elimination. TCE is well absorbed by all routes,
19 although volatility limits dermal absorption unless
20 occluded. TCE is widely distributed in the body but
21 partitions heavily into adipose tissues. TCE is
22 extensively metabolized by both oxidative and
23 conjugative pathways. And the resulting reactive
24 metabolites are believed to be responsible for most of

1 TCE's toxicity. TCE has a relatively quick half-life
2 of 44 to 50 hours in humans and much faster in
3 rodents.

4 We're on Slide 51. For this risk
5 evaluation, EPA utilized the physiologically based
6 pharmacokinetic, or PBPK, model, published as part of
7 the 2011 IRIS assessment. This model allows for
8 cross-species and route to route extrapolation of
9 toxicity data and also includes a probabilistic
10 representation of human variability. In this manner,
11 an external dose via either inhalation or ingestion in
12 an animal study can be translated into the equivalent
13 internal human dose, the most sensitive one percent of
14 the population. The PBPK model for TCE does not
15 contain a dermal compartment. It can only be used for
16 inhalation and oral data.

17 Slide 52, based on the 2018 problem
18 formulation, EPA considered liver toxicity, kidney
19 toxicity, neurotoxicity, immunotoxicity, reproductive
20 toxicity, developmental toxicity, overt toxicity
21 following acute or short-term exposure and
22 carcinogenicity in the risk evaluation. Acceptable
23 studies were available via inhalation and oral but not
24 dermal routes. Oral points of departure, or PODs,

1 were extrapolated to dermal exposure. Based on the
2 weight of scientific evidence and availability of
3 adequate quantitative data, all but overt acute
4 toxicity was carried forward to dose response
5 analysis.

6 Slide 53, EPA only selected medium- or
7 high-quality studies with adequate quantitative
8 information available for consideration in dose
9 response analysis. For acute risks, EPA identified
10 four relevant studies, covering three developmental
11 endpoints and one immunotoxicity endpoint. The three
12 developmental toxicity endpoints were prenatal
13 mortality, developmental neurotoxicity and congenital
14 heart defects, or CHDs. Based on EPA guidance, it is
15 assumed that these developmental outcomes can present
16 following only a single day of exposure during a
17 sensitive window, despite the data coming from longer-
18 term studies. Of note, the draft risk evaluation
19 included a detailed discussion of considerations for
20 CHD benchmark response, or BMR, selection.

21 While EPA acknowledges dose response
22 uncertainties, including nonmonotonicity of the dose
23 response and other concerns, it was determined that a
24 one percent BMR was still most appropriate, based on

1 the severity of the endpoint and a good benchmark dose
2 model fit. The immune outcome is mortality in
3 response to infection, following an acute three-hour
4 TCE exposure. The data from this study was not PBPK
5 modeled. However, it was extrapolated to a dermal
6 dose using breathing rate and bodyweight values from
7 the mouse species tested. The POD was adjusted to 24-
8 hour HEC value for occupational but not consumer risk
9 because CEM can provide three-hour exposure estimates
10 to match study duration.

11 Slide 54, for chronic effect, EPA
12 identified many more relevant studies for each hazard
13 domain, often covering multiple endpoints within each
14 domain. Therefore, studies were selected that best
15 represent each endpoint. In selecting the most
16 representative studies and PODs, EPA considered the
17 following factors: data quality evaluation score;
18 species, i.e. was it an animal study or in humans;
19 exposure duration; dose range; and cumulative
20 uncertainty factor, as well as relevance to the
21 endpoint of interest and human exposure scenarios.
22 Risk estimates were provided for all of these
23 endpoints in the risk calculator. However, only the
24 most sensitive endpoint within each domain was

1 presented in the body of the risk evaluation in order
2 to most succinctly represent overall risk for that
3 domain.

4 For liver, there was a single study
5 representing the general endpoint of liver toxicity
6 that was selected, and the same was true for kidney.
7 Representative studies were identified for both
8 decreased wakefulness and trigeminal nerve effects
9 within the neurotoxicity domain. And the risk
10 estimates for decrease wakefulness were presented in
11 Section 4. Both autoimmunity and immunosuppression,
12 chronic PODs, were derived in the assessment, with
13 autoimmunity risk estimates presented. Both male and
14 female reproductive effects were identified, and the
15 risk estimates for male effects were presented. The
16 developmental effects were the same as described for
17 acute risks, with risk estimates for heart defects
18 presented in Section 4 to represent the domain.

19 We're now on Slide 55. While EPA
20 presented risk estimates for all the endpoints
21 previously described, individual endpoints had to be
22 chosen in order to succinctly present the best
23 representative overall risk estimates for each
24 condition of use. Therefore, EPA identified the most

1 robust and representative acute and chronic noncancer
2 PODs from among endpoints that it deemed to be
3 adequately sensitive. For acute exposure, EPA
4 identified the immunosuppression endpoint and POD from
5 Selgrade and Gilmour 2010 as most robust.

6 In this study, mice were infected in
7 the lungs with bacteria following three-hour
8 inhalation exposure to various doses of TCE.
9 Mortality was assessed at all doses in a large number
10 of mice, while other indicators of immunosuppression
11 were confirmed in smaller assays. The pulmonary
12 effect was extrapolated to a systemic response based
13 on other studies demonstrating systemic
14 immunosuppression. And the interspecies uncertainty
15 factor, or UF, was reduced based on assumed PPM
16 equivalence across species. This study was selected
17 as the most robust acute endpoint because it scored a
18 high-end data quality, used a broad dose range, showed
19 a consistent dose response, was actually from an acute
20 exposure study, and, despite mortality being a very
21 frank effect, the endpoint is based on the results of
22 multiple assays.

23 The selected chronic endpoint is
24 autoimmunity from Keil et al. 2009. In that study,

1 mice were exposed via drinking water for 27 to 30
2 weeks at low doses. And both thymus effects and DNA
3 autoantibodies were observed at the lowest dose. The
4 selected POD was based on the autoantibodies as a
5 better marker of an adverse effect, which resulted in
6 a decreased uncertainty factor for extrapolation from
7 lowest adverse effect level, or LOEL, due to being a
8 subclinical marker of disease. This study was
9 selected based on scoring high for data quality, being
10 of chronic duration, and the use of an early sensitive
11 clinical marker that's also associated with thymus
12 effects.

13 Slide 56, while the reasonably
14 available information clearly determined that the
15 developmental toxicity domain overall was supported by
16 the weight of scientific evidence, further analysis
17 was conducted for the congenital heart or CHD
18 endpoint, which has been greatly debated in various
19 manuscripts and assessments over the years. The
20 primary studies for this endpoint are Johnson 2003 and
21 Dawson '93, both from the same lab. Johnson 2003
22 consolidated data from several cohorts, including the
23 Dawson data, over a six-year period, examining the

1 incidence of CHDs following TCE administration to
2 pregnant females.

3 This data is supported by evidence from
4 epidemiological and mechanistic studies. However, the
5 mammalian in vivo findings from Johnson 2003 have not
6 been confirmed by other laboratories via multiple
7 exposure routes. Multiple weight of evidence
8 assessments of this endpoint have been published with
9 differing conclusions depending on the focus of the
10 assessment.

11 Slide 57, the Johnson 2003 study has
12 some significant strengths and also several
13 limitations. Strengths include blinded examination,
14 the fact that only unanimous agreement resulted in a
15 positive finding of a defect, the use of a detailed
16 dissection protocol, the provided description of
17 preservation and examination methods, the fact that
18 dams were randomly assigned to control a treatment
19 group, and the fact that several variables such as the
20 methods, supplier, and investigators remained
21 consistent over time. As for limitations, the major
22 critiques involved the fact that controls were pooled
23 from multiple studies and some of these controls used
24 tap water while others used distilled. Although, EPA

1 did not find any statistically significant difference
2 between controlled data from the different
3 experiments.

4 The study took place over six years
5 with a several year gap, allowing for potential
6 genetic drift in the study population. Additionally,
7 individual fetus data could not be connected to a
8 particular dam or mother. The original publications
9 had several deficiencies in transparency about these
10 issues and data reporting. However, many of these
11 concerns were addressed by subsequent errata and
12 communications with EPA. Details provided in this
13 later documentation include: individual fetal cardiac
14 malformation data for each litter, individual maternal
15 terminal bodyweight data, additional description of
16 fetal evaluation procedures, additional information on
17 animal husbandry and randomized group assignment of
18 dams, and transparency regarding experimental
19 variables across the dates of the experiments. When
20 considering all available information, not only what
21 was originally published, both the Johnson and Dawson
22 studies received a medium in data quality evaluation.

23 Slide 58, in an attempt to clarify some
24 of the uncertainty over the endpoint, Charles River

1 Laboratories attempted to replicate Johnson 2003, for
2 other in vivo studies had not previously used the same
3 administration method or dosage. In this study,
4 retinoic acid, or RA, was additionally added as a
5 positive control. Charles River reported only a
6 minimal, non-statistically significant increase in the
7 incidence of cardiac defects, ranging from 2.5 percent
8 in fetuses and controls to 3.5 percent at the highest
9 dose. For comparison, Johnson 2003 data ranged from a
10 similar 2.2 percent in controls up to 10.5 percent at
11 the highest dose. The ratio of effected litters
12 ranged from 16.4 percent to 66.7 percent in Johnson
13 and was 25 percent in both controls and the highest
14 dose in the Charles River study.

15 Now on Slide 59, interestingly, the
16 entirety of the incidence from Charles River
17 represented only a single defect, the only one
18 identified for TCE treated animals and controls,
19 ventricular septal defects, or VSDs. Johnson 2003, on
20 the other hand, identified a constellation of varied
21 defects. The table on the right shows some examples
22 of the defects observed in Johnson 2003, alongside
23 Charles River, as well as another study, Fisher 2001,
24 which administered TCE via gavage and had the lead

1 author from Johnson 2003 as a consultant for
2 dissection and examination. On the left side of the
3 table is a comparison of defects observed following
4 TCE administration in all three studies and on the
5 right shows RA positive control data from Charles
6 River and Fisher.

7 As you can see, a multitude of defects
8 were observed in both Johnson, the yellow column on
9 the left, and Fisher, the white column to the right,
10 while a very limited set of defects were observed even
11 in the positive control in Charles River, shown in the
12 center. The most important defect not identified in
13 Charles River is atrial septal defect, indicated with
14 red arrows, which show the strongest dose response in
15 Johnson had a higher incidence than VSDs and were also
16 observed in multiple other RA studies in a broader
17 literature. It is clear from this table that for
18 whatever reasons the Charles River study did not
19 identify as broad of a set of defects as other
20 studies, either from TCE or retinoic acid. Therefore,
21 the Charles River methodology may result in a pre-
22 disposition of extra sensitivity for VSDs, perhaps at
23 the expense of other defects. This presumed focus on
24 VSDs is supported by the discussion section in the

1 academic publication version of this study, DeSesso et
2 al. 2009. However, that publication did debate the
3 significance of the non-VSD malformation.

4 Slide 60, these observed differences
5 may be due to methodological differences between the
6 two studies. Charles River used the Stuckhardt and
7 Poppe dissection method, which based on published
8 methodology would not be expected to include close
9 examination of the atrial septum. Major differences
10 in the dissection method include the examination of
11 fix first fresh tissue for Johnson versus Charles
12 River, as well as differing angles of cut for
13 dissection. The Johnson method as described is likely
14 to be more sensitive to atrial, valvular, and other
15 defects. Other study differences include different
16 sources and strains of rats, unavoidable genetic drift
17 over time resulting in different sensitivities, fetus
18 selection, variations in TCE loss and differences in
19 animal husbandry.

20 The Johnson and Charles River studies
21 both use concurrent controls. However, as previously
22 mentioned, the controls in Johnson were pooled from
23 among multiple experiments and were a mix of tap and

1 distilled water. The table to the right highlights
2 these and other comparisons between the two studies.

3 This is Slide 61. Based on the
4 questions concerning whether Charles River was fully
5 inclusive in its examination of CHDs, EPA determined
6 that a more thorough weight of evidence analysis was
7 needed for this endpoint. Therefore, Charles River
8 and Johnson were considered along with all other
9 identified relevant studies for their contribution to
10 the overall weight of evidence, 45 studies in total.
11 EPA decided to evaluate evidence on a semiquantitative
12 scale on the basis of three factors: reliability or
13 data quality, outcome strength, and relevance. This
14 allowed a transparent and unbiased conclusion of each
15 study based not only on the quality of the study but
16 also how useful the study is for the endpoint and how
17 strong the observed positive or negative response
18 really was.

19 Using this method, EPA determined an
20 independent summary score for each evidence area of
21 epidemiology, in vivo animal, and mechanistic studies.
22 The summary score was determined by integrating the
23 overall grades for each study within the evidence
24 area. Of note, this weight of evidence analysis also

1 included studies on relevant TCE metabolites.

2 Overall, the database provides positive evidence that
3 TCE may produce congenital cardiac defects in humans
4 based on positive evidence from epi data, ambiguous
5 evidence from in vivo animal data, and stronger
6 evidence from mechanistic data. Therefore, the
7 congenital heart defects endpoint was carried through
8 for dose response analysis.

9 We are on Slide 62. For dose response
10 analysis, administered doses or air concentrations as
11 reported in the tox study were run through the PBPK
12 model to obtain an internal dose point of departure,
13 or idPOD. The idPOD was benchmark dose modeled when
14 possible, and benchmark response values were selected
15 based on the severity of the effect, along with other
16 factors. The PBPK model outputs a human equivalent
17 concentration, or HEC, or dose, HED, value at various
18 percentiles, representing human variability. HECs
19 were also adjusted to 24-hour exposure duration
20 values.

21 Uncertainty factors considered for
22 determining the benchmark MOE were a UF for
23 interspecies, which was three if PBPK modeled or
24 otherwise scaled; an intraspecies UF for human

1 variability that was three when the 99th percentile
2 PBPK output was used; a LOEL to NOEL UF, which was
3 either three or ten if the POD was based on the LOEL
4 and one otherwise; and a subchronic to chronic UF,
5 which was ten for chronic risk estimates if a study
6 duration covered less than ten percent of lifetime.
7 Of note, the risk evaluation utilized HEC and HED 99
8 percentile values, which for most cases were
9 approximately threefold lower than the 50-percentile
10 output. And this was identical to the toxicokinetic
11 UF component that was eliminated through its use.

12 Here on Slide 63 is an exposure
13 response array displaying the relative range of the
14 acute PODs, in terms of HEC and HED 99s, along with
15 the applied concentration or dose range tested in the
16 study. The graph is split with the single
17 immunological effect on the left and three
18 developmental endpoints on the right, displayed in
19 order of decreasing POD. All of these PODs are below
20 the PEL, and three of four are below the odor
21 threshold. The blue ranges and HEC values represent
22 inhalation concentrations, while the orange ranges and
23 HEDs represent oral doses.

1 Cumulative uncertainty factors are
2 displayed on the top row, along with study data
3 quality score on the bottom. As you can see, the
4 acute endpoints cover over three orders of magnitude.
5 The cardiac endpoint is substantially lower than the
6 others. However, note that differing uncertainty
7 factors are also accounted for in assessing risk
8 relative to benchmark.

9 Slide 64 contains an exposure response
10 array for chronic effect laid out similarly to the
11 array for acute endpoints. All chronic endpoints are
12 well below the PEL and odor threshold. These
13 endpoints are displayed with higher PODs on the left
14 and lower PODs on the right. And you will notice that
15 the three most sensitive endpoints representing
16 kidney, immune, and developmental effects are all
17 within an order of magnitude. When accounting for
18 uncertainty factors, the risk estimates for these
19 three endpoints differ by within threefold.

20 Slide 65, now moving on to cancer. The
21 cancer assessment in the 2014 risk assessment was
22 based on a series of meta-analyses on epidemiology
23 literature performed in the 2011 IRIS assessment. To
24 determine the weight of evidence for cancer hazard,

1 EPA performed an updated series of meta-analyses on
2 the entirety of the epi database for the three most
3 well supported cancers: kidney cancer, liver cancer,
4 and non-Hodgkin Lymphoma, or NHL. EPA utilized the
5 same methodology as in for the 2011 IRIS assessment
6 and is recommended from National Academy of Sciences.
7 However, novel analyses were conducted for this risk
8 evaluation, incorporating TSCA's systematic review
9 principles.

10 EPA also included sensitivity analyses,
11 including removal of an overly large but low
12 sensitivity study and stratification by data quality
13 score with an example for liver cancer shown on the
14 left. When considering study heterogeneity, tests for
15 publication bias, and a sensitivity analyses
16 performed, the results indicate positive associations
17 between TCE exposure and cancer for all three tumor
18 types. This confirms EPA's existing hazard
19 classification of TCE as a known human carcinogen.

20 Slide 66, now for discussion of the
21 cancer mode of action, or MOA. There is clear
22 evidence of a genotoxic mode of action for kidney
23 cancer through formation of reactive conjugative
24 intermediate. Toxicokinetic data supports metabolite

1 formation, and genotoxicity of the metabolites has
2 been observed in both in vitro and in vivo. There are
3 likely multiple mechanisms involved for liver cancer,
4 including both genotoxicity and PPAR alpha activation.
5 However, tumorigenesis occurs at lower doses than both
6 of these are observed. There's also limited evidence
7 for other mechanisms such as epigenetic DNA changes.
8 There's insufficient available data to suggest any
9 particular MOA for NHL. The data supports use of
10 accumulative linear non-threshold model based on the
11 clear genotoxic MOA for kidney cancer, the combined
12 relative contributions of multiple tumor types, and
13 positive associations observed in human data at low
14 level environmental exposures.

15 Slide 67, POD for cancer in the form of
16 an inhalation unit risk or oral slope factor was
17 derived from the high-quality kidney cancer data from
18 Charbotel et al and then adjusted upward based on the
19 additional relative potency of the other two sites.
20 Based on the same positive association identified for
21 all three cancer sites, EPA derived the same
22 inhalation unit risk oral slope factor, or IUR and
23 OSF, values as was used in the 2011 IRIS and 2014 risk
24 assessment. The IUR is 0.22 per PPM. OSF is 0.0464

1 per mgs over kg, with a benchmark of one times 10 to
2 the negative four, which is based on OSHA and NIOSH
3 items.

4 We're on slide 68. Uncertainties and
5 limitations in the human health hazard assessment
6 include uncertainty in the appropriateness and
7 sensitivity of DMR and UF determinations, uncertainty
8 in the PBPK outputs for GSH metabolites -- although,
9 there is less uncertainty in rat data -- and
10 uncertainty in the dose response analysis for the
11 heart defects endpoint. EPA was also unable to derive
12 the POD to account for observed developmental
13 immunotoxicity in a single study. And it is unknown
14 whether the approach for adjusting the cancer POD
15 resembles the true combined risk of additional sites.
16 Confidence determinations considered the above points,
17 along with the range of PODs, and the relative
18 influence of various other assumptions.

19 Overall, confidence in acute endpoints
20 is medium. Overall confidence in chronic noncancer
21 endpoints is high. And confidence in cancer endpoints
22 is medium to high. Confidence was raised for all
23 endpoints through the use of a PBPK model and the
24 breadth of the database. And there was high

1 confidence for the two selected representative acute
2 and chronic endpoints of autoimmunity and
3 immunosuppression.

4 And finally, here I will overview the
5 human health risk characterization which can be found
6 in Section 4.2 of the draft risk evaluation and
7 relates to Charge Question 6.1 through 6.5. This is
8 Slide 69. Here we are on Slide 70. The diagram on
9 the left shows a breakdown of the receptors and
10 exposure routes evaluated in the risk evaluation, as
11 were shown earlier.

12 Both acute and chronic risks were
13 evaluated for occupational scenarios, while acute
14 risks were estimated for consumers. Noncancer risks
15 were calculated by comparing the MOE, the ratio of the
16 POD to the exposure to the benchmark MOE. For cancer,
17 extra risk is calculated by multiplying the lifetime
18 exposure estimate by the IUR or OSF. All risk
19 estimates were presented both with and without PPE,
20 and EPA indicated for which scenarios respirator use
21 is not expected. Risks were not aggregated across
22 routes due to large uncertainties without a dermal
23 compartment in the PBPK model.

1 Here on Slide 71 is an example of an
2 occupational risk characterization table for a single
3 OES: manufacturing. As you can see, risk estimates
4 were presented for all acute endpoints, each chronic
5 hazard domain, and cancer. Risks are shown for
6 workers assuming both no PPE and PPE with ABF up to 50
7 and glove ABF up to 20, as well as for ONUs who are
8 not expected to use PPE. For this particular example,
9 monitoring or modeling data was not reasonably
10 available for ONUs. So EPA assumed that ONU exposure
11 may be comparable to worker central tendency values.
12 It is clear that for this OES risks are identified as
13 shown in shading for most endpoints, via both
14 inhalation and dermal exposure and even with PPE.

15 Here on Slide 72 is an example of the
16 risk characterization table for a consumer COU: break
17 and parts cleaner. As you can see, risks are
18 identified to users and bystanders for multiple
19 endpoints at various user intensities via both
20 inhalation and dermal exposure. This is Slide 73,
21 covering assumptions and key sources of uncertainty
22 for the human health risk characterization. As one
23 key source of uncertainty, EPA did not quantify
24 chronic risk consumer uses of TCE containing products.

1 However, chronic hazards are not applicable for the
2 vast majority of consumers based on typical frequency
3 of use.

4 There is also uncertainty associated
5 with the assumption that ONU exposure estimates in the
6 absence of data are comparable to worker central
7 tendency values. Additionally, the absorption modeled
8 parameters and assumptions may under- or overestimate
9 risk for any individual on a given day. Dermal risk
10 estimates are extrapolated from oral POD values, and
11 worker PPE assumes proper training, fitting, and use
12 during the work activity.

13 This is Slide 74. EPA identified
14 potentially exposed or susceptible subpopulations, or
15 PESS, based on the definition from TSCA. Groups
16 having greater exposure than the general population
17 include workers and ONUs, which include women of
18 childbearing age and adolescence, along with consumer
19 users and bystanders, which include children. Groups
20 with greater biological susceptibility include those
21 with certain genetic or polymorphisms, developmental
22 life stages, pre-existing health conditions, and other
23 environmental factors. Another major susceptibility
24 factor is age, especially for older mothers, due to

1 increased association with congenital heart defects in
2 epi studies. The risk evaluation accounted for PESS
3 by providing distinct risk estimates for women of
4 childbearing age and different consumer life stages,
5 the use of 99 percentile PBPK outputs, inclusion of
6 the congenital heart defects endpoint which may only
7 present in certain susceptible subpopulations, and the
8 use of an acute immunosuppression endpoint for
9 protection of subpopulations with preexisting
10 infection.

11 Slide 75 covers an overall summary of
12 the human health risk characterization. For most OES,
13 occupational inhalation risks were identified in
14 multiple endpoints for both workers and ONUs, with
15 risks for all OES at high end exposures, including
16 with PPE. There were risks for all OES to workers via
17 dermal exposure, including with PPE. Risk conclusions
18 did not change for the majority of occupational
19 exposure scenarios, whether based on cardiac defects
20 or autoimmunity.

21 Acute risks were identified to consumer
22 users and bystanders for all COUs and for all except
23 pepper spray based on the most robust acute endpoint.
24 For most COUs, there were acute risks at all intensity

1 levels and through multiple endpoints for both users
2 and bystanders. The risk conclusions were not very
3 sensitive to endpoint selection. And in many cases,
4 the MOEs were orders of magnitude below benchmark.

5 On this last slide, Slide 76, I would
6 like to close the presentation by bringing forward the
7 risk characterization consideration for the
8 procedures, for chemical risk evaluation under the
9 amendment Toxic Substances Control Act, or TSCA. The
10 same considerations go into the Administrator's
11 determination about unreasonable risk. These include
12 integration of the hazard and exposure assessment into
13 quantitative and/or qualitative estimates of risk for
14 the identified populations, including potentially
15 exposed or susceptible subpopulations; describing
16 whether aggregate or sentinel exposures under the
17 conditions of use were considered, and the basis for
18 their consideration, not considering costs or other
19 non-risk factors; taking into account where relevant
20 the likely duration, intensity, frequency, and number
21 of exposures under the conditions of use of TCE; and
22 describing the weight of the scientific evidence for
23 the identified hazards and exposures. With that, I
24 would like to conclude this presentation, and I thank

1 you all for your attention. And that's the last
2 slide.

3 **DR. TODD PETERSON:** Thank you very
4 much. This is Todd Peterson, the DFO. Usually at
5 this point Ken Portier and I coordinate when we're
6 sitting elbow to elbow at the table. I just would
7 like to suggest something, and Ken can confirm it.
8 And then we'll be off for a break. Schedule says
9 we'll have a break until 12:00. Thank you, Keith, for
10 your presentation. It was very timely and clear. I
11 think what we'll do is add five minutes to the break
12 time to come back at 12:05 Eastern Time. One thing I
13 want to say is, for all those online, I would ask that
14 you keep your line open and don't disconnect or be
15 dialed back in again. That way, after a 15-minute
16 break, I'll be able to pick up again.

17 Because this is a virtual meeting and
18 because of all the preparations we've done, I think
19 the DFO can comment at this point that, when we come
20 back, Ken Portier will lead the panel in a discussion
21 about the presentation they just heard. At some
22 point, panel members may have a question of OPPT. And
23 what I would like to say is sometimes there may be a
24 bit of a lag while the RAD team tries to figure out

1 who they want to have to answer a question. So there
2 may be -- Hello? There may be a pause from time to
3 time before someone speaks. And finally, critical to
4 all this is make sure that if you're a panel member or
5 an OPPT person to announce your name before you speak.
6 And I think that will be good. So Ken, if you agree,
7 chime in and then we can start the break until 12:05.

8 **DR. KENNETH PORTIER:** I agree. Let's
9 return at 12:05. At that point, the host will be
10 controlling the slide set, so EPA won't have to do
11 that. We're having some network issues, and that's
12 going to hopefully save some of those issues. Let's
13 break until 12:03.

14 (BREAK)

15
16 **SACC DISCUSSION ON OPPT TECHNICAL PRESENTATION**

17
18 **DR. TODD PETERSON:** Good afternoon to
19 East Coasters and still good morning to those on the
20 West Coast. It's 12:05. As I just mentioned before,
21 this will be time for the SACC committee members, the
22 peer reviewers, ad hocs, to talk about our
23 presentation that they've just seen. So I will turn
24 the floor over to Ken Portier.

1 **DR. KENNETH PORTIER:** Yeah. Good
2 afternoon and good morning. I see -- at this point,
3 we're going to open up the discussion to the panel
4 with comments and questions on the presentation. And
5 I see that Dr. Schlenk wants to start this. Dan?
6 Remember to unmute your phone.

7 **DR. DANIEL SCHLENK:** Okay. Can you
8 hear me?

9 **DR. KENNETH PORTIER:** Yes.

10 **DR. DANIEL SCHLENK:** Okay. Dan Schlenk
11 here. I had a question about the monitoring data or
12 the data that was actually used for the discharge
13 numbers that E-FAST was used for. It was more the
14 actual -- the data that was used -- let me see if I
15 can find the slide -- the DMR data that was -- in the
16 document, when I read the data in the document, it
17 indicated that NPDS data was actually used --
18 monitoring data was used for certain calculations.
19 And I'm wondering was that actual monitoring data or
20 what actually NPDS data was actually utilized in the
21 estimates for the discharge rates?

22 **DR. STANLEY BARONE:** Hi, this is Stan
23 Barone. I hope Stephanie Sarraino, Dr. Sarraino can
24 address that question, if you can unmute her line.

1 **MS. STEPHANIE SARRAINO:** Yes, hi.

2 Thank you for the question. So as far as the NPDS
3 data, the only thing from the NPDS permits that was
4 used was the flow -- the receiving water body stream
5 flows in modeling. So no -- aside from the DMR data
6 that the engineers used in the occupational exposure
7 assessment that informs some of their release
8 estimates, which was also used.

9 **DR. DANIEL SCHLENK:** So just to
10 clarify, so none of the release -- there was no
11 effluent monitoring data that was obtained from NPDS
12 then; is that correct?

13 **MS. STEPHANIE SARRAINO:** So from -- the
14 DMR reporting does contain that. So that's an
15 important exposure estimate. Not all of them, some of
16 them were informed by TRI release estimates. But for
17 a number of the sites, the discharge monitoring report
18 obtained based on the NPDS permits did inform the
19 release estimates.

20 **DR. DANIEL SCHLENK:** Okay. So there
21 was no NPDS monitoring data that was used for TCE?

22 **MS. STEPHANIE SARRAINO:** Well, I
23 believe some of the DMR reporting may have included
24 effluent monitoring, and some of it was effluent

1 estimates. I'm not sure if possibly the engineer
2 might be able to further answer that on as far as how
3 they treated the DMR data from NPDS to inform some of
4 the releases. I'm not sure if that fully answers your
5 question.

6 **DR. DANIEL SCHLENK:** It doesn't, but
7 that's okay. Thanks anyway.

8 **DR. KEITH JACOBS:** Kara, do you have
9 anything to add to that? Are you on the line, Kara?

10 **MS. KARA KOEHRN:** This is Kara. Can
11 you hear me?

12 **DR. KENNETH PORTIER:** Yes.

13 **MS. KARA KOEHRN:** Okay. Yeah.
14 Stephanie is right that some of the DMR information
15 that goes into E-FAST as well as some of the TRI data
16 going into E-FAST would be monitoring data. But at
17 least, I know for the TRI data it could also be mass
18 balance or some other kind of estimation.

19 **DR. DANIEL SCHLENK:** Yeah. This is Dan
20 Schlenk again. Yeah. That was my understanding was
21 the TRI data was all mass-based in terms of inputs.
22 But the monitoring data was actually obtained -- well,
23 at least it said in the document the DMR had NPDS
24 data. But it seemed that that was only for flow

1 estimates but not any monitoring data for TCE from the
2 NPDS data. That's what I sort of took from the DRE
3 thing.

4 **MS. KARA KOEHRN:** Yeah. We can double
5 check maybe on the next break, but I'm pretty sure
6 that some of the DMR data is monitored data depending
7 on the facility that it's coming from.

8 **DR. DANIEL SCHLENK:** Okay. Thanks.
9 That's all I had, Ken.

10 **DR. KENNETH PORTIER:** Okay. Thanks.
11 All right. Dr. Kissel, you're next.

12 **DR. JOHN KISSEL:** So the fourth slide
13 gave the physical-chemical properties of
14 trichloroethylene, which should correspond to Table
15 1.1 on page 41 of the draft risk evaluation. There
16 are substantial differences in boiling point, melting
17 point, vapor pressure, log KOW, aqueous solubility,
18 and specific gravity. Can we assume that EPA actually
19 believes the numbers that are in the draft risk
20 evaluation and that Slide 4 is just a transcription
21 error of some kind?

22 **DR. KEITH JACOBS:** So this Keith
23 Jacobs. I'm going to allow Wen to chime in if I say
24 anything incorrect. We did identify at least one typo

1 for solubility, and the solubility is 1.3, not 13.
2 And it is possible that there was a transcription
3 error for some other properties as well, but we didn't
4 get to review all of those. So yes, it is possible.
5 Wen, are you on the line if you have anything else to
6 add beyond that? Wen, if you're trying to speak, make
7 sure you're not muted.

8 **MR. WEN-HSIUNG LEE:** Okay. Can
9 everyone hear me?

10 **DR. KEITH JACOBS:** Yes.

11 **MR. WEN-HSIUNG LEE:** Okay. Yeah. The
12 original organic chemist that collected all the data,
13 he left. And I'm the predecessor, so yeah. I stepped
14 in. So some of the slides are original. Yeah. It's
15 quite a little bit different. But you start our
16 document as the final. Yeah.

17 **DR. KEITH JACOBS:** So yes, it's a
18 transcription error is the takeaway. Sorry. We
19 apologize for that. The values in the document are
20 correct.

21 **MR. WEN-HSIUNG LEE:** Yes.

22 **DR. KENNETH PORTIER:** Thank you. Was
23 that it, John?

24 **DR. JOHN KISSEL:** Yeah. I'm good.

1 **DR. KENNETH PORTIER:** Dr. Cobb, you're
2 next. George, you're unmuted, but we don't hear you.
3 I don't see Dr. Cobb's phone connected to the system,
4 so he may have dialed into the activity site instead
5 of to the panel site. Dr. Cobb check your email. You
6 may need to connect differently. Sorry. Dr.
7 Doucette?

8 **DR. WILLIAM DOUCETTE:** Yeah. I just
9 took my hand down, but I had the same comments as Dr.
10 Kissel. The data in the slide presented is incorrect
11 because I'm looking at EPI Suite. The data within the
12 DRE does look to be correct. So just clarification.
13 That's all I have.

14 **DR. KENNETH PORTIER:** Okey-doke. Dr.
15 Hossain?

16 **DR. MUHAMMAD HOSSAIN:** Yes. Can you
17 hear me?

18 **DR. KENNETH PORTIER:** Do you want to
19 ask your question? I see -- yes, we can hear you.

20 **DR. MUHAMMAD HOSSAIN:** I have a
21 question regarding the environmental hazard on Slide
22 19. And that is the effective concentration for
23 hazard for fish. My question is that there are
24 several kinds of fishes, so some are maybe more

1 sensitive animals. So what kind of fish are used in
2 the acute hazardous and chronic hazardous for the EC50
3 and EC20?

4 **DR. STANLEY BARONE:** Kara Koehn, could
5 you address the species sensitivity issues?

6 **MS. KARA KOEHRN:** Yeah. This is Kara.
7 The EC20 that was the value that we based the chronic
8 COC was based on fathead minnows. And that was the
9 most sensitive chronic value we had for fish, so
10 that's what we used. We were able to do a species
11 sensitivity distribution using the acute data but not
12 the chronic.

13 **DR. MUHAMMAD HOSSAIN:** Okay.

14 **DR. KENNETH PORTIER:** Is that it Dr.
15 Hossain?

16 **DR. MUHAMMAD HOSSAIN:** Thank you.

17 **DR. KENNETH PORTIER:** Dr. Lash?

18 **DR. LAWRENCE LASH:** Okay. I think I'm
19 unmuted. Hey, this is Larry Lash. Well, I had a --
20 and I'm not sure this is quite the right place to make
21 the comment because it does come up in review of the
22 charge questions, but I noticed it on the slide.
23 There were two points on Slide 50. I mean, it's
24 really a minor point. But the slide that talked

1 about, I guess, it was toxicokinetics, and it
2 mentioned -- it said that it's pretty well-regarded
3 that the adverse effects, with the exception of I
4 guess in very high levels due to solvent effect, are
5 pretty much due to metabolites.

6 But the statement reads that it's for
7 the reactive metabolites, all the adverse effects.
8 But that's not really true because, with the exception
9 of the effects due to the glutathione conjugation
10 pathway, which are due to reactive metabolites, most
11 of the other target organs the effects are due to --
12 are ascribed to TCA and trichloroacetate,
13 dichloroacetate, chloralhydrate, which are not really
14 reactive. So it's a minor issue, but I think it's an
15 important correction.

16 The other point had to do with Slide
17 66, which is on the MOA for kidney cancer. And again,
18 both here and in the document, with regard to the MOA,
19 I think that the slide as well as the document seems
20 to present it in a more definitive manner than really
21 the data supports. DCVC has been clearly demonstrated
22 to be a mutagen, but it's fairly weak. And it is the
23 only metabolite that's been demonstrated to be
24 mutagenic. But as far as its relative quantitative

1 contribution, compared to what are the other
2 hypothesized mechanism, which is repeated cycles of
3 cytotoxicity and repair and regeneration, that's
4 really unclear. So I just thought I wanted to make
5 those points. That was it.

6 **DR. KEITH JACOBS:** Thank you.

7 **DR. KENNETH PORTIER:** Thank you, Dr.
8 Lash.

9 **DR. KEITH JACOBS:** These are important
10 clarifications and will help us -- as you said, we'll
11 discuss later in the week, but will help us in our
12 edit of the document as we move forward.

13 **DR. KENNETH PORTIER:** Thank you. Let
14 me go back to Dr. Cobb and see if he's able to unmute.
15 Somebody mentioned you may need to unmute your phone
16 and unmute WebEx. Dr. Cobb?

17 **DR. GEORGE COBB:** Am I here?

18 **DR. KENNETH PORTIER:** I see you
19 unmuting. Now, I've got you. Thank you. We can hear
20 you.

21 **DR. GEORGE COBB:** Okay. Thank you. So
22 I have several questions. I think I'm just going to
23 tick through them quickly and maybe we can come back

1 to them in discussion because I don't want to keep
2 things from moving along.

3 My first question was how EPI Suite
4 handled the density of TCE and how that might make
5 things move to the bottom rather than the top of the
6 water column and if whether that had any effect on
7 whether EPI Suite considered that at all? Also, on
8 the river runs and the monitoring data, I was really
9 pleased to see the monitoring data. But the hydraulic
10 connectivity between those sites, I have some question
11 about how that was handled or how that was assured to
12 make sure that you weren't simply monitoring
13 background instead of downstream concentrations.

14 I also would like some explanation, or
15 some discussion at some point, of how the Detoro
16 (phonetic) article was used in the probabilistic
17 assessments to actually get concentrations that were
18 compared to the toxicity values because how you
19 actually choose a value out of that distribution is
20 important. And I think I'll leave the rest for later.
21 I at least wanted to tick those through and get them
22 on the discussion.

23 **DR. KENNETH PORTIER:** EPA, do you want
24 to tackle any of those?

1 **DR. KEITH JACOBS:** Can you clarify what
2 the specific questions is or was it more just
3 comments?

4 **DR. GEORGE COBB:** Well, the first
5 question is how does EPI Suite handle the density of
6 the compound, if at all? Because if TCE is not
7 miscible with the water that it enters, it will end up
8 at the bottom where it combines sediments more
9 readily, and if it's simply soluble in the water
10 column? That's the first question.

11 **MR. WEN-HSIUNG LEE:** This is Wen. I'm
12 the predecessor. Yeah. For EPI Suite, we used the
13 structure. So we used the simulation to do all the
14 estimates. But whenever we have some kind of good
15 data from the study, like density -- like that
16 endpoint and solubility, we put it into EPI Suite as
17 well. And I know the density of 1.4 is a sinker -- we
18 consider a sinker. And for this kind of calculation
19 and exposure, we do not use that. We just use the
20 solubility that is 1.3 grams per liter.

21 So for this kind, we're thinking about
22 (inaudible) and all are set into the sediment. I did
23 not calculate it using EPI Suite. We just used the
24 kind of -- most I used EPI from the structure. We do

1 all the calculates, include on STP model that's for
2 estimating and the distribution in the water.

3 And for our EPI Suite modeling, we just
4 find out it's most of them, it just vaporized -- yeah
5 -- it's in the air. So only very limited we estimated
6 were treated with water treatment. Most of them are
7 just -- yeah -- close to the volatility, just change
8 into air. So we do not have an estimate. We consider
9 this a kind of sinker, the kind of phenomena.

10 **DR. GEORGE COBB:** Yeah. That's kind of
11 what I thought. And I guess the next big question is,
12 when you have a monitoring value in a stream, how are
13 you certain that that monitoring value in the stream
14 is actually downstream of a TCE source that's being
15 modeled in the assessment?

16 **MR. WEN-HSIUNG LEE:** Yeah. This maybe
17 I need to answer about exposure. If the exposure
18 folks calculate the distribution of the concentration
19 because our model -- E-FAST did not have the fate
20 property still inside. And if you have some kind of
21 certain kind -- the absorption to soil, it was
22 different from the release point from up the stream or
23 down the stream will be different. But we do not have

1 the -- we did not use the model that can include this
2 kind of fate properties.

3 **DR. KEITH JACOBS:** Stephanie, can you
4 chime in on this to help clarify?

5 **MS. STEPHANIE SARRAINO:** Yes. So as
6 far as whether or not monitoring data could be
7 associated with the releasing sites, we did do --
8 there was an attempt to do a geospatial analysis
9 aligning or seeing if there was alignment between any
10 of the monitored values from literature against some
11 of the facilities that were modeled. There was not
12 much alignment at all in our assessment. And the
13 geospatial analysis is in the document, and I can try
14 to get more details for you as we go on that. But
15 there was not much alignment in this case. There were
16 a couple cases where they were in the same watershed
17 unit or HUD. But there was not a strong association
18 with any of the monitoring sites being downstream,
19 which is why we regarded most of them as more
20 reflective of ambient water levels rather than the
21 near facility levels predicted by the modeling.

22 **DR. GEORGE COBB:** Right. Okay. And
23 that's what I thought, but then did you not use those

1 ambient concentrations as one of the reasons that you
2 were considering low or negligible risk?

3 **MS. STEPHANIE SARRAINO:** I may have to
4 pass -- defer that to our eco-toxicologist who did the
5 risk characterization. Kara, can you chime in on
6 that?

7 **MS. KARA KOEHRN:** Yeah. This is Kara.
8 So most of the monitoring data that we had in the
9 water quality portal was measuring ambient water. It
10 was not very close to facilities. Or if it was even
11 in the same watershed, it was very far downstream.

12 **DR. STANLEY BARONE:** He's asking the
13 same question over and over.

14 **MS. KARA KOEHRN:** Can you guys hear me?

15 **MS. STEPHANIE SARRAINO:** Yes.

16 **MS. KARA KOEHRN:** Yes. The exception
17 was one study from the published literature, U.S. EPA
18 1977, and that had near facility monitoring. It was
19 from a long time ago, but that was the exception to
20 the monitoring data that we had. So for most of the
21 monitoring data, we labeled that as ambient water
22 monitoring. And then that one study from 1977 was a
23 near facility monitoring study.

24 **DR. GEORGE COBB:** Okay. Thank you.

1 **MS. KARA KOEHRN:** Sure.

2 **DR. KENNETH PORTIER:** George, is that
3 all of yours?

4 **DR. GEORGE COBB:** Yes. That's it, Ken,
5 and thank you for bearing with me. I think what
6 happened was I actually hung the phone up by accident.
7 I pushed the hang up instead of mute button.

8 **DR. KENNETH PORTIER:** Yeah. It's fun.
9 Dr. Johnson?

10 **DR. MARK JOHNSON:** Yes. Thank you. My
11 question's in regard to Figure 3.2. I guess that's
12 the invertebrate and the fish species sensitivity
13 distribution. Am I correct in I think what I read
14 where it's a mix of median lethal and median sublethal
15 values on that distribution?

16 **MS. KARA KOEHRN:** Yeah. This is Kara.
17 So I tried to stick to just lethal values. The
18 exception is for invertebrates I used both lethal and
19 immobilization or mortality and immobilization because
20 it's very hard to tell the difference between the two.
21 So I would say, for the most part, it's mortality.

22 **DR. MARK JOHNSON:** Well, that's
23 important. If your immobilized or necrosis, you're

1 food, right? You're good as dead anyway, right,
2 potentially?

3 **MS. KARA KOEHRN:** Yeah. Exactly. And
4 just a note, we went back and forth on this, so we'd
5 be happy to have your comments on it. But we did have
6 some amphibian data that measured developmental
7 effects that we did not put in the specie sensitivity
8 distribution because we had mortality data for them,
9 too. And to stay consistent among the data, we tried
10 to stick to mortality or things measuring mortality.
11 So if you have other thoughts on that, please let us
12 know.

13 **DR. MARK JOHNSON:** Okay. Sure.
14 Another operational question, I don't have a whole lot
15 of experience with SSDs. I've seen them a lot but
16 never built one. How can you -- the EC of five, I'm a
17 correct in saying that you're 95 percent sure that the
18 median lethal values are covered in that distribution?

19 **MS. KARA KOEHRN:** That's right.

20 **DR. MARK JOHNSON:** Okay. Because it's
21 a percentage of the medians then?

22 **MS. KARA KOEHRN:** Yeah. So the HC05
23 we're thinking is a concentration that's protective of
24 95 percent of the species in the curve.

1 DR. MARK JOHNSON: Well, that's a
2 different -- we're saying something different, then, I
3 think, because --

4 MS. KARA KOEHRN: Oh, sorry.

5 DR. MARK JOHNSON: -- you're not really
6 protective. You're just looking at the distribution
7 of your median lethal values. So you're 95 percent
8 sure that the median lethal value is below that value
9 or above that value, excuse me?

10 MS. KARA KOEHRN: Yes, I think that's
11 correct.

12 DR. MARK JOHNSON: All right. Thank
13 you. That's all I have.

14 DR. KENNETH PORTIER: Thank you. Dr.
15 Doucette?

16 DR. WILLIAM DOUCETTE: Yes. I've just
17 got two clarification questions. One is following up
18 on Dr. Cobb's comment, and you mentioned some of the
19 monitoring data you considered ambience. So in other
20 words, it was quite a ways away from what you
21 perceived the source was going to be. And I'm
22 wondering then how can -- if TCE, according to all
23 your documentation is supposed to quickly volatilize
24 from the stream and not be an issue, how can I have

1 ambient concentrations of TCE in the monitoring data?
2 Is that question clear, or do you understand what I'm
3 getting at? It runs counter to the argument that TCE
4 would not stay in the surface water.

5 **MS. STEPHANIE SARRAINO:** Hi, yes, this
6 is Stephanie Sarraino. And we might have Wen, our
7 fate expert, also weigh in on this one. Most all of
8 the ones that we are referring to as ambient were
9 quite low. I believe averages were well below five
10 parts per billion or the MCL. There was, I think, one
11 study that showed up to 17 parts per billion. Some of
12 the monitoring data that did show higher levels were
13 from a 1976, I believe, or 1970s study near
14 facilities, which may be -- which were closer to what
15 we were predicting in the modeling. So I may need to
16 defer to the fate expert for anything more on that,
17 whether the level that we did show in the ambient
18 water of being below five parts per billion would
19 still comport with this observation that we're making
20 that you pointed out.

21 **DR. WILLIAM DOUCETTE:** Okay. Thank
22 you. One other question, and I'm just not sure where
23 this is addressed or if this is even appropriate to
24 address under this TSCA draft risk assessment. But

1 who would address surface water contamination that
2 comes from contaminated ground water seeping into a
3 surface water site? I've been at four or five
4 different sites where that was a concern. We actually
5 measured surface water concentrations that were the
6 result of contaminated ground water seeping into the
7 surface water. Is that under a different
8 jurisdiction, or is that something that would be
9 considered here?

10 **DR. STANLEY BARONE:** Dr. Doucette, this
11 is Stan Barone. Actually, you're raising an important
12 issue, but it is part of the regulatory nexus with our
13 sister offices and the other regulatory authorities
14 between our Office of Land and Emergency Response and
15 then also the Office of Water.

16 **DR. WILLIAM DOUCETTE:** Okay. I just
17 wanted to get that clarified. Thank you.

18 **DR. KENNETH PORTIER:** Thank you, Bill.
19 Dr. Apte?

20 **DR. UDAYAN APTE:** Hi, can you hear me?

21 **DR. KENNETH PORTIER:** Yes.

22 **DR. UDAYAN APTE:** Okay. My question is
23 about route of exposure. It seems that you see
24 significantly dissolved in the ground water. There

1 is, of course, volatilization of the surface water.
2 When you guys presented data on routes of exposure,
3 mainly concerned was dermal and inhalation route. And
4 oral route wasn't considered in the analysis. And I
5 was just a bit confused about, if the groundwater is
6 contaminated, why are we not looking at that?

7 **DR. KEITH JACOBS:** Are you talking
8 about general population human exposures, to clarify?
9 This is Keith Jacobs.

10 **DR. UDAYAN APTE:** Yeah. I think I'm
11 talking about general exposures.

12 **DR. KEITH JACOBS:** So general
13 populations, for the same reasons as Dr. Barone just
14 stated, was not part of this risk evaluation. It is
15 covered by other statutes. And we only evaluated
16 occupational and consumer exposure. And in
17 occupational and exposure scenarios, oral exposure is
18 not expected.

19 **DR. UDAYAN APTE:** That makes sense.
20 Thank you.

21 **DR. STANLEY BARONE:** Just to add to
22 that -- this is Stan Barone. You were kind of -- I
23 thought you were going to go to the vapor intrusion

1 issue. We are also not addressing vapor intrusion in
2 residential or occupational settings.

3 **DR. UDAYAN APTE:** Yeah. My question
4 was specifically on drinking water contamination. But
5 if you're thinking about occupational exposure, then I
6 understand the premise behind this.

7 **DR. KENNETH PORTIER:** Thank you. Dr.
8 Bennett? Dr. Bennett, you're on mute.

9 **DR. STEVEN BENNETT:** Ah. Let me try
10 that again. Sorry about that. I hit the wrong
11 button.

12 **DR. KENNETH PORTIER:** We can hear you
13 now.

14 **DR. STEVEN BENNETT:** Okay. Thank you.
15 The previous risk evaluation for TCE under the
16 workplan was completed and the proposed rules were
17 issued. But I'm trying to better understand how those
18 uses were incorporated into this current risk
19 evaluation. I think from the presentation you
20 indicated that they are considered completely from the
21 beginning, but I want to make sure that I completely
22 understand how they differentiate from how they're
23 previously evaluated. That's my first question.

1 **DR. KEITH JACOBS:** Are you asking if
2 they were included, the previous uses, or specifically
3 laying out the differences?

4 **DR. STEVEN BENNETT:** What I want to try
5 to understand is how they were evaluated this time
6 versus previously. So in other words, were they
7 building off of what they were done previously, or was
8 this a completely new evaluation under the new
9 parameters of reformed TSCA? I guess that's my -- I
10 think it's the later, but I just want to make sure I'm
11 clear on that.

12 **DR. KEITH JACOBS:** Well, our engineer,
13 Franklyn Hall, can talk specifically about the
14 occupational and Stephanie can talk specifically about
15 the consumer.

16 **DR. STANLEY BARONE:** But the -- this is
17 Stan Barone. The short answer to your question, Dr.
18 Bennett, is the later. Yes, these are considered
19 under the new TSCA requirement. The previous
20 conditions of use that were in the 2015 final risk
21 assessment on TCE are overlapping with the conditions
22 of use that are in this risk evaluation. And there
23 are more conditions of use. We have additional

1 monitoring and modeling that was not in the previous
2 risk assessment that are presented here.

3 **DR. STEVEN BENNETT:** Okay. Thank you.
4 And anyone else have any additional add on that? But
5 I think that covers that. The other piece were
6 indications that I believe roughly 80 -- I believe
7 recorded 83 percent of the TCE is used for processing
8 of the intermediate for formation of HFC134A. Have
9 you incorporated any of the changes to HFC134A
10 production post 2015-2016, given that that is, I'll
11 say, partially -- well, it was banned under the SNAP
12 rule, under the Clean Air Act program? But I think
13 those would be significant changes, even in the market
14 you stated where you report the IHS data from 2014
15 versus 2017. There's a notable shift in the
16 percentage of that. But I just wondered if there's
17 any lessons or any pieces that will be either
18 incorporated or whether that was something that would
19 be updated in the final version of the risk
20 evaluation?

21 **DR. STANLEY BARONE:** Dr. Bennett, we'll
22 have to follow up with you on that. We need to do a
23 little bit of conferencing amongst the team with our
24 economist and risk management group as well.

1 DR. STEVEN BENNETT: All right. Thank
2 you.

3 DR. KENNETH PORTIER: Thank you. I see
4 that Dr. Doucette, Dr. Cobb, and Dr. Bennett and Dr.
5 Apte still have their hands up. I'm assuming Dr.
6 Bennett's going to get around to putting his hand down
7 and Dr. Apte's put his down. Dr. Cobb, did you want
8 to have a follow-up question? Nope? Dr. Cobb, if you
9 have a question -- there we go. You're unmuted.

10 DR. GEORGE COBB: No, I don't have a
11 question. I'm trying to put my hand down right now.

12 DR. KENNETH PORTIER: So, Dr. Cobb,
13 before you go, Dr. Grant mentioned that you missed one
14 of your three questions. You didn't follow up on it.

15 DR. GEORGE COBB: There's more
16 discussion about that, and that's more a discussion
17 point than any clarification from the Agency at this
18 point, I think.

19 DR. KENNETH PORTIER: Okey-doke.

20 DR. GEORGE COBB: Is that okay?

21 DR. KENNETH PORTIER: Yeah. That's
22 good. We'll just keep that for the question
23 discussion. Anyone else on the panel wish to comment
24 at this point? Dr. Johnson?

1 **DR. MARK JOHNSON:** Yeah. Ken, this is
2 Mark. Just another quick question regarding the value
3 that was chosen from Figure 3.2. Actually, as I
4 understand it, the figure -- the value used to address
5 acute effects of aquatic organisms was not based on
6 the HC05. It was based on the EC20. Is that correct?
7 It was growth of fish, I believe.

8 **MS. KARA KOEHRN:** This is Kara. So the
9 acute value was based on a geometric mean of the
10 aquatic invertebrates. I think there were three
11 species, and a geometric mean was taken of those three
12 species because that taxa was the most sensitive to
13 acute exposures. If I had taken the HC05 from the
14 SSB, it would have been less protective. So because
15 the three aquatic invertebrates were the most
16 sensitive species on the curve, we decided to use the
17 more protective value.

18 The SSB is still valuable because it
19 shows the various sensitivities. But the aquatic
20 invertebrates are clearly on the lower left-hand part
21 of the curve showing more sensitivity, and then the
22 amphibians and fish are sort of distributed
23 throughout. And just to follow up on the previous
24 question about fish sensitivities, it was the EC20

1 from a chronic study that was used for the chronic
2 COC. It was based on fathead minnows. And if you
3 look at the acute SSB, fathead minnows are the second
4 most sensitive fish species.

5 **DR. MARK JOHNSON:** Okay. And so an
6 EC05, the value isn't a whole lot different than --
7 and the geometric means you calculated wasn't between
8 a NOEC and a LOEC, right?

9 **MS. KARA KOEHRN:** Right. No, it was
10 three EC50s.

11 **DR. MARK JOHNSON:** Okay. So why do you
12 think that a geometric mean would be the way to go to
13 harmonize those three values, not a arithmetic mean?

14 **MS. KARA KOEHRN:** Well, they were all
15 pretty close, and our policy is to use a geometric
16 mean to use appropriate weighting between the three
17 values. And yeah. I guess it's just a nice -- the
18 SSB HC05 is a good second line of evidence showing
19 that the values weren't too far away from each other.

20 **DR. MARK JOHNSON:** Yeah. I totally
21 agree. Why not just take the lowest EC50?

22 **MS. KARA KOEHRN:** We could, and you
23 could definitely suggest that. We were trying to
24 integrate all the data we had. And because all three

1 values were pretty close, we thought that we would
2 have more confidence in a value that represented three
3 species than simply taking the most sensitive one.

4 **DR. MARK JOHNSON:** Okay. Thanks.

5 **MS. KARA KOEHRN:** Yeah.

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

7 Anyone else on the committee have a comment, a
8 clarifying question? We have a few more minutes,
9 about 15 more minutes allocated to this discussion.

10 **DR. THOMAS ROSOL:** Yeah. Ken, this is
11 Tom Rosol. I have a question, please.

12 **DR. KENNETH PORTIER:** Yeah. Tom?

13 **DR. THOMAS ROSOL:** Yeah. This relates
14 to genotoxicity. I was curious. Did the EPA consider
15 using a weight of evidence approach for the
16 genotoxicity such that a table was generated that
17 lists all the in vitro and -- published in vivo and in
18 vitro genotoxicity assays for TCE and metabolites and
19 then considered that in the deliberation? And then
20 also for the kidney MOA, I was wondering why GSH
21 intermediates were restricted to the kidney MOA and
22 not considered for cancers and other organs,
23 particularly the liver. Thank you.

1 **DR. STANLEY BARONE:** This is Stan
2 Barone. We're sort of getting into the discussion of
3 the MOA. But in brief, we have heard from the
4 committee before about tabulating the genetic tox
5 data, both in vitro and in vivo, and are pursuing that
6 recommendation. We did not have that tabulate
7 information for the draft assessment. But that is
8 definitely something worthy of your recommendation.

9 On the other part of the conversation
10 with regard to GSH metabolites and other targets, in
11 our systematic review, we looked for literature and
12 did not find anything that was dispositive for a
13 mutagenic mode of action or GSH related metabolites
14 and other organs or other targets. And we speak to
15 that in the risk evaluation, but we actually don't
16 have direct evidence for that. So the strongest
17 evidence that we cite is for the kidney, and that's
18 why we focused there.

19 **DR. KEITH JACOBS:** This is Keith
20 Jacobs, just adding on to your second question. The
21 processing of the conjugative metabolites into those
22 reactive species primarily occurs in the kidney.
23 That's my understanding, and that is why the kidney is
24 the primary source of where those have an effect.

1 DR. THOMAS ROSOL: Thank you very much.

2 DR. KENNETH PORTIER: Thank you. Dr.
3 Lash, do you have another follow up comment/question?

4 DR. LAWRENCE LASH: Yeah. Not really a
5 question, I was just going to briefly comment. I know
6 we don't want to maybe get into this in detail but
7 just to address the comment about the MOA and
8 genotoxicity. I would just add that, for DCVC --
9 well, there's two points. The only data that suggests
10 that -- where it's cancer is kidney, where DCVC is the
11 penultimate metabolite. So it's only relevant for
12 that in terms of how the metabolism occurs and the
13 metabolites are distributed. But there actually are
14 several papers that relate to female reproductive
15 toxicity where it's thought that glutathione derive
16 metabolites do play a role. And those were actually
17 omitted -- I comment on that later -- from the
18 document. So that was all I wanted to say, just to
19 clarify.

20 DR. KENNETH PORTIER: Thank you. Dr.
21 Pessah?

22 DR. ISAAC PESSAH: Yes, thank you. I
23 was just wondering. This pertains solely to cancer
24 MOA -- the statement from Dr. Barone -- or extents to

1 noncancer MOA, about the glutathione issue? Because
2 there is some literature on glutathione in the brain,
3 but we can discuss that later.

4 **DR. KENNETH PORTIER:** Well, that
5 sounded like a clarifying question. EPA?

6 **DR. STANLEY BARONE:** So with regard to
7 -- this is Stan Barone again. With regard to Dr.
8 Pessah's comments, my response was to the cancer mode
9 of action, clarification of the cancer mode of action.
10 We did not include an extensive mode of action
11 discussion for noncancer.

12 **DR. ISAAC PESSAH:** Okay. We can get
13 there later, I guess. Thank you.

14 **DR. KENNETH PORTIER:** Yeah. Any
15 additional comments from the panel, clarifying
16 questions? Unmute and ask.

17 **DR. MARK JOHNSON:** Dr. Portier, this is
18 Mark Johnson again. One other quick question. It's
19 mentioned that there's lots of, I guess, high quality
20 mechanistic information supporting fetal cardiac heart
21 malformations. When I looked through the text, what I
22 saw was just some references to genomic information.
23 Having seen some of those data, that can be incredibly
24 confusing. It's difficult alone just to do the

1 statistics with it. So I was wondering could you
2 speak more to the high-quality mechanistic information
3 that points to TCE causing fetal cardia heart
4 malformations?

5 **DR. KEITH JACOBS:** This is Keith
6 Jacobs. So the weight of evidence data is presented
7 in one of the appendices. It might be G, but I don't
8 have the document in front of me. The full weight of
9 evidence break down is presented in G. And then the
10 study by study assessment where we actually have a
11 written evaluation for each of those three metrics,
12 the reliability, the relevance, and the strength, is
13 in one of the supplemental files. It's an excel
14 document where we go through every single study. So
15 that might be where you can get the information you're
16 looking for if you want to review the individual study
17 by study assessment. And then the overview is in
18 Appendix G.

19 **DR. MARK JOHNSON:** Okay. Well, I'll go
20 back to Appendix G and take another look. I was just
21 curious if you knew exactly what molecules was
22 responsible and what kind of things had to happen to
23 cause that. And I didn't see that in the DRE, but
24 I'll go back again and look. Thank you.

1 **DR. KEITH JACOBS:** So are you talking
2 about a specific mechanisms or just a discussion of
3 the studies and mechanistic information available?

4 **DR. MARK JOHNSON:** I did not see a
5 specific mechanism. That's what I was lacking.

6 **DR. KEITH JACOBS:** Okay. There is --
7 it's unclear on if there's any specific overarching
8 mechanism. It's more likely that it's a constellation
9 of mechanisms and different things going on. But
10 there is a -- we do touch on that in the actual body
11 of the assessment, in the weight of evidence for the
12 cardiac, right after we present the kind of overview
13 synopsis of the weight of evidence conclusion. There
14 is a paragraph or two about potential mechanisms and
15 mechanistic information. And then, again, you'll see
16 more breakdown of the actual weight of evidence for
17 those in the appendix and the supplemental file.

18 **DR. MARK JOHNSON:** Okay. Let me ask a
19 clarifying question, then. It sounds like we have a
20 body of evidence that supports that TCE could cause
21 fetal cardiac heart malformations. But we still lack
22 a mechanism that defines it. Would that be accurate?

23 **DR. KEITH JACOBS:** There is a lack of
24 any specific individual mechanism that is definitive.

1 There are potential for several contributing
2 mechanisms that may act additively or independently.

3 **DR. MARK JOHNSON:** Okay. Thank you.

4 **DR. KENNETH PORTIER:** I think I'll make
5 a last call for any clarifying question from the
6 panel. Dr. Grant, I see your hand's up.

7 **DR. STEPHEN GRANT:** Yeah. May I just
8 make a suggestion that, if we are going to add a table
9 of data supporting genotoxicity, this cardia defects
10 question is in the same realm and always a huge --
11 pages of text can be condensed into a table where
12 possible, even though we don't have a mechanistic
13 link. It might be a good idea to be able to look at
14 the breadth of data altogether rather than going to
15 appendices or supplemental files.

16 **DR. KENNETH PORTIER:** So Dr. Grant,
17 that sounds like a good comment for the last question
18 where we talk about the content of the report. Make a
19 note. Bring it back up again. Anyone else? I don't
20 see or hear anyone. At this point, I have 12:53
21 Eastern Time, and we're a little bit ahead of our
22 break. But I think I'll go ahead and break for lunch.
23 And we will return at -- let's return at 1:40. It may

1 take us a few minutes to get back together and make
2 sure we've got everyone on the line.

3 So let's return at 1:40 Eastern and
4 begin the public comment. Those members of the public
5 that are scheduled to speak before the panel, we're
6 aware of you. Many of you have provided slide
7 material that we'll be able to display. And at this
8 time, I'll just remind others that you need to contact
9 the DFO, Todd Peterson, if you wish to speak. But I
10 think our timeframe for public comments is pretty full
11 at this point.

12 **DR. TODD PETERSON:** Yeah. Ken, I'll
13 just --

14 **DR. KENNETH PORTIER:** So let's break
15 and return at 1:40. Yeah. Todd?

16 **DR. TODD PETERSON:** Yeah. This is Todd
17 Peterson. I concur. 1:40 is a good time. That'll
18 give us several minutes for us to do the roll call to
19 make sure all the reviewers are online. And I just
20 sent a note out to all the public commenters to have
21 them make sure that they'll be available a minute or
22 two early. So actually, when we get to the public
23 comments, we'll be right on track and on schedule with

1 the 1:45 agenda time. So go have a good lunch, and
2 we'll see you back a one four zero p.m. Eastern Time.

3 **DR. KENNETH PORTIER:** Dr. Apte, I see
4 your hand's up.

5 **DR. UDAYAN APTE:** Yeah. Just quick
6 question, is it okay to log out and log back in or
7 should we remain on the call?

8 **DR. KENNETH PORTIER:** So don't log out
9 of the WebEx. If your phone hangs up, like mine did
10 earlier, you click on the phone icon, or you click on
11 the communicate button and ask WebEx to dial you back
12 in, to call you back on your number to reestablish the
13 connection. I'm going to just let my phone be
14 connected for the whole time. Just a reminder, there
15 is a lot of pressure on the internet and on WebEx
16 right now. So if you do hang up, you may not be able
17 to easily get back in again. That's an issue. But
18 remember, if you do hang up or get hung up, please use
19 the WebEx call in option to reconnect. That way I see
20 you as a panelist, and I can see your hands going up
21 and down. Okay. Let's break. Thank you.

22
23 (BREAK)

PUBLIC COMMENTS

DR. TODD PETERSON: Okay. So let's open up the afternoon session, and you go ahead and do the roll call. And when you're all set, let me go ahead, and I will help coordinate the oral commenters.

DR. KENNETH PORTIER: Fine. Dr. Anderson, are you in? Dr. Bennett?

DR. STEVEN BENNETT: I'm here.

DR. KENNETH PORTIER: Thank you. Dr. Barton? Dr. Blystone?

DR. SHERI BLYSTONE: I am here.

DR. KENNETH PORTIER: Dr. Bruckner? Dr. Bruckner? Dr. Cory-Slechta?

DR. DEBORAH CORY-SLECHTA: I'm here.

DR. KENNETH PORTIER: The rest of you should probably unmute your phones so we can quickly go through this. And then we can mute it after. Dr. Davies?

DR. HOLLY DAVIES: Yes, I'm here.

DR. KENNETH PORTIER: Dr. Doucette?

DR. WILLIAM DOUCETTE: Yes, I'm here.

DR. KENNETH PORTIER: Dr. Jimenez-Gonzalez?

1 DR. CONCEPCION JIMENEZ-GONZALEZ: Here.

2 DR. KENNETH PORTIER: Thank you. Dr.

3 Gilbert?

4 DR. KATHLEEN GILBERT: I'm here.

5 DR. KENNETH PORTIER: Dr. Johnson?

6 DR. MARK JOHNSON: I'm here.

7 DR. KENNETH PORTIER: Dr. Kaufman?

8 MR. ALAN KAUFMAN: Here.

9 DR. KENNETH PORTIER: Dr. Kissel?

10 DR. JOHN KISSEL: Here.

11 DR. KENNETH PORTIER: Dr. Rowlands?

12 DR. CRAIG ROWLANDS: Here.

13 DR. KENNETH PORTIER: Dr. Schlenk?

14 DR. DANIEL SCHLENK: Here.

15 DR. KENNETH PORTIER: Dr. Apte?

16 DR. UDAYAN APTE: I'm here.

17 DR. KENNETH PORTIER: Dr. Cobb? Dr.

18 Cobb? Dr. Grant?

19 DR. GEORGE COBB: I'm here, Ken. Can
20 you hear me? Can you hear me?

21 DR. KENNETH PORTIER: Who is that, Dr.
22 Grant or Cobb?

23 DR. GEORGE COBB: Yeah. George Cobb.

24 DR. KENNETH PORTIER: George. Okay.

1 DR. STEPHEN GRANT: Grant here.

2 DR. KENNETH PORTIER: Dr. Grant?

3 DR. STEPHEN GRANT: Here.

4 DR. KENNETH PORTIER: Hossain?

5 Jenkins?

6 MS. ALLISON JENKINS: Here.

7 DR. KENNETH PORTIER: Lash?

8 DR. LAWRENCE LASH: I'm here.

9 DR. KENNETH PORTIER: Dr. Morandi?

10 DR. MARIA MORANDI: Here.

11 DR. KENNETH PORTIER: Dr. Morris?

12 DR. JOHN MORRIS: I'm here. Dr.

13 Morris.

14 DR. KENNETH PORTIER: Got it. Dr.

15 Pessah? Dr. Rosol?

16 DR. ISAAC PESSAH: Sorry. I'm here.

17 Pessah is here.

18 DR. KENNETH PORTIER: Okay. Dr. Rosol?

19 Dr. Vorhees? We're missing Rosol, Vorhees, Dr.

20 Anderson. I know he's been teaching. Dr. Barton?

21 DR. CHARLES BARTON: I'm here. I
22 couldn't get my phone off mute earlier.

23 DR. KENNETH PORTIER: Got it. Okay.

24 Well, we have a quorum. Todd, do you want to proceed

1 with introducing the public commenters and we'll
2 scroll up their slides?

3 **DR. TODD PETERSON:** Okay. So I did
4 send out a couple communications to the oral
5 commenters, so they know the order that they'll be
6 speaking in. And that order was determined by when
7 people made requests. There was no other particular
8 reason for the order, and that's how that was
9 determined, in case anyone's curious. And I sent out
10 a couple of notes, and one of them was I'll announce
11 the first person. We'll make sure that you're on the
12 line. So the WebEx crew, if they can bring up the
13 slides for Jennifer McPartland. We'll make sure the
14 slides are there. Okay. And Jennifer McPartland, are
15 you on the line?

16 **DR. JENNIFER MCPARTLAND:** I am on the
17 line. Can you hear me?

18 **DR. TODD PETERSON:** I can.

19 **DR. JENNIFER MCPARTLAND:** Great.

20 **DR. TODD PETERSON:** Let me do one other
21 thing for fairness. Let me set up my timer. I didn't
22 do that ahead of time. All right. So you're ready.
23 You're slides are ready. Remember to say "next slide"

1 when you want the team here to advance it. And you
2 may start. You have five minutes.

3 **DR. JENNIFER MCPARTLAND:** Perfect.

4 Thank you. Good afternoon. I am Dr. Jennifer
5 McPartland, Senior Health Scientist at Environmental
6 Defense Fund. I must open my remarks by expressing
7 utter dismay at the Agency's decision to hold this
8 meeting in light of the COVID-19 pandemic and the very
9 real burden it is putting on individuals and
10 communities across the country, including SACC
11 members, who as a result are unable to fully and
12 meaningfully participate today. Next slide.

13 My comments focus on our concerns with
14 the human health hazard assessment of the draft risk
15 evaluation. The most significant and consequential
16 flaw is EPA's decision to make determinations of acute
17 and chronic risks based on immune related endpoints.
18 EPA relied on a 2010 study by Selgrade and Gilmour to
19 derive the point of departure for acute noncancer
20 risks and a 2009 study by Keil et al for chronic
21 noncancer risks. It is worth emphasizing that
22 mortality is the endpoint used from the Selgrade and
23 Gilmore study. Next slide.

1 EPA's use of immune related endpoints
2 is at odds with previous Agency TCE assessments,
3 including the 2011 IRIS toxicological review and the
4 2014 OPPT workplan risk assessment. Both assessments
5 base TCE risks on fetal cardiac malformations, the
6 most sensitive endpoint. TCE induced fetal cardia
7 malformations are supported by several scientific
8 studies across multiple lines of evidence, including
9 epidemiological, animal, and mechanistic.

10 Indeed, EPA's draft in the case that
11 this endpoint is supported by the weight of the
12 scientific evidence. EPA also correctly maintains
13 that the Johnson et al 2003 study remains appropriate
14 for characterizing risk of fetal cardia malformations.
15 However, when reaching its determinations of risk, EPA
16 switched endpoints as documented in an in-depth
17 investigation by Elizabeth Shogren of *Reveal News*.
18 Extensive revisions made to EPA's draft after White
19 House intervention resulted in determinations of risk
20 based on immune related effects rather than fetal
21 cardiac malformations. Next slide.

22 EPA and other scientific authorities
23 have repeatedly examined and reaffirmed the fetal
24 cardiac effects. This slide provides a snapshot of

1 these extensive reviews, and I will not belabor all
2 these reviews, just to leave it at this is a topic --
3 this is an issue that has been examined repeatedly by
4 scientific experts. Next slide. The ACC and HSIA
5 funded study by Charles River Laboratories,
6 subsequently published by DeSesso et al, does not only
7 not negate findings from Johnson et al 2003, it has
8 serious shortcomings, including using an insensitive
9 heart dissection methodology, downplaying observed
10 ventricular septal defects, and ignoring extensive
11 literature showing fetal cardiac effects below 1,000
12 parts per million. Next slide.

13 EPA's reliance on the TSCA systematic
14 review method remains fundamentally flawed. It's use
15 of numerical study scoring defies consistent
16 recommendations in the field of systematic review,
17 including those made in the 2014 Academies review of
18 the IRIS program. Such scoring plays a particularly
19 nefarious role in this draft, whereby EPA claims the
20 evidence for fetal cardiac defects are of medium
21 quality while that for immune effects is of high
22 quality, leaving EPA to rely on risk estimates orders
23 of magnitude less than should be the case.

1 EPA's reliance on Whycap (phonetic) et
2 al 2018 as part of its rationale is flawed. Among
3 other concerns, this paper grossly distorts the
4 national toxicology program's OHAT risk of bias tool
5 to erroneously assert that the Johnson study has
6 greater risk of bias. We discuss other flaws in this
7 publication extensively in our written comments. Next
8 slide.

9 EPA acknowledges a wide variety of
10 potentially exposed or susceptible subpopulations in
11 the draft. However, EPA should explicitly acknowledge
12 the following additional groups that represent key
13 susceptible subpopulations: individuals with
14 compromised liver or kidney function; individuals with
15 cardiac arrhythmias; individuals co-exposed to
16 chemicals that interact with TCE metabolisms,
17 including chlorinated hydrocarbons, which commonly co-
18 occur in drinking water and phenobarbital, a
19 medication used to treat epilepsy. Thank you.

20 **DR. TODD PETERSON:** Okay. Thank you
21 very much. And I'll turn off the timer. I just had -
22 - let's see. Come on. All right. Excuse me. I just
23 had an email about a couple of the commenters don't
24 seem to be on the line. And what I mentioned in the

1 email is we'll go down the list. If somebody's not on
2 the line, we will go back and make sure that we go
3 down and get everybody called at least twice. So the
4 next set of the slides for the host, can you please
5 put up the slides for Richard Denison? And is Richard
6 Denison on the line?

7 **DR. RICHARD DENISON:** Yes, I am, Dr.
8 Peterson.

9 **DR. TODD PETERSON:** Okay. So slides
10 are there. Say next slide when you want to advance,
11 and we'll start you right now.

12 **DR. RICHARD DENISON:** Thank you. I'm
13 Dr. Richard Denison with EDF. TSCA requires that the
14 SACC include representatives that have specific
15 scientific expertise in the relationship of chemical
16 exposures to women and children, as well as other
17 potentially exposed or susceptible subpopulations.
18 Such expertise is especially relevant to TCE. This
19 panel has only two medical doctors.

20 If they, or others, with this expertise
21 cannot attend all parts of this virtual meeting
22 because, for example, they are on the frontlines of
23 the COVID-19 crisis, then holding this meeting they
24 violate both TSCA and FACA's balance requirement.

1 EPA's insistence on proceeding with this meeting is
2 deeply disrespectful of those panelists and, for that
3 matter, the entire panel. And it will lead to a
4 compromised peer review of a critical risk evaluation.
5 Next slide.

6 EPA has made three decisions that
7 deviate from scientific best practices, defy
8 requirements under the law, ignore longstanding Agency
9 policy, and are not sufficiently health protective,
10 including of pregnant women, infants, children, and
11 workers. Each decision is directly relevant to the
12 SACC's charge as each of them results in serious
13 underestimations of TCE's risks. Next slide. First,
14 EPA has failed to base its risk assessment on the most
15 sensitive endpoint and the most sensitive
16 subpopulation.

17 Instead, EPA relies on its 500-fold
18 less sensitive endpoint that is also not the most
19 relevant to the most sensitive subpopulations. This
20 unprecedented decision contradicts multiple previous
21 Agency assessments of TCE, Agency guidance, and expert
22 advice of the NAS to use the most sensitive endpoint
23 and protect the most sensitive group.

1 Our written comments identify these
2 strong precedents that EPA is now casting away. EPA's
3 decision also flouts TSCA's requirement to protect
4 vulnerable subpopulations, explicitly including
5 pregnant women and children. EPA's choice of this
6 endpoint does not adequately identify or protect
7 against risks for these subpopulations. If EPA
8 protects against the most sensitive endpoint, then
9 we'll also generally protect against other effects.
10 In contrast, EPA asserts without a shred of evidence
11 that it expects that addressing risks from immune
12 effects would address other identified risks. EPA
13 should be ashamed of itself. Next slide.

14 EPA has again assumed that workers
15 throughout the value chain and lifecycle will use
16 universally effective PPE in almost all cases. EPA
17 presents no supporting evidence and ignores
18 significant evidence to the contrary. Worker exposure
19 to TCE in the absence of PPE must be considered
20 reasonably foreseen, at a minimum. EPA does find
21 unreasonable risk for most conditions of use, but it
22 has dramatically underestimated the magnitude of that
23 risk by assuming PPE.

1 As a result, it may well forgo it's
2 only opportunity to ensure that the PPE it assumes
3 will actually be used. EPA's decision flouts the
4 long-established industrial hygiene hierarchy of
5 controls, which puts PPE as the last resort. And it
6 flouts TSCA's requirements to rely on the best
7 available science and provide special protection for
8 workers. An analysis that we provide to the SACC
9 shows that EPA's assumption underestimates acute risks
10 from TCE by an average of 16-fold and acute inhalation
11 risks by 50-fold. Next slide.

12 EPA again applies a cancer risk
13 benchmark up to two orders of magnitude less
14 protective than warranted. By allowing cancer risks
15 as high as one in 10,000, EPA contravenes TSCA by
16 providing far less protection to workers and the
17 general population, let alone other vulnerable
18 populations. EPA cites policy and practice under
19 other laws and by other agencies, ignoring the fact
20 that those standards differ fundamentally from TSCA's.

21 EPA failed to identify unreasonable
22 risk from its estimate in at least 11 occupational
23 exposure scenarios that even a one in 100,000 cancer
24 benchmark would have flagged. And where EPA did

1 identify such unreasonable risk use its lax benchmark,
2 it understated the magnitude of the cancer risk and
3 the needed reduction in exposure by at least tenfold.
4 Thank you.

5 **DR. TODD PETERSON:** Okay. Thank you
6 very much. And the next person we have on the list is
7 Lindsay McCormick, and there are slides. Host, can
8 you pull up the slides for -- okay. There we go.
9 Lindsay McCormick, are you on the line?

10 **MS. LINDSAY MCCORMICK:** I am. Can you
11 hear me?

12 **DR. TODD PETERSON:** Yes. And you may
13 start now.

14 **MS. LINDSAY MCCORMICK:** Good afternoon.
15 I'm Lindsay McCormick with Environmental Defense Fund.
16 I must also start by expressing my deep concern that
17 EPA has insisted on holding this peer review meeting
18 during a time of national emergency from COVID-19.
19 Some SACC members were not able to be here today, and
20 so others likely unable to prepare sufficiently, given
21 competing personal and professional priorities. With
22 that said, I will discuss four significant areas of
23 concern with EPA's draft. Next slide.

1 First, EPA has inappropriately excluded
2 all general population exposures to TCE, asserting
3 without support that they have been assessed and
4 effectively managed under other laws. Aside from the
5 absent legal basis, these exclusions prevent
6 significant health concerns and mean that EPA has
7 failed to comprehensively evaluate exposures to TCE.
8 For example, when TCE is regulated as a hazardous air
9 pollutant under the Clean Air Act, those standards are
10 set for individual source categories and even by EPA's
11 own account do not eliminate risk to exposed
12 populations.

13 Exposures from multiple sources in
14 combination are never considered. The releases and
15 exposures EPA ignores are far from trivial. Despite
16 the existing regulations under other laws EPA relies
17 on, facilities still release two to three million
18 pounds annually of TCE into the air, water, and land.
19 EPA's approach effectively pretends this quantity is
20 zero.

21 This is particularly troubling for TCE,
22 which is one of the most pervasive and toxic chemical
23 pollutants in our environment. EPA and ATSDR have
24 documented the following key exposure pathways:

1 outdoor air, indoor air and vapor intrusion,
2 groundwater and drinking water wells, food, and breast
3 milk and formula. Of note, TCE is one of the most
4 frequently detected chemical contaminants in
5 groundwater. Shallow private drinking and irrigation
6 wells are particularly vulnerable, and neither are
7 monitored or regulated by the Safe Drinking Water Act.
8 Next slide, please.

9 Second, EPA has failed to consider
10 those that face greater exposure due to their
11 proximity to conditions of use. On page 177, EPA
12 acknowledges that it has underestimated exposure to
13 consumers by failing to consider aggregate background
14 exposures in the assessment, specifically mentioning
15 populations living near facilities emitting TCE.
16 Despite this acknowledgement, EPA erroneously limits
17 its analysis of potentially exposed or susceptible
18 subpopulations to those that might face greater
19 susceptibility. With exception of workers and
20 consumers, EPA did not consider whether the general
21 population or specific subpopulations face a greater
22 risk due to greater exposure. Next slide, please.

23 Of particular concern, EPA does not
24 consider people who live or work near manufacturing,

1 processing, use or disposal sites or provide any
2 analysis of the extent to which they are at greater
3 risk. This includes people living near the 731 active
4 superfund sites containing TCE in the U.S. Next
5 slide, please.

6 Third, EPA's failed to assess how
7 exposure combines to increase risk. First, even from
8 single condition of use, EPA's failed to assess how
9 inhalation exposure and dermal exposure combine. EPA
10 quickly dismisses this approach by invoking, quote,
11 "uncertainties present in the current exposure
12 estimation procedures," end quote. EPA's decision not
13 to apply an additivity approach because of
14 uncertainties will necessarily result in an
15 underestimate of exposure and, thus, risk. Second,
16 EPA also failed to combine any exposures for multiple
17 conditions of use. Instead, EPA looked at each
18 condition of use separately and never considered the
19 possibility the same person may be exposed to TCE
20 through multiple conditions of use. Next slide,
21 please.

22 Fourth, EPA also erroneously invokes
23 uncertainty to dismiss unreasonable risk to the
24 environment. Among the numerous flaws in EPA's

1 environmental assessment, EPA's own analysis found
2 excessive risk to aquatic organisms from 521
3 facilities, in one case exceeding the concentration of
4 concern by 1,000-fold. But EPA dismisses the actual
5 unreasonable risk it found merely by invoking
6 uncertainty. Even had EPA not actually found risk,
7 uncertainties in EPA's analysis should counsel in
8 favor of finding unreasonable risk. Uncertainty
9 increases the chance of unreasonable risk and does not
10 diminish them. Thank you for the opportunity to
11 comment.

12 **DR. TODD PETERSON:** Okay. Thank you.
13 The next person I have on the list is Eleni Kapatou,
14 and are you on the line? We don't seem to see you in
15 the list at the moment. Okay. I will get an update
16 from the host should this presenter join us. So the
17 next individual who requested to make an oral comment
18 is Nicholas Chartres, and he has some slides. Can you
19 bring up the slides? There we go. So is Nicholas
20 Chartres on the line, please?

21 **DR. NICHOLAS CHARTRES:** Yes, I'm here.
22 Thank you.

23 **DR. TODD PETERSON:** Okay. You may
24 start when you're ready.

1 **DR. NICHOLAS CHARTRES:** Good morning.

2 My name is Nicholas Chartres, and I'm a research
3 scientist at the University of California, San
4 Francisco. My comments today will focus on our
5 concerns with the application of the systematic review
6 in the trichloroethylene draft risk evaluation. Next
7 slide, please. I have no conflicts to disclose. Next
8 slide, please.

9 EPA's required by TSCA statute to use
10 the best available science and the weight of
11 scientific evidence to make decisions about chemical
12 risks. EPA defined the weight of the scientific
13 evidence in its 2017 risk evaluation rule as a
14 systematic review method that uses pre-established
15 protocols to comprehensively, objectively,
16 transparently, and consistently identify and evaluate
17 each evidence -- or each stream of evidence, including
18 strengths, limitations, and relevance of each study
19 and to integrate evidence as necessary and
20 appropriate. However, EPA states in the draft risk
21 evaluation for TCE that although EPA will make an
22 effort to adopt as many best practices as practicable
23 for the systematic review community the EPA expects
24 modifications to the process to ensure timely

1 regulatory decision making under the aggressive
2 timelines of the statute. Authority bodies, U.S.
3 agencies, and academic scientists have developed and
4 implemented validated environmental health systematic
5 review methods, including those that the National
6 Toxicology Programs Office of Health Assessment
7 Translation and UCSS Navigation Guide. If EPA uses
8 one of these aforementioned methods, the Agency would
9 not have to make an effort to adopt as many best
10 practices as practicable. Next slide, please.

11 We highlight the previous comments and
12 recommendations made by the SACC to EPA on the issues
13 they have identified in previous draft risk
14 evaluations in each step of the systematic review
15 process. These include the need to publish peer
16 reviewed, pre-established protocols prior to
17 performing the actual risk assessment. The number of
18 items that have been rejected for each criterion
19 should be summarized to enable raters to determine
20 what studies were excluded and the need for improved
21 clarity of the data integration process. Next slide,
22 please.

23 As you can see on this slide, we
24 highlight that EPA has failed to again address any of

1 these comments and recommendations made by the SACC in
2 the systematic review for TCE draft risk evaluation,
3 therefore leading to a biased evaluation of the
4 evidence. Today, we will highlight that EPA is not
5 systematically reviewing the studies relied on in the
6 evaluation and is inappropriately excluding a
7 significant proportion of the body of evidence. Next
8 slide, please.

9 This is the TCE literature flow diagram
10 for human health hazards in which EPA states 180
11 studies went through data evaluation. In Section
12 1.5.2 of the TCE draft risk evaluation, EPA states
13 that EPA evaluated the quality of the on topic TCE
14 study reports identified in the TCE bibliography
15 supplemental file for the TSCA scope document and gave
16 all studies a confidence rating during data
17 evaluation. However, in this TCE bibliography
18 supplemental file, there are 49 pages of on topic
19 references for human health hazards with approximately
20 25 citations per page, totaling approximately 1,200 on
21 topic references.

22 Again, as you can see here in the flow
23 diagram, only 180 studies have been referenced for the
24 data evaluation step. Of further concern, as noted in

1 the bottom right-hand corner of the slide, there are
2 119 animal and mechanistic studies and 96
3 epidemiological studies that go through data quality
4 evaluation as cited in the systematic review
5 supplemental file's data quality evaluation of human
6 health hazard studies, totaling 215 studies that go
7 through data quality evaluation for human health
8 hazards. Therefore, there are 35 data sources that
9 EPA has not accounted for in this flow diagram. Such
10 inconsistencies are deeply concerning and threaten the
11 validity of the TCE draft risk evaluation. Next
12 slide, please.

13 How EPA has accounted for the included
14 studies in each step of the literature flow diagram
15 for human health hazards is inconsistent with the
16 approach used here in Figure 1A, "Literature flow
17 diagram for environment hazards," that includes the
18 appropriate additional step of reporting a number of
19 studies that are evaluated at the title and abstract
20 stage and the number at the full text screening stage.
21 It is deeply concerning that EPA uses two different
22 approaches to report how the included and excluded
23 data sources were evaluated in the TCE draft risk
24 evaluation. Next slide, please.

1 Finally, for data integration, EPA
2 states that the EPA literature search did not identify
3 any new evidence that significantly contributes to or
4 challenges the previously established weight of
5 evidence conclusions for this hazard, other than
6 congenital heart defects. In order to address the
7 complete results in the previous weight of evidence
8 assessment in support of this risk evaluation, EPA
9 performed another weighted evidence analysis. EPA
10 adopted the methodologies described in weight of
11 evidence in ecological assessments. While we commend
12 EPA's efforts to move towards a more transparent
13 grading of the overall quality of the evidence and
14 data integration process, we recommend EPA use one of
15 the validated peer reviewed methods such as NTP or the
16 HATS method for this.

17 **DR. TODD PETERSON:** That's your five
18 minutes, please.

19 **MR. NICOLAS CHARTRES:** Thank you for
20 your time.

21 **DR. TODD PETERSON:** Thank you. So the
22 next person on the list is Terri Pace, and she does
23 not evidently have any slides. And I was told earlier
24 she may not be on the phone. Has Terri Pace shown up

1 in the queue? Okay. I'm going to move to the next
2 name, Anthony Tweedale. Is he on the line? I see
3 his slide. Thank you. Is Anthony Tweedale on the
4 line? I believe he may be having a problem with a
5 connection. We'll come back to him. The next speaker
6 is Daniele Wikoff, and Daniele has slides. Can you
7 bring up -- okay? So Daniele, are you on the line?

8 **DR. DANIELE WIKOFF:** Can you hear me?
9 I'm here. Hello?

10 **DR. TODD PETERSON:** Yes, we can.

11 **DR. DANIELE WIKOFF:** Super.

12 **DR. TODD PETERSON:** Can you hear me?

13 **DR. DANIELE WIKOFF:** Yes.

14 **DR. TODD PETERSON:** Okay. So when you
15 start, I'll start the timer. Go right ahead.

16 **DR. DANIELE WIKOFF:** Okay. Super.
17 Thank you so much and thank you for the opportunity to
18 provide comments on the systematic review component of
19 the risk evaluation. Next slide, please. My name's
20 Daniele Wikoff. I'm the health sciences practice
21 director. I'm a toxicologist specializing in use of
22 evidence-based methods, including systematic review,
23 to facilitate hazard in risk assessment. In addition
24 to being a practitioner, I'm also engaged in a number

1 of activities globally related to development of best
2 practices for systematic review. The comments in this
3 brief presentation and the written comments are, based
4 on my collective experience, both reasonable to expect
5 from the systematic review perspective, as well as
6 achievable by the TSCA scientists. Next slide,
7 please.

8 In this slide, we tried to give a
9 snapshot of the written comments we submitted to the
10 docket. Focusing first on the black text, we have
11 emphasized the recognized goal of using systematic
12 review. That is to ensure that the review is
13 complete, unbiased, reproducible, and transparent. In
14 the center, Figure 3.3. is from the risk evaluation,
15 demonstrating how systematic review is used relative
16 to the risk evaluation process.

17 Now moving to the red boxes, starting
18 with the left, we have overlaid a summary of the
19 written comments provided in the docket. These cover,
20 first, the lack of transparency and reproducibility in
21 the search, identification, and selection of evidence,
22 aspects which Nicolas just addressed; second, in the
23 bottom center box, aspects related to data quality in
24 which it was not conducted in a systematic or

1 reproducible manner. We would like to emphasis that
2 these aspects would not be apparent to the SACC
3 members without conducting an independent review of
4 each study quality assessment. And third, on the
5 right in the area it summarizes comments related to
6 the lack of systematic approach, transparency, and
7 reproducibility of the data integration and weight of
8 evidence, which I will say more about in the next
9 slide. Next slide, please.

10 Here, again, if we begin focusing on
11 the black text, weight of evidence is defined as a
12 systematic review method which comprehensively,
13 objectively, transparently, and consistently
14 identifies and evaluates each stream. Now moving to
15 the table, again in the black, we want to show that
16 there were different approaches used for different
17 endpoints. In the second column, different types of
18 evidence were evaluated for each of these endpoints.
19 Data quality, in the third column, is conducted for
20 individual studies. However, then for only one
21 endpoint, studies were again evaluated for study
22 quality, that is, now looking at the blue text, two
23 separate but overlapping approaches were applied to
24 individual studies.

1 These resulted in different
2 categorizations of quality. Then, a weight of
3 evidence for this single endpoint was determined using
4 an approach designed and implemented specifically for
5 this endpoint and assessment that is not applied in
6 any other TSCA evaluation. This approach was
7 described in less than two pages in the appendices,
8 not enough to assess the rigor of this methodology,
9 which was also addressed recently by Nicolas. Next
10 slide.

11 In this slide, we have provided an
12 example of the level of granularity we think is needed
13 during the peer review process. We highlight some of
14 the lack of consistency and systematic and
15 reproducible approaches. These include, for example,
16 looking at the red text, first, in the middle under
17 data quality evaluation, a number of these studies
18 were not scored according to the criteria as described
19 in the TSCA systematic review guidance.

20 Second, on the left on the bottom of
21 the slide, there is inconsistency with respect to
22 conducting -- sorry, with respect to contacting study
23 authors. In one instance, there was extensive
24 communication with study authors where in another

1 instance the full study reports, which would have
2 addressed the issues with reporting, were completely
3 disregarded. Similarly, there was lack of consistency
4 in carrying forward studies to the weight of evidence.
5 There was not rationale provided for why a number of
6 the studies with negative findings were not carried
7 forward. And then last, in the last column, there was
8 not transparency in the method for selecting what is
9 described as the most representative pod for the
10 endpoint. Next slide.

11 So in closing, we would really
12 encourage the SACC to review the comments submitted to
13 the docket regarding systematic review, those from Tox
14 Strategies, as well as others, including those from
15 EDF posted to the docket just this morning, as well as
16 others that we have heard already during the public
17 comment period. Thank you again.

18 **DR. TODD PETERSON:** Okay. Thank you.
19 So the next person on our list is Robert Sussman. And
20 I don't see that he has any slides. So we can just
21 put up the holding slide between speakers. And is
22 Robert Sussman on the line?

23 **MR. ROBERT SUSSMAN:** Yes, can you hear
24 me?

1 **DR. TODD PETERSON:** Yup. Are you on a
2 speaker phone? If you can --

3 **MR. ROBERT SUSSMAN:** This is the best I
4 can do. I will speak loudly.

5 **DR. TODD PETERSON:** Okay. Well, you're
6 clear enough, so when you start, I'll start the timer.
7 Go ahead.

8 **MR. ROBERT SUSSMAN:** Okay. Good
9 afternoon. I'm Bob Sussman, and I'm appearing today
10 on behalf of Safer Chemicals Healthy Families. We are
11 very troubled by the eleventh-hour political decision
12 to overrule career EPA scientists and exclude TCE
13 related fetal heart defects from EPA's determination
14 of unreasonable risk.

15 This decision has significant public
16 health implications. The immune related effects that
17 EPA is emphasizing occur at significantly higher dose
18 levels than heart malformation. Thus, an unreasonable
19 risk will still exist if EPA bases exposure limits on
20 the less sensitive immune endpoints. For example,
21 EPA's analysis of acute exposure scenarios shows that
22 the HEC99 for immune effects is 470 times higher than
23 the HEC99 for fetal heart malformations.

1 It's worth emphasizing that fetal heart
2 malformations are a significant, often lethal, and
3 irreversible effect and can impact a person's health
4 for a lifetime. There is no credible justification
5 for ignoring fetal heart defects and the serious
6 dangers they pose to pregnant women and fetuses. EPA
7 has repeatedly found that the weight of evidence
8 demonstrates that TCE causes fetal heart defects. And
9 the available data are sufficient for dose response
10 analysis.

11 I want to read a statement from the
12 draft risk evaluation, which states EPA's position.
13 Quote, "Overall the database is both reliable and
14 relevant and provides positive overall evidence that
15 TCE may produce cardiac defects in humans based on
16 positive evidence from epidemiology studies, mixed
17 evidence from animal toxicity studies, and stronger
18 positive evidence from mechanistic studies."

19 Secondly, the only change since EPA's
20 earlier TCE assessments is the recent industry study
21 that purports to find that TCE does not cause heart
22 malformations. However, the draft evaluation
23 concludes that this study's methodology was likely of
24 reduced sensitivity and did not sufficiently examine

1 the complete range of potential cardiac effects.

2 Moreover and significantly for the narrow category of
3 cardiac defects it addressed, the study found a dose
4 related increase in malformations remarkably similar
5 to the increase reported in the 2003 Johnson study.

6 Third, the TCE draft selects immune
7 effects as, quote, "a representative endpoint that
8 should drive risk determinations to the exclusion of
9 more sensitive endpoints." This is a dangerous and
10 unprecedented approach that would allow sensitive
11 endpoints supported by the weight of the evidence to
12 be ignored based on a subjective judgement that the
13 data for other endpoints warrants greater confidence.
14 To my knowledge, EPA has never done this before. And
15 in fact, EPA's risk assessment guidelines underscore
16 that risk managers and risk assessors should protect
17 against the most sensitive health effects adequately
18 demonstrated by the available science.

19 Finally, while TCE's immune effects are
20 serious, the implication that the data supporting them
21 are significantly more certain than the evidence of
22 heart defects is an after-the-fact invention,
23 contradicted by the rest of the draft. The evaluation
24 repeatedly states that EPA has, quote, "high

1 confidence in all the endpoints selected as points of
2 departure." Moreover, when the strengths and
3 limitations of the two bodies of evidence are
4 objectively compared, the uncertainties are not
5 materially different and do not justify concluding
6 that the immune effects should be used to determine
7 unreasonable risk but the heart defect data should
8 not. Thank you very much.

9 **DR. TODD PETERSON:** That's your five
10 minutes. Thank you very much. Okay. And cancel.
11 All right. So I'm going to go down the list. I've
12 had one-person call -- write an email saying they're
13 back online. So we'll definitely go back to other
14 names. But the next name I have on the list is
15 Jennifer Sass, and she does not have any slides. So
16 Jennifer, are you on the line? Can you hear me?

17 **DR. JENNIFER SASS:** Yes. Can you hear
18 me?

19 **DR. TODD PETERSON:** Yeah. Okay.
20 You're good to go. I will start the timer when you
21 start.

22 **DR. JENNIFER SASS:** Okay. Thank you
23 for the opportunity to give comments and thank you to
24 the EPA career staff and the SACC members for all the

1 hard work that you've done throughout this process,
2 including in this assessment. I'm going to submit
3 written comments later today, but I've been listening
4 to the SACC meeting. So thank you.

5 Here are my main points. I'm going to
6 be focusing on the halogenated solvents industry,
7 association, the HSIA report on the cardiac
8 malformations. I have two major points. One is the
9 HSIA report had major flaws in it that would
10 underestimate risk. And my second point is that it
11 actually confirms the EPA's analysis of the cardiac
12 malformation. So it's actually a confirmatory study.

13 Some of the major flaws which I'll
14 touch on is that they used pairwise statistics. A lot
15 of them were statistical -- misuse of statistical
16 analyses. They used pairwise instead of a trend
17 analysis, which is a lot weaker. EPA cancer
18 guidelines say you can use either. So EPA should use
19 whichever shows a response to TCE. That's page 46 of
20 the cancer guidelines.

21 They also use litter instead of
22 individual pup data as the unit of statistical
23 analysis, which is very weak considering they only had
24 20 litters. It's a dramatic reduction in statistical

1 power or the ability to detect an effect. Typically,
2 EPA would use both litter and individuals. It would
3 be nice to see the statistics on both.

4 The HSIA report used only two-sided
5 statistical analysis, which is meant for something
6 like a drug treatment where the effects could be
7 either harmful or beneficial. That's not the case
8 with this toxicology study, and it should have used
9 only one-sided tests, which is more appropriate when
10 the alternative hypothesis is to no effect is harm,
11 not benefit. And IRIS would normally do a one-sided
12 test for this reason. It would dramatically increase
13 the statistical power to detect an effect.

14 I've done some of the corrected
15 statistics, and if one used a Cochran-Armitage trend
16 test, which is a one-sided p-value test for discrete
17 data, which these are, and if you considered -- run
18 the ventricular septum effects on an individual animal
19 basis through the Cochran-Armitage trend test, you
20 would get a p-value of 0.0196 or 0.02, which is
21 statistically significant effect. There is a saying
22 amongst statisticians that some people use statistics
23 as a drunkard uses a lamppost for support rather than
24 illumination. I would suggest that, in this case, the

1 TSCA program would be drunk if they were to rely on
2 this study as not showing an effect.

3 It also misuses historical controls.
4 They were pieced together post hoc from old
5 publications from labs in China in the 1960s and early
6 1970s, which is so far out of the range of appropriate
7 use of historical controls. And they've also made no
8 argument why they should use historical controls. And
9 they've only used historical controls from some of the
10 effects.

11 Despite some of these flaws and ones
12 that my colleague Jennifer McPartland and others have
13 listed, as well as EPA career staff, the HSIA report
14 actually does provide evidence of ventricular septal
15 defects in the developing heart when rats are treated
16 prenatally with TCE. The reason why this study is so
17 important is because it's a study that supports risk
18 estimates and, therefore, regulations based on an
19 acute endpoint. It requires protection of a pregnant
20 woman or women of reproductive age because anywhere
21 during the formation of heart tissue, any exposure,
22 even low dose or even transient, could lead to an
23 effect.

1 And this means that regulations would
2 have to protect women of reproductive age rather than
3 exposures being averaged over a lifetime across the
4 population, which would accommodate a much higher peak
5 or short-term exposures. And that's what the key to -
6 - the importance of being able to develop a dose
7 response from the study is and why the HSIA, the
8 Halogens and Solvents Industry, wants so much for EPA
9 to move away from these data areas.

10 I've also done some graphing of all the
11 values in the study to demonstrate the similarity
12 between EPA's analysis, the IRIS' analysis and the --
13 that is the Johnson study and the current study. And
14 I'll submit those with my written comments. Thank
15 you.

16 **DR. TODD PETERSON:** Thank you. Get the
17 timer to turn off. Okay. So the next speaker on the
18 list is David Michaels, and there are no slides for
19 Dr. Michaels. Is David Michaels on the phone?

20 **DR. DAVID MICHAELS:** Yes, thank you.

21 **DR. TODD PETERSON:** Okay. I will start
22 the timer when you start.

23 **DR. DAVID MICHAELS:** Excellent. Thank
24 you. Thank you all. Some background on who I am, I

1 served as the Assistant Secretary of Labor for OSHA
2 for seven plus years under President Obama. During
3 the Clinton administration, I was Assistant Secretary
4 of Energy for Environment Safety and Health, charged
5 with protecting workers, the environment, communities
6 around the nuclear weapons complex. I'm a member of
7 the Board of Scientific Counselor in the National
8 Toxicology Program, and for five years I was chair of
9 the Trachekiet (phonetic) Council.

10 In my limited time today, I'd like to
11 address just one important issue in which aspects of
12 this draft risk evaluation are fundamentally, fatally
13 flawed. So that's the hierarchy of controls in PPE.
14 The hierarchy represents decades of OSHA policy and
15 practice. OSHA is very clear that it's unacceptable
16 use PPE as the primary means to protect workers.

17 Now, this risk evaluation acknowledges
18 the hierarchy of controls but bases worker exposure
19 measures, estimates, in three unstated assumptions
20 about PPE, all of which are unfounded and don't
21 represent the reality of work places: first, that
22 workers will be given PPE, in this case respirators,
23 by their employer; second, they will be able to use
24 that PPE -- they'll be trained to use it correctly and

1 they don't have medical conditions that will preclude
2 that use -- and third, that the PPE will be effective
3 in protecting them. This draft risk evaluation seems
4 to think that a recommendation for providing
5 respiratory protection in a safety datasheet means
6 every employer will do that.

7 In fact, OSHA does not require
8 employers to follow recommendations in safety
9 datasheets. OSHA's only requirement is that employers
10 maintain those sheets, and the worker protection
11 recommendations on those sheets are only that:
12 recommendations. Anyone who has spent time in worker
13 protection knows that many employers do not always
14 follow recommendations. Many don't even comply with
15 OSHA's legal requirements. But the authors of this
16 draft don't seem to get that.

17 I call your attention to a statement on
18 page 377. "EPA expects there is compliance with
19 federal and state laws, such as worker protection
20 standards, unless cases specific facts indicate
21 otherwise. And therefore, existing OSHA regulations
22 for worker protection and hazard communication will
23 result in appropriate PPE consistent with applicable

1 safety datasheets." This statement is simply and
2 demonstratively false.

3 Existing OSHA regulations for worker
4 protection and hazard communication will not result in
5 appropriate PPE use. The haz-com standard is that.
6 It's hazard communication. It's a requirement to make
7 datasheets available to workers. The authors seem to
8 think that OSHA requires employers to follow those
9 recommendations. In many cases, smaller employers
10 don't even read the safety datasheets, let alone
11 follow them.

12 Now, everything I've said to this point
13 applies to chemical exposures in general. When you
14 focus on TCE, it gets far worse. The OSHA permissible
15 exposure limit, or PEL, for PPE is 100 parts per
16 million averaged over an eight-hour day with a ceiling
17 of 200 PPM. In contrast, California has an
18 occupational exposure limit of 25 PPM. The ACJ has
19 lowered theirs to 10. NIOSH recommends a REL of two
20 in certain situations, 25 in others.

21 The draft notes that OSHA recommends
22 employers follow more protective occupational exposure
23 limits. I made that recommendation. The gap between
24 OSHA's current standards and levels that would

1 actually protect workers led me to recommend that
2 employers should look to other standards. The OSHA
3 standard for TCE is only a permissible exposure limit.
4 It's not a comprehensive standard. There's no
5 requirement for the application of hierarchy of
6 controls or use of PPE or any sort of training or
7 education or medical monitoring.

8 This situation actually incentivizes
9 its employers not to provide PPE to their employees,
10 the opposite of what the draft assumes. The authors
11 of the draft think that employers will not care that
12 the OSHA standard asks little of them, but when those
13 exposures occur below the old OSHA standards,
14 employers will offer PPE anyway. This will occur,
15 according to the draft, even when exposure is far too
16 high above NIOSH's recommendation but below the OSHA
17 legal limit.

18 But if employers do as EPA assumes they
19 will and provide appropriate PPE, in particular
20 respirators, the employers must, under the OSHA rule,
21 provide medical monitoring, fit testing, and much
22 more. It's a very big deal, not simply give out
23 respirators. It's expensive, and very few employers
24 will do that.

1 So I can assure you that many employers
2 will not do this voluntarily, yet, in its analysis,
3 EPA assumes the use of PPE, which leads to incorrect
4 risk assessments of exposure, as Dr. Denison said,
5 drastically underestimating risks by orders of
6 magnitudes. So to get this right, EPA should go back
7 and make determinations of unreasonable risk, assuming
8 many workers will not use appropriate PPE. Thank you
9 for considering my comments and thank you for your
10 service to the country.

11 **DR. TODD PETERSON:** Thank you. So the
12 next person I have on the list does have slides, and
13 that's Jon Urban. And I'll wait for the slides to
14 come up. There we go. And Jon Urban, are you on the
15 line?

16 **DR. JON URBAN:** I am on the line. Can
17 you hear me?

18 **DR. TODD PETERSON:** I can hear you.
19 And when you start speaking, then I will turn on the
20 timer.

21 **DR. JON URBAN:** Great. I appreciate
22 that. Good afternoon and thank you for this
23 opportunity to present comments related to EPA's
24 weight of the evidence assessment of the fetal cardiac

1 defects. My name is Jon Urban. I'm a managing
2 scientist with ToxStrategies, and I'm presenting on
3 behalf of the American Chemistry Council.

4 Overall, the EPA's systematic review
5 and assessment of the weight of the evidence
6 concerning the association of the utero exposure to
7 TCE and the developmental fetal cardiac defect have a
8 number of shortcomings that raise serious concerns
9 about the integrity of the assessment. Given the
10 limited time I have for this presentation today, I'd
11 like to point the committee to the ACC's written
12 comment submitted last week for a thorough review of
13 all the shortcomings identified during the review of
14 the draft risk evaluation. Next slide, please.

15 The first major issues was the Agency's
16 fetal cardiac analysis was not conducted in a
17 consistent, objective, transparent, or complete
18 manner, thus undermining fundamental principles of
19 systematic review. A couple of the many examples I'll
20 highlight here include the inconsistent application of
21 the TSCA study quality metric criteria, as well as a
22 failure to apply all relevant study quality metrics.
23 Next slide, please.

1 Second, there's clear evidence of
2 reviewer bias in the quality scoring of the animal
3 studies. This is an evidence base in which only one
4 of 13 animal studies reported an association between
5 TCE exposure and cardiac defects, and this would be
6 the Dawson-Johnson study you've heard of. The table
7 on this slide lists some of the ways in which the
8 reviewers afforded more weight and latitude in scoring
9 the Dawson-Johnson study when compared to the rest of
10 the animal studies, thus, again, violating fundamental
11 principles of systematic review regarding consistency
12 and transparency. Next slide, please.

13 Third, contrary to EPA's conclusion
14 that the animal toxicity studies provided mixed
15 ambiguous evidence for an effect of TCE, overall, the
16 animal studies provide the most reliable and
17 consistent evidence compared to either the human or
18 the mechanistic evidence streams. In fact, within
19 this dataset, it is the Dawson-Johnson study that's
20 the outlier, being the only study that was rated
21 unreliable for risk assessment when the TSCA study
22 quality metrics were applied consistently and the only
23 study to report an association between TCE and fetal
24 cardiac defects, as illustrated in the dose response

1 summary figured published in Wykoff et al 2018. Next
2 slide, please.

3 In fact, we recently published
4 independent systematic evaluations of this literature.
5 Wykoff et al was a systematic review of the human and
6 animal evidence stream, while Urban et al
7 systematically reviewed the mechanistic studies and
8 then integrated all three evidence streams to assess
9 the overall weight of the evidence.

10 Wykoff et al found human data were
11 insufficient to determine a relationship between TCE
12 and fetal cardiac defects but concluded that the
13 animal study strongly support a lack of association.
14 More recently, Urban et al addresses some of the
15 questions of mechanism and mode of action raised
16 earlier by Dr. Mark Johnson during committee
17 discussion.

18 After conducting a systematic review of
19 the mechanistic study data, we were surprised that EPA
20 concluded that this represented the strongest evidence
21 and supported their conclusions regarding association
22 between TCE and fetal cardiac defects, given the high
23 heterogeneity in the model types, endpoints, and
24 inconsistency in outcomes and the largely unreliable

1 study quality if scored using the same TSCA study
2 quality metrics. Additionally, claims that the TCE
3 directed gene expression alterations in fetal hearts
4 support the association are limited by the lack of
5 phenotypic anchors in a reliable mammalian model.

6 And the current database does not
7 support the putative adverse outcome pathways proposed
8 by Macrus et al in 2016. Integration of all three
9 evidence streams ultimately led us to conclude that
10 the typicality of the evidence does not support fetal
11 cardiac defect as the critical effect in TCE human
12 health risk assessment. Next slide, please.

13 Finally, while EPA included oral
14 studies of the oxidative metabolites of TCE as a part
15 of the evidence base, these studies were not included
16 in the formal assessments of either Wykoff or Urban,
17 though they were discussed. The reason for not
18 including the metabolite studies in our systematic
19 reviews was the fact that TCA and DCA dose levels
20 administered in these studies were so high that
21 estimates of TCE equivalent dose -- that is the TCE
22 dose levels needed to achieve the same internal levels
23 in metabolites as those produced by the administration
24 of metabolites themselves that would be lethal,

1 exceeding the document rat oral LD50s for TCE. It's
2 also notable to point out that the EPA's 2011 IRIS
3 risk assessment for TCA, which is the primary TCE
4 oxidative metabolite, reviewed the metabolite studies
5 who included that the fetal cardiac defects should not
6 be considered a critical effect due to inconsistent
7 findings and questions of interpretation.

8 So again, the issues highlight in this
9 brief presentation represent just a few of the many
10 issues with the Agency's assessment of this endpoint.
11 And we encourage the committee to review the ACC's
12 written comments for a thorough delineation of all the
13 shortcomings identified. Again, thank you for your
14 time.

15 **DR. TODD PETERSON:** Okay. Thank you
16 for being right on time. So the next speaker has
17 slides. It's the last slide set, other than one that
18 we'll go back to. John DeSesso, and the host has
19 those up. So is John DeSesso on the line, please?

20 **DR. JOHN DESESSO:** Yes, I am. Can you
21 hear me?

22 **DR. TODD PETERSON:** I can hear you.
23 You're loud and clear. So you start, and I'll start
24 my timer once you're going.

1 DR. JOHN DESESSO: Thank you very much.

2 Well, hello. My name is John DeSesso. I'm a
3 developmental toxicologist with 45 years of
4 experience. I'm employed by Exponent, which is a
5 science and engineering consulting firm, and
6 Georgetown University's Medical School, where I'm an
7 adjunct professor having taught embryology, anatomy,
8 and teratology for 37 years. Next slide.

9 In brief, the cardiac defects portion
10 of EPA's TCE toxicological assessment is flawed
11 because it relies primarily on a single drinking water
12 study. It does not incorporate robust developmental
13 toxicity studies that found no increase in heart
14 defects, and it fails to incorporate toxicokinetic
15 data showing minimal systemic TCE concentrations after
16 oral exposure. Next slide.

17 So why conduct another drinking water
18 study? Next slide. The Johnson study has been
19 heavily criticized in the literature, and the new
20 Charles River Study addressed as many of the
21 criticisms as possible. The results were published in
22 the journal *Birth Defects Research*, and the cardiac
23 defects did not repeat. Next slide.

1 Well, this table contrasts the Johnson
2 and Charles River studies. You can see that the
3 exposure ranges of the two studies are similar.
4 However, the group size is different. Johnson had 55
5 control litters but only 9 to 13 litters of TCE
6 groups, whereas Charles River used 23 to 24 litters
7 per group. Johnson acquired her data over six and a
8 half years or more, and the analyzed portion of the
9 Charles River study was about a month long. Charles
10 River included both the toxicokinetic arm and a
11 positive control group. Johnson had neither. The
12 Charles River data were available for independent
13 review, but the records for Johnson's studies were
14 lost.

15 Another important difference is that
16 Johnson used a unique heart dissection method that
17 removed the atria and physically manipulated the
18 heart. Next slide. Whereas, Charles River used the
19 standard first initial dissection technique, which is
20 the method cited by EPA in its test guidelines for
21 prenatal developmental toxicity studies. Next slide.

22 EPA has concluded the Charles River
23 study is not adequately sensitive to cardiac
24 teratogens. Next slide. However, their conclusion is

1 based on an assessment of the positive control data,
2 which EPA indicates did not indicate all cardiac
3 defects that had been attributed to retinoic acid.
4 EPA's assessment lacks transparency. They tabulated
5 35 cardiac defects that appeared in 25 published
6 studies using retinoic acid, but the papers were not
7 identified. The doses, length of exposure, durations
8 of treatment, and frequency of occurrence were not
9 given. The criteria for OCD effects were not
10 described. And additionally, they included some
11 findings that were observed only in mice or hamsters
12 but not rats and some non-mammalian data from chickens
13 or zebra fish, which have no placentae and develop
14 outside the mother. Next slide.

15 Now, this table presents the
16 frequencies of the studies, not the frequency in
17 fetuses, that reported those 35 cardiac findings.
18 Twenty of the 35 findings were reported in only a
19 single study, and only 11 findings were reported in
20 three or more studies. So none of the studies found
21 all of the defects. Next slide.

22 Charles River study -- the defects is
23 the seven circled findings on the graph -- next slide
24 -- plus the three additional findings listed. You'll

1 note that on the left side there were ventricular
2 septal defects observed but no defects in valves or
3 the atrial septum. Next slide. But Johnson's
4 methodology also has a similar sensitivity. Next
5 slide.

6 While Johnson did not have a positive
7 control group, she co-authored and evaluated hearts in
8 the Fisher 2001 study, which did have a retinoic acid
9 positive control group. Next slide. Fisher's
10 positive control data are circled here. And as you
11 can see, they also reported -- next slide, I think.
12 No, go back. I think we got ahead of me here. Go
13 back one. Do you see the circles there? You can see
14 they have a spectrum of -- not all the cardiac
15 defects. And on the left side notice that there were
16 no ventricular septal defects or atrial septal defects
17 or valve defects. So the Johnson study is not more
18 sensitive. Next slide.

19 If we classify any cardiac defect as
20 being an abnormal heart, we can compare across the
21 three oral studies. Next slide. The data from the
22 two drinking water studies and the Fisher gavage study
23 are shown here. TCE exposures increased from left to
24 right. Next slide.

1 If we pay attention to the percentage
2 of fetuses with abnormal hearts, we can see that as
3 the dose increases by 12,500 times the percentage of
4 abnormal hearts remains in the range of 1.4 to 5
5 percent. But notice circled there that there's a lone
6 value outside that range, which is the dose of the
7 Johnson study -- the high dose -- which had only nine
8 litters. Next slide. The toxicokinetic arm of the
9 Charles River study adds implausibility to the TCE --
10 that TCE causes cardiac defects. Next slide.

11 This table's from *Birth Defects*
12 *Research*. Next slide. Never mind. Don't do that
13 because -- you'll notice in red that TCE was not
14 detected in internal plasma after drinking water
15 exposures in both the Charles River and Fisher
16 studies. The green box, however, shows that exposure
17 did occur because TCA, a non-volatile metabolite of
18 TCE, was detected in dams that were exposed to at
19 least 350 parts per million and greater.

20 If we conservatively estimate that the
21 high dose TCE was at half the maternal plasma levels
22 and (inaudible) extrapolate to zero, you can see in
23 the green boxes -- the blue boxes -- that the span

1 includes all the doses that TCA used in its in vitro
2 studies for this assessment. Thank you.

3 **DR. TODD PETERSON:** Thank you. Okay.
4 This is the last slide set. If we can bring -- I know
5 we have one more speaker, but there's one other person
6 that we think is trying to be on the line. Can we try
7 one more time? Is Anthony Tweedale on the phone? Can
8 we bring up Anthony Tweedale?

9 **MR. ANTHONY TWEEDALE:** You can't hear
10 me, I guess.

11 **DR. TODD PETERSON:** Oh, now I can hear
12 you. Can you hear me?

13 **MR. ANTHONY TWEEDALE:** Oh, good. Yes.
14 I can hear you.

15 **DR. TODD PETERSON:** Good. Okay. Hold
16 on one second. Just stay there. And host, can you go
17 back to the one slide? It's actually a portrait PDF
18 file. There we go. So Anthony Tweedale, you start
19 speaking, and I'll start the timer when you start.

20 **MR. ANTHONY TWEEDALE:** Great. I'm an
21 American. I live in Brussels and work in Brussels.
22 And I work on risk assessment. And all over the
23 world, at least in America and Europe, I find that
24 academia's literature is being ignored and pre-market

1 risk assessments, in other words risk assessments that
2 are performed for the purpose of authorizing a
3 chemical to either go onto or stay on the market.

4 So I congratulate EPA under its new
5 TSCA responsibilities. It's trying to evaluate all
6 the literature. And it's, in this case, using a
7 published study from academia, which I know is quite
8 controversial. So I'm not going to get into that.

9 What I set out to focus on is in this
10 slide. I did a PubMed search using the search term I
11 used to find toxicity studies. It turned up 3,700
12 potential studies. And a quick look at the titles of
13 the studies, I'd estimate half of those were toxicity
14 studies. And if you add at least 20 percent that are
15 not in PubMed, other toxicity studies on TCE, there
16 might be 2,000 to 2,500 published studies finding
17 toxicity on trichloroethylene.

18 So as the previous speaker from UCSF
19 highlighted, this risk assessment shows that, even
20 though EPA's search found many, many studies, almost
21 all were classified as off topic, that is to say not
22 relevant. And sure enough, I looked at the list of
23 those many thousands of studies, the titles, and
24 clearly, essentially all of them seem to be off topic.

1 But there's something wrong with EPA's search term.
2 If I can find roughly almost 2,000 published studies
3 of toxicity on TCE, EPA only found 500 and some --
4 it's there in my slide -- when you add together both
5 the human health and the ecological or the ecotox
6 searches which were performed as separate searches.
7 So that's my basic point.

8 I want the committee to ask EPA to go
9 back, not just for trichloroethylene, but in all its
10 TSCA systematic review assessments and do this first
11 step right. If you don't do the first step right,
12 you'll never get a good reliable result, which is what
13 systematic review is all about.

14 So two very quick things, at the end of
15 my slide I mention just by chance I saw one of the
16 published studies regarding this big controversy over
17 the developmental heart defects of TCE. And so I
18 decided to look, and it doesn't seem that EPA found
19 that. It was published last year, and I give the
20 citation at the bottom of this slide. That's just a
21 random indication that EPA's literature search was not
22 very good.

23 And then the very last thing is I went
24 to look at the IRIS websites, EPA's database IRIS, and

1 the -- same goes for chronic exposure -- is based on
2 the same study that EPA is now using, the 2009 authors
3 that was previously mentioned. But there's a tenfold
4 difference, roughly, in the safe dose. In IRIS, it's
5 tenfold lower than EPA's proposing today. Now, there
6 could be perfectly valid reasons for that, but I would
7 like the committee to ask of EPA why there's a tenfold
8 difference when they are based on the same study. It
9 probably has something to do with the toxicokinetics.
10 Okay. Thank you very much.

11 **DR. TODD PETERSON:** And thank you. We
12 have one last speaker, and that's James Bus, who does
13 not have any slides. I'm just going to make a DFO
14 comment at this point. For all of the speakers, the
15 slide sets that you sent forward, they are in a share
16 folder and also have been emailed to the panel. And
17 those of you who have submitted comments in relation
18 to your oral comments, those are also in the share
19 folder and available to the committee members.

20 I know that some of you will send in
21 comment documents related to your oral presentation
22 during or just after the meeting, and I will certainly
23 post those to the docket for you. And they will be
24 made available to the members. So we're doing due

1 diligence to make sure that those materials are
2 distributed. So the last speaker is James Bus. Are
3 you on the line?

4 **DR. JAMES BUS:** Yes. I am. Can you
5 hear me?

6 **DR. TODD PETERSON:** I can hear you.
7 And when you start, I'll start the timer.

8 **DR. JAMES BUS:** Thank you. Good
9 afternoon. My name is Dr. James Bus, and I'm a
10 toxicologist at Exponent, a consulting company. My
11 comments are offered on behalf of the Halogenated
12 Solvents Industry Alliance, or HSIA. I certainly want
13 to extend my personal thanks and those of HSIA for the
14 commitments of the members of this science advisory
15 committee to assist the EPA on the use of the best and
16 most appropriate science in its deliberations on the
17 health and environmental risk of trichloroethylene.

18 I'm here to specifically address the
19 cancer risk evaluation that relies on key assumptions
20 presented in the 2011 EPA IRIS trichloroethylene
21 assessment. In that assessment, the mode of action of
22 trichloroethylene kidney cancer in laboratory animals
23 and humans was concluded as operating by a mutagenic
24 mode of action attributed to formation of DNA reactive

1 metabolites secondary to formation of the
2 trichloroethylene glutathione conjugate derived
3 metabolites, dichloro vinylglutathione, or DCVG, and
4 its downstream metabolite, dichloro vinylcystene, or
5 DCVC. The IRIS cancer modeling relied in part on two
6 key 1999 literature studies from a single laboratory
7 reporting that substantial amounts of DCVG were
8 present in the blood of volunteers exposed for four
9 hours to 50 or 100 parts per billion of
10 trichloroethylene and also in in vitro incubations
11 with human liver hepatocytes or liver and kidney
12 subcellular fractions.

13 Importantly, however, the DCVG analyses
14 in these studies relied only on an HPLC
15 spectrophotometric method that had substantial
16 potential for chromatographic overlap with peaks of
17 endogenous metabolites. I was the co-author on an
18 HSIA sponsored study published as Zhang et al in 2018
19 that conducted a side by side comparison of the
20 performance of the nonspecific spectrophotometric
21 method to a trichloroethylene metabolite specific HPLC
22 mass spec, mass spec method. That method demonstrated
23 that the spectrophotometric method substantial
24 overestimated the concentrations of DCVG in rat blood,

1 liver, and kidney and in human blood by up to four
2 orders of magnitude.

3 Additional mass spectrometry analyses
4 confirm that the overestimation was attributable to a
5 chromatographically interfering peak to DCVG that was
6 primarily endogenous glutamate. These new analytical
7 data indicate that the DCVC concentrations reported in
8 the early literature studies are not reliable for
9 modeling human kidney cancer risks of
10 trichloroethylene. The Zhang and coworker findings
11 are also consistent with a recent study using a
12 structure specific HPLC ESI mass spec, mass spec
13 method demonstrating that the concentrations of DCBG
14 and DCVC in kidneys of mice receiving a high oral dose
15 of trichloroethylene were approximately five orders of
16 magnitude lower than metabolites derived from
17 oxidative metabolism.

18 Importantly, none of these critical new
19 data using state of art analytical methods are
20 considered in the current draft risk assessment.

21 Finally, the new and analytically robust data showing
22 that glutathione conjugate derived metabolism is only
23 a very minor pathway of trichloroethylene metabolism
24 in rodents and humans also challenged the hypothesis

1 that this pathway is plausibly consistent with a
2 mutagenic mode of action in rodents and humans. Thank
3 you for your attention.

4 **DR. TODD PETERSON:** Okay. Just had to
5 unmute myself. So okay. This is Todd Peterson, the
6 DFO. We had a communication from one individual,
7 Terri Pace, who's on the list. She's had problems
8 connecting and has sent an email that she's going to
9 forward her comments so that they can be placed in --
10 to the attention of the committee and also in the
11 docket.

12 That means that I'm going back to the
13 one other person on my list who we didn't hear from,
14 and I don't see any indication she's on the line. But
15 I'm going to ask. Is Eleni Kapatou on the line?
16 Okay. One last time, Eleni Kapatou? Okay. Well,
17 unfortunately for whatever reason, that individual is
18 not able to communicate today, and maybe they will
19 also supply their comments in written form as well.
20 At this point, we are done. This is the last of the
21 oral public comments that were requested. And I will
22 turn the meeting over to Dr. Portier.

23 **DR. KENNETH PORTIER:** Thank you, Todd,
24 and thank you to all the public commenters. At this

1 point, I'm always amazed at how everyone views this --
2 each risk assessment and all the different points that
3 can be brought out in that kind of review. At this
4 time, I think the committee is ready to begin the
5 charge questions. But I think I'd like to take about
6 a ten-minute break at this point, Todd. There's a
7 couple of issues I need to talk with you about. And
8 we can get the charge questions brought up. So let's
9 take a little break until about 3:05, please.

10 **DR. TODD PETERSON:** That's fine by me.

11 **DR. KENNETH PORTIER:** Panel, we'll be
12 ready to begin at 3:05.

13
14 (BREAK)

15
16 **DR. KENNETH PORTIER:** Good afternoon,
17 again. I think it's -- go ahead, Todd.

18 **DR. TODD PETERSON:** Go ahead, Ken. You
19 go -- good to go.

20 **DR. KENNETH PORTIER:** I was just going
21 to say I think it's time for us to reconvene. I
22 wanted to make a short announcement that I've heard --
23 we've heard from the commenters that they are, shall
24 we say, disappointed that EPA decided to move forward

1 with this public meeting over a virtual channel given
2 the extraordinary situation that we are in at this
3 time. And I realized that while I've been party to
4 some of the conversations that justified this meeting,
5 the committee and the public have not been party to
6 those discussions and that EPA has not really made a
7 statement as to why they decided to move forward.

8 So in a back channel I've asked EPA to
9 put together that statement, and they're working on
10 it. In the meantime, I think we're going to move
11 forward as a committee to address the charge
12 questions. And once I receive confirmation that the
13 appropriate statement and individual to present that
14 statement have been identified, we'll take a short
15 break and have that statement made.

16 So at this point, we're going to move
17 forward with the questions, and I'm going to turn to
18 Dr. Heidi Bethel who'll be reading the questions into
19 the docket so that the panel can begin the
20 discussions. Dr. Bethel?

21 **DR. HEIDI BETHEL:** Hi. This is Heidi
22 Bethel. Can you all hear me okay?

23 **DR. KENNETH PORTIER:** Yes.

1 DR. HEIDI BETHEL: Okay. Perfect. So
2 I'm going to go through the question. You want me to
3 go through the entire Question 1, Dr. Portier?

4 DR. KENNETH PORTIER: Up to Question
5 1.1.

6 CHARGE QUESTION 1 (1.1)
7

8 DR. HEIDI BETHEL: Okay. So Question 1
9 is on the environmental fate and exposure section of
10 the document. EPA qualitatively analyzed the
11 sediment, land application, and biosolids pathways
12 based on TCE's physical/chemical and fate properties.
13 Exposure estimates to the environment were developed
14 for the conditions of use for exposures to aquatic
15 organisms.

16 Question 1.1. states: Please comment on
17 EPA's qualitative analysis of pathways based on
18 physical/chemical and fate properties from Section 2.1
19 of the document.

20 DR. KENNETH PORTIER: Thank you. And
21 we've asked Dr. Blystone to lead the conversation or
22 the comments on Question 1.1. Dr. Blystone?

23 DR. SHERI BLYSTONE: Yes. Hi, this is
24 Sheri Blystone. So I did get comments from pretty

1 much everyone, and those that didn't will, of course,
2 speak up during the meeting or correct any of the
3 mistakes that I made. I will say that I tried to
4 bucket the comments that I got under each of the
5 questions. If it wasn't specifically placed there,
6 it's also -- if I miss it in the one that you think it
7 should be there, please go ahead and speak up for that
8 as well.

9 So just going through the comments on
10 Question 1.1, there are some general comments here as
11 well. One commenter found that the environmental fate
12 evaluation for TCE to be very similar to previous
13 reviews, for instance methylene chloride and carbon
14 tet, and that the cookbook approach to conducting a
15 fate evaluation results in repeating most of the same
16 shortcomings that were identified in previous reviews.
17 This commenter also found the document to be less
18 concise and more difficult to read than some of the
19 other risk assessments out there.

20 We had a question that I think came up
21 during the clarifying about groundwater to surface
22 water and is that considered relevant for TSCA's
23 estimates, so we might get some more discussion around
24 that. Another discussant also mentioned that landfill

1 releases to surface water should be included, that
2 they represent current uses, and any current
3 contribution to surface water must be included to
4 prevent unnecessary risk to humans and our natural
5 resources. If the partitioning to sediments and soil
6 is considered minimal, than the risk to groundwater,
7 especially unregulated drinking water sources, must be
8 objectively determined.

9 According to this commenter, the
10 committee has repeatedly commented that exclusion of
11 groundwater on the basis of regulation under Clean
12 Drinking Water or Safe Drinking Water statutes is
13 erroneous, at least according to some committee
14 member's view. And private wells are not regulated
15 under the Clean Water Act and the Safe Drinking Water
16 Act and that storm water also must have derived from a
17 TCE use and should be assessed. Another comment said
18 that the analysis was adequate but that we did need a
19 diagram that displayed the pathways and rates, I think
20 similar to what we saw in the slides this morning.

21 There was a comment that, in general,
22 the Agency has discounted the findings of their own
23 2014 TCE workplan. For example, the environmental
24 fate sections in that document state there are several

1 factors that can contribute -- that can limit the
2 aerobic biodegradation of TCE, including TCE
3 concentration, PH, and temperature. Toxicity of the
4 degradation products, for instance, dichloroethylene,
5 vinyl chloride, chlorofluoromethane, to the degrading
6 microorganisms may also reduce the rates of
7 biodegradation of TCE in aerobic soils.

8 There were a couple of comments around
9 degradation and hydrolysis products. One is that what
10 we know about them should be mentioned, specifically
11 what are the degradation products and hydrolysis
12 products. There was a comment that it was stated in
13 several sections of the DRE that anaerobic
14 biodegradation of TCE was rapid. However, this isn't
15 always the case. And in many situations, toxic
16 biodegradation intermediates are formed, including
17 dichloroethylene and vinyl chloride. Atmospheric
18 photolysis via OH radicals also can result in the
19 formation of chloroform and other chlorinated
20 biproducts.

21 For the physical/chemical properties,
22 compared to other compounds evaluated there are many
23 experimental physical/chemical properties for TCE.
24 It's not clear in the document how the physical

1 properties listed in Table 1 were selected over other
2 values in the literature or why a range of values was
3 not provided. The data, or lack thereof, from the
4 targeted National Sewage Sludge Survey and EPA's
5 biennial review for biosolids is purported to be
6 strong support for the decision not to quantitatively
7 assess this pathway, but it wasn't clear if TCE is
8 even analyzed for. That was actually my comment. I
9 didn't see it listed as a analyte for the TNSSS.

10 Another discussant also commented that
11 there's no mention of the influence that TCE density
12 has on environmental fate. I think that came up this
13 morning a little bit as well. TCE density and
14 partitioning to suspended sediments means that TCE
15 will deposit in bottom sediments, where it may form a
16 dense, nonaqueous phase liquid. Although the density
17 dependent deposition to sediments is acknowledged in
18 Section C.1.2 of the U.S. EPA 2014 workplan for TCE,
19 none of this is considered in the draft risk
20 assessment.

21 The draft risk assessment stated that
22 TCE was not found in biosolids. This statement should
23 be modified according to one of the commenters. It
24 was stated that TCE is not anticipated to partition to

1 biosolids during wastewater treatment. EPA stated
2 that to further support this analysis TCE was not
3 detected in EPA's targeted National Sewage Sludge
4 Survey, nor was it reported in the biosolids during
5 EPA's biennial review, like I've already mentioned.

6 The methods we're using to analyzing
7 the biosolids are not suitable to TCE, and the
8 targeted analysis did not appear to actually look for
9 TCE. So that's at least two of us that caught that.
10 The Agency used the model program EPI Suite to predict
11 fate of TCE from discharges. Excuse me -- I think I
12 might have -- no, I'm still on track. Sorry. I'm
13 getting a little confused in my own analysis here.

14 EPI Suite to predict the fate -- the
15 program estimated 80 percent loss to the air, and one
16 percent would be an aqueous discharge, based on the
17 log KOW and predicted log KOC. The Agency predicted
18 limited partitioning into biosolids. This was
19 confirmed with targeted National Sludge Survey data,
20 which did not detect TCE. While a similar argument is
21 made for partitioning into sediments, there is no
22 measured data to support this qualitative assessment -
23 - estimate.

1 Additional text regarding uncertainties
2 for the predictions are needed. For example, the
3 Agency indicates that TCE would not bioaccumulate
4 based on the log KOW of about two. This value
5 indicates that TCE would partition into the organic
6 phase 100 times more than the aqueous phase. If TCE
7 is continuously discharged into aquatic systems,
8 pseudo-persistent exposure would occur because there
9 is limited biodegradation, according to Bio Win.
10 While only one percent is predicted to be discharged
11 into surface water from EPI Suite, based on the
12 production volume and multiple detections observed in
13 surface waters across the United States, persistent
14 exposure may be a possibility and should be addressed
15 as an uncertainty.

16 In Section 2.1.2, the EPI Suite model
17 indicates that the model was run with default
18 settings, so settings have equal releases to air,
19 water, and soil. That is not the scenario that exists
20 in the environment. The Agency presented data
21 suggesting that the releases -- the release ratios in
22 air, soil, and water and 37,800 to 960 to one. Using
23 these ratios all divided by two instead of the default

1 1,000 kilograms per hour into each compartment
2 produces a large net flux of TCE to water from air.

3 This simple comparison demonstrates
4 that the Agency's entire assumption of air emissions
5 not impacting environmental risk is in serious error.
6 It is not apparent that EPI includes the density of
7 chemicals that are being assessed. This would
8 influence sediment deposition rates in water.

9 It should also be noted that the EPI
10 Suite overall half-life in the Agency scenario
11 described is nearly one week, but the half-life in
12 water is over one month. And the half-life in soil
13 and sediment are 1.8 and 8.1 thousand hours. These
14 half-lives do not imply rapid dissipation to air.
15 And that's all I had for Question 1.1.

16 **DR. KENNETH PORTIER:** Thank you. I'm
17 going to next call on the four associates just to see
18 if they have anything to add. Dr. Doucette?

19 **DR. WILLIAM DOUCETTE:** Yeah. I think
20 Sheri covered -- I gave her comments, and I think she
21 addressed all of them. It was a little disappointing
22 for me just to have some of the same things that we
23 brought out in the methylene chloride and carbon tet
24 assessment repeated in this one. I realize that the

1 timing of all these -- they were done probably
2 simultaneously. And some of these didn't get caught.
3 That was a little bit disappointing for me because it
4 seemed like, at least in the carbon tet one, most of
5 the comments that we had made for methylene chloride
6 they had tried to do a better job of addressing.
7 That's all I have. Sheri caught the rest.

8 **DR. KENNETH PORTIER:** Thank you. Dr.
9 Kissel?

10 **DR. JOHN KISSEL:** I have three general
11 topic areas to comment on, and I provided a slide. I
12 wonder if that could be put up. And while I'm waiting
13 for that -- oh, there it is. The first thing is
14 Figure 1.1, the life cycle diagram on page 55, I would
15 just like to emphasis that it would be really nice to
16 have actual numbers there besides the input.

17 The lifecycle literature and the mass
18 low in society kind of literature needs numbers to be
19 informative. And we need to know what's going in, and
20 we need to know what's coming out and try to assess
21 what fraction -- for all of these solvents, we have
22 historically an enormous problem with chlorinated
23 solvents because they don't degrade rapidly in
24 groundwater. And that's leakage out of the system.

1 And we really need some national estimates of how much
2 of the total throughput is finding its way into soil
3 and then into groundwater. So I would urge EPA to
4 start thinking bigger in terms of mass balances on
5 these compounds as we continue to go forward. Okay.

6 The second point is illustrated by the
7 slide that is up, which is a display of a natural
8 chromatography experiment. This study was done in the
9 '80s in a shallow clean sand aquifer in Canada. The
10 release point -- so this is a series of university
11 investigators -- deliberately released chlorinated
12 solvents into a shallow aquifer and then monitored the
13 consequence. And what you're seeing there is movement
14 of center of mass of different -- well, two chemicals
15 and a tracer.

16 So the top plume is chloride, which is
17 basically showing the movement of water. The release
18 point was zero, zero on that plot. And in a little
19 less than 22 months or so -- so the water has moved
20 about 60 meters. And in that same time, I don't have
21 -- these guys didn't do trichloroethylene, so we don't
22 have trichloroethylene on here. But we have carbon
23 tet, which was our last compound. And we have
24 perchloroethylene, which is coming up.

1 And they are moving more slowly than
2 the water because they are absorbing to solids. You
3 can estimate from the retardation factors roughly what
4 fraction of the agent is actually in the water, as
5 opposed to absorbed to solids, at any given time. And
6 for TCE, this will be a good test of whether EPA is
7 paying attention and is modifying their results. If
8 when we get the PCE document it still says that, well,
9 it's mostly going to be in water and it's quite
10 mobile, this figure is kind of a shot across the bow
11 because it says very clearly that PCE is not
12 overwhelmingly in water, given the choice.

13 And in my view, this is clean sand
14 aquifer. The estimated fraction of organic carbon in
15 this aquifer is 0.02 percent, so way, way, way less
16 organic carbon than you would find in surface water,
17 sediment, or sewage sludge or other matrices. And you
18 still see retardation of these compounds because they
19 are absorbing to solids and absorbing and desorbing,
20 which gives you the chromatographic effect.
21 Chlorinated solvents have been a problem long enough
22 that we know something about how they move in
23 groundwater. And I find that these documents we're

1 getting kind of overlook that literature, so I wanted
2 to make that point and show this figure.

3 The third point that I wanted to make
4 is that I submitted -- it's taking me a while -- as we
5 keep going through these and we keep having repeat
6 experiences, I find I'm saying the same things over
7 again with a little elaboration. But for carbon
8 tetrachloride, I submitted a list of physical/chemical
9 parameters that are pertinent to understanding dermal
10 absorption. And basically, I will insert that same
11 list of physical/chemical parameters or dermal
12 absorption parameters and recommend that they be
13 included.

14 Now, we haven't actually finished the
15 report for carbon tetrachloride, so EPA hasn't seen
16 them. But I'm giving them notice that they're going
17 to get the same list of recommendations. Given that
18 dermal absorption is generally not well understood by
19 the public or even much of the technical community, I
20 think greater discussion on that topic and elucidation
21 of that topic would be appropriate. And that's what I
22 have.

23 **DR. KENNETH PORTIER:** Thank you, John.
24 Dr. Schlenk?

1 **DR. DANIEL SCHLENK:** Hello? Can you
2 hear?

3 **DR. KENNETH PORTIER:** Yeah, Dan.

4 **DR. DANIEL SCHLENK:** Okay. Yeah. I
5 sent all my stuff to Sheri, and she pretty much stated
6 everything I had to say. So no further comments.

7 **DR. KENNETH PORTIER:** And Dr. Cobb?
8 While Dr. Cobb's trying to come on, Dr. Doucette? Oh,
9 there he is. George?

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

11 **DR. KENNETH PORTIER:** Yeah.

12 **DR. GEORGE COBB:** Yeah. Something
13 keeps happening. Every time I click this microphone
14 button on my screen, it just pops something up, and it
15 doesn't actually make my microphone turn on. So
16 please bear with me.

17 First of all, thank you to Sheri for
18 capturing the vast majority of my comments. She did a
19 great job with that. I did have a couple of things
20 that have come up since the discussion started I
21 wanted to kind of get in here.

22 The first thing is, on Slide 13 of the
23 EPA's presentation, there were some arrows that were
24 showing everything moving from sediment -- all the TCE

1 moving from sediment to water and all moving from
2 water to air. And I'm not sure that's quite right.
3 Check those arrows out a bit before you publish that.

4 The other thing was that on page 89,
5 line 502, the way that EPA described the cleansing
6 process for data to make sure that they were using
7 appropriate monitoring data was very cursory. And I'm
8 not expecting paragraph upon paragraph, but a little
9 bit more about how things were disqualified and what
10 would, for instance, constitute sample contamination.
11 With modern analytical techniques, you can find almost
12 anything you're looking for in almost any matrix,
13 including what you think is clean glassware, just as
14 an example. And other than that, I think that's it
15 and thank you.

16 **DR. KENNETH PORTIER:** Thank you,
17 George. Dr. Doucette?

18 **DR. WILLIAM DOUCETTE:** Yes. I wanted
19 to follow up on Dr. Kissel's comment. I've worked on
20 field sites, TCE contaminated field sites for probably
21 20 years. He brought up the point of sorption, and I
22 put this in my written comments.

23 There's been a ton of sorption studies,
24 for example, for TCE. And I found values of log KOC.

1 It went as high as 4.2. And it really depends on --
2 again, log KOC is a simplification. It ignores
3 absorption to other surfaces, other than organic
4 carbon. And I guess I just wanted to reiterate that
5 TCE is fairly data rich in terms of most of the
6 properties, and certainly sorption is one of them.
7 And there should be some more information provided or
8 a range of values. And it's really hard, given John's
9 example showing sorption -- it's really hard to
10 believe a statement basically saying that TCE sorption
11 is not environmentally relevant and it's all going to
12 be found in the pore water and it's all going to
13 volatilize quickly.

14 I got involved in several projects
15 where we actually used trees to monitor contaminated
16 groundwater. And we monitored concentrations in the
17 trees over the winter when they weren't moving water.
18 And the concentrations didn't change much. So the
19 idea that its rapid volatilization really depends on
20 the environmental conditions and that continued
21 wording that's in these documents, it just needs to be
22 more accurate and more careful.

23 The other point I wanted to make that
24 Sheri touched on briefly -- but the use of the STP

1 model within EPI Suite and some of the percent
2 removals, 81 percent for volatilization, one percent
3 removal via sorption -- those estimates -- and that's
4 all that they are -- don't -- at least in how they're
5 used, they don't assume any air associated with it.
6 In other words, is it 70 to 90 percent? Or is it zero
7 to five percent in terms of sorption? It seems like
8 the effort that went into modeling some of the human
9 endpoints -- and rightfully so because those are the
10 most important -- but the level of sophistication and
11 effort spent in doing the human exposure modeling is
12 way greater than the environmental modeling. And it
13 would just seem, if it's Environmental Protection
14 Agency, we should at least spend a little bit more
15 time dealing with some of those issues.

16 And the other point that was brought up
17 and I'm going to reiterate one more time is the
18 biodegradation pathways. Oftentimes, it's well known
19 that TCE starts dechlorinating under anaerobic
20 conditions. But oftentimes, it ends at vinyl
21 chloride, which is obviously a serious issue. And at
22 least some discussion of that, the biochemical or
23 biodegradation pathways and potential production of

1 toxic byproducts, needs to be incorporated into these
2 documents. Thank you.

3 **DR. KENNETH PORTIER:** Thank you. Dr.
4 Cobb?

5 **DR. GEORGE COBB:** Okay. So I agree
6 with Bill and John on the KOC/KOW aspects and sorption
7 to sediments. I'd also like to point out that part of
8 the conundrum we are in and why that big range that
9 Bill was mentioning may exist in KOW is that, in the
10 field, water has a realistic ionic strength. And when
11 you're measuring a KOW or a KOC in the lab, you're
12 using pure water, most often. So that's going to add
13 some complexity that we're not accounting for when
14 we're modeling things. And I think that's worth
15 noting. And that's all.

16 **DR. KENNETH PORTIER:** Thank you. Any
17 additional comments on Question 1.1? Not hearing any,
18 I think we're going to move on -- oh, yes?

19 **DR. WILLIAM DOUCETTE:** I tried to raise
20 my hand. George just reminded me there are -- because
21 TCE is so data rich, there are several publications
22 that actually look at TCE solubility and Henry's Law
23 constant as a function of temperature and of ionic
24 strength. And so I think there's just a lot more

1 information available for TCE than other compounds
2 that really should be incorporated into this
3 environmental risk assessment.

4 **DR. KENNETH PORTIER:** Bill, do you have
5 references to some of that that you can include in the
6 comments?

7 **DR. WILLIAM DOUCETTE:** Yes, I do. And
8 I will send them to Sheri.

9 **DR. KENNETH PORTIER:** Thank you. Dr.
10 Bethel, why don't we move on to Questions 1.2 and 1.3?

11
12 **CHARGE QUESTION 1 (1.2 AND 1.3)**

13
14 **DR. HEIDI BETHEL:** Okay. Question 1.2,
15 please comment on the data, approaches, and/or methods
16 used to characterize exposure to aquatic receptors
17 from Section 2.2?

18 And Question 1.3, please comment on
19 EPA's assumption that TCE concentrations in sediment
20 pore water are expected to be similar to the
21 concentrations in the overlying water or lower in the
22 deeper part of sediment, in which anaerobic conditions
23 prevail. Thus, the TCE detected in sediments is
24 likely from the pore, Section 4.1.3.

1 **DR. KENNETH PORTIER:** Thank you. Dr.
2 Blystone, I don't know if you're going to answer these
3 separately or together. Why don't we begin with
4 Question 1.2?

5 **DR. SHERI BLYSTONE:** That was going to
6 be my -- do you want me to just go through all the
7 comments for both and then the rest of the discussants
8 can --

9 **DR. KENNETH PORTIER:** Let's go ahead
10 and -- let's just do 1.2.

11 **DR. SHERI BLYSTONE:** I can go right
12 from 1.2 to 1.3, let you know when I've made the
13 change, and then everybody else can just chime in with
14 anything I missed.

15 **DR. KENNETH PORTIER:** Okay.

16 **DR. SHERI BLYSTONE:** Okay. Because at
17 least several commenters talked about there's also a
18 lot of overlap with Question 2, so some of these
19 things may come up again there, or some people may be
20 reserving their comments for Question 2. So we should
21 be aware of that.

22 Dr. Doucette just talked again about
23 some of the physical/chemical properties. I had some
24 comments from him in here, as well, to justify --

1 using the log KOC and high volatilization to justify
2 not evaluating sediment and terrestrial organism, even
3 though TCE is one of the most widespread groundwater
4 and soil contaminants in the U.S. We have to think
5 about that. I think that's already been sort of gone
6 over enough at this point. His comments about the STP
7 model I also had here, but he just reiterated those.
8 So I won't go into that again.

9 There were comments on the E-FAST model
10 not being appropriate for volatile organic compounds
11 according to EPA's own documentation. The comment is
12 "Why spend the time an effort and a large section of
13 the document on a comparison between modeled and
14 measured data if the model is not appropriate for TCE?
15 What data should be used in appropriate modeled data
16 or limited monitoring data? Which should be given
17 more weight? Is it even appropriate to make the
18 comparison?" I'm sure Bill can go into that a little
19 bit more. This is Dr. Doucette's comments. He also
20 recommended that we make it more clear that tables
21 2.7, 2.8, and 2.9 are estimated aqueous
22 concentrations. Table titles and figure captions
23 should stand alone and better distinguish between
24 estimated and measured aqueous concentrations.

1 There were some comments -- I think
2 these are from Dr. Portier -- on Table 2.2. and
3 associated text. Though not indicated in table
4 captions, these are water releases. It depends
5 heavily on TRI and DMR data for 2016 and assumes 260
6 days of operations per year, impact of TRI data coming
7 only from those manufacturers, processors having ten
8 full time employees and that handle greater than
9 25,000 pounds. So there are some limitations there.

10 Impact on DRM data of requirement to
11 load major discharger data but optional to load minor
12 discharge data, in fact, that distinction between
13 major and minor is set independently by each state.
14 If releases to lake water -- is daily averaging an
15 appropriate measure of average water concentration?
16 There is an issue of carryover of undegraded fraction
17 from day one added to releases on day two. That's
18 sort of a question/comment. Wipe cleaning used towel,
19 rag, paper. Where did those contaminated products end
20 up? Into landfills, toxic waste dumps that are just -
21 - also, does this show release of TCE to the
22 environment?

23 Footnote A to Table 2.2 assumes 260
24 days of operations per year in assessing annual

1 releases, but Appendix I, where there is a discussion
2 of the approach to estimating water releases from
3 manufacturing sites using effluent guidelines,
4 apparently assumes and justifies the use of 350
5 operating days per year. The footnotes lead to
6 Appendix 1-2I-2. So what is the basis for the range
7 of estimates for manufacturing estimated daily
8 releases in Table 2.2?

9 Appendix I discusses the approach to
10 estimating water releases from manufacturing sites
11 using effluent guidelines where TRI and DMR data were
12 not available or where TRI and DMR data did not
13 sufficiently represent releases of TCE to water for a
14 condition of use. It would be useful to know what
15 fraction of manufacturing sites had water releases
16 that were estimated by this approach and what fraction
17 used monitoring data directly. Similarly, what
18 fraction of processing facilities under each condition
19 of use were represented by estimates and which by
20 monitoring? This has direct relevance on the
21 uncertainty that would be assigned to arrange
22 estimates reported in Table 2.2. And then this table
23 should refer to Table 2.4 for clearer description of
24 assumption on release days.

1 There was a comment that they had
2 difficulty justifying pounds per day values in Table 2
3 with kilograms per site day estimates in Appendix I.
4 Another comment on Footnote A to Table 2.2. justifies
5 that the OTCD range of water releases for multiple
6 other degreasing, cleaning, and metal working
7 applications because releases were estimated using TRI
8 and DMR data. This sounds less like a justification
9 than an acknowledgement that you only have strong
10 water release data from larger OTCD operations.

11 In Table 2.3, what does it mean when
12 you report a range for the number of facilities? For
13 line two of the table reports five to 440 facilities
14 that are in the scenario processing as a reactant.
15 Should we assess that this is EPA acknowledging that
16 we are not sure of the number of facilities? Is this
17 something like we know of five but there could be as
18 many as 435 more facilities that do this?

19 On the estimate of release days in
20 Section 2.2.2.2.2.3 -- I might have that wrong -- are
21 they really assumptions, not estimates? There are no
22 data on exactly how these facilities operate. Did
23 anyone ask?

1 Everything is assessed as having medium
2 confidence. It's not clear there are any rules as to
3 what is qualified as high or low. This is in overall
4 confidence in release estimates. There seems to be a
5 lot of uncertain components that go into a medium
6 confidence assessment. Medium confidence for
7 commercial printing and copying is unjustified based
8 as it is on one facility that is not likely
9 representative of the whole industry. This should be
10 an example of low confidence in occupational exposure
11 water release estimate.

12 On Table 2.11, the NR value should be
13 replaced with values calculated from the underlying
14 data from tabulated publications. I think this is
15 where Dr. Cobb is going to show something in a little
16 bit, so I'm going to pass over this and let him talk
17 about that later. There's a comment that all
18 references to concentration ranges must be clear what
19 is being reported. The range of 0.4 to -- this is on
20 page 99, line 788. The range of 0.4 to 477 is not the
21 observed concentration range. The range is actually
22 0.05 micrograms per liter to 990 micrograms per liter.
23 And as such, the text is misleading as written.
24 Again, that was on page 99, line 788.

1 In notes from supplemental document 10,
2 environmental data extract, data from Lake Charles PPT
3 facility released TCE that produced mean surface water
4 concentrations of 282 micrograms per liter, a median
5 of 353 micrograms per liter. Throughput surface water
6 concentrations ranged from 0.9 to 126 micrograms per
7 liter. All of these studies report ranges in standard
8 deviations, but the table format seems to indicate
9 only one detection for each. That value of one of the
10 fraction of samples with detectable concentration.

11 The Agency should incorporate a maximum
12 likelihood estimate or tobit, or equivalent for
13 releases from the 668,400 facilities that are likely
14 to use TCE but that do not report TRI data. This
15 approach uses distribution of known observations to
16 predict the unknown observation, or non-detects,
17 68,600 potential or likely users from Table 2.3 and
18 183 facilities reported plus eight wastewater
19 treatment plants. The problem formulation indicates
20 that recycling and disposal at 172 reporting
21 facilities total 91 million pounds, yet the Agency has
22 chosen to assess only 52 pounds of release.

23 It is scientifically indefensible to
24 disregard 91 million pounds of report emissions from

1 reporting facilities and base a nationwide
2 environmental risk assessment on 0.003 percent of the
3 known releases. Similarly, the reported 91 million
4 pounds released is a fraction of the 172 million
5 pounds used in commerce problem formulation. Table
6 2.4, much of the remainder's unaccounted. So again, I
7 think this is going towards that mass balance type
8 issue that the committee has brought up previously.

9 The exclusion of spills in TCE draft
10 risk evaluation is appropriate as the spills resulted
11 from TCE uses in commerce. This emission stems from
12 an unprotective decision to allow hazardous spill
13 emission from the problem formulation. Watershed
14 assessments using the AQC approach can be valuable if,
15 and only if, assessments establish links between
16 facility locations to downstream monitoring data
17 point. Otherwise, the approach is likely to under-
18 report TCE concentrations downstream of manufacturing
19 facilities.

20 That was what I had for 1.2, with the
21 exception of the comments from Dr. Cobb that we'll go
22 into in a minute. On Question 1.3, the comments are
23 as follows. It appears likely that TCE pore water
24 concentrations are similar to overlying water. The

1 movement from sediment is dependent upon the organic
2 carbon content of the sediment. With a predicted log
3 KOC of about two, there is 100 times more likelihood
4 that TCE will be an organic carbon. However, the lack
5 of detected TCE in sewage sludge, which has high
6 concentrations of organic carbon, suggest partitioning
7 into pore water does occur even with this log KOC.

8 There's a comment that the Agency seems
9 to be operating as if all systems are at thermodynamic
10 equilibrium and kinetics to not exist. This is
11 incorrect. Water in sediment pore water and overlying
12 water can only be at equilibrium after an extended
13 distance of turbulent swell along a river reach. In
14 sediments of rivers with low turbulence, only the
15 first centimeters of sediment are in equilibrium with
16 overlying water. There is virtually no advection
17 between stationary sediment and water. Measurements
18 of TCE in sediments near commercial releases are
19 needed.

20 It's also commented that since
21 anaerobic systems most often degrade chlorinated
22 hydrocarbon to be a reductive dichlorination any
23 diminution in TSC in anaerobic sediments will produce
24 dichloroethylene TCE and thus does not eliminate

1 toxicity. TCE production in toxicity has not been
2 assessed in any way for this DRE. So again, we're
3 talking about degradation products.

4 Further comment, how can there be a low
5 partition coefficient to sediments and no exposure
6 route to terrestrial organisms if TCE is present in
7 soil? These contradicting statements by the Agency
8 make no sense, and the inconsistency must be resolved.
9 Either there's low partition to sediment and soil and
10 that slices soil sediment dwelling organism at acute
11 risk, or there's high partition to soil and sediment
12 and the risks would be considered -- would more likely
13 be chronic. The partition coefficient for measured
14 data in U.S. EPA 1977 shows field measured partition
15 coefficients of 0.076 and 0.32 when using geometric
16 mean and arithmetic mean, concentrations in water and
17 sediment media. The Agency must justify that 0.32 or
18 32 percent represents low partitioning to sediment.

19 Finally, there was a comment the review
20 of available data raised questions regarding the
21 extent to which TCE may be present in sediments. Yet,
22 no monitoring studies have been conducted to refute
23 the available data. Thus, the Agency erroneously
24 states that review and evaluation of reasonably

1 available information on TCE confirmed problem
2 formulation conclusions. And that is all that I had,
3 like I said, with the exception of the table that Dr.
4 Cobb is going to discuss.

5 **DR. KENNETH PORTIER:** Thank you, Sheri.
6 Dr. Doucette, your hand's up.

7 **DR. WILLIAM DOUCETTE:** Oh, sorry. I
8 want to hear George's comments before I comment any
9 more. So I'll lower my hand. Sorry.

10 **DR. KENNETH PORTIER:** Okay. Why don't
11 we jump to Dr. Cobb?

12 **DR. SHERI BLYSTONE:** And this is Sheri
13 again. There was a slide. Yeah.

14 **DR. GEORGE COBB:** It's up here.

15 **DR. SHERI BLYSTONE:** I think that's not
16 the latest one you did, George. I'm sorry.

17 **DR. GEORGE COBB:** Do not worry. It's
18 all good. So first of all, thank you to Sheri for
19 reading all of that in for all of us. She does a much
20 better job than I do at that.

21 The point of this slide is that the
22 available data that EPA has from actual monitoring
23 data, even if it is from 1977 -- this is the data that
24 we have for monitoring data. Part of the point here

1 is that trichloroethylene in water -- the mean,
2 whether you're using arithmetic or geometric mean, are
3 all substantially higher than anything that's in the
4 risk assessment. I should have stated that clearly --
5 are often higher than anything that's in the risk
6 assessment.

7 And if you look at the middle of that
8 graph there, maybe lower middle part, you see a
9 centile, a 92nd centile and a 76th centile, of all of
10 the data from all of those sites is 447 micrograms per
11 liter. And the 76th centile is 179 micrograms per
12 liter. So these are both higher than the estimates
13 that are in the DRE. And failing any other available
14 data, I submit that the 92nd or the 76th centile of
15 these estimates be used. There are ways to get to a
16 90th centile or 75th percentile mathematically if the
17 Agency would choose. But the big point is those data
18 are available.

19 The other point I'd like to make is
20 that the sediment data are also there. And those data
21 demonstrate clearly that TCE partitions to sediment in
22 riverine environments. One of these may have been
23 eserine. I'm not -- I need to kind of clarify that a
24 little bit. But there are sediment data. There are

1 water data, and the data clearly show the TCE
2 partitions into sediments. And with that -- that's
3 all I had to say. I think EPA either needs new data
4 or they need to use the existing data, which look to
5 be this data from 1977. That's it.

6 **DR. KENNETH PORTIER:** Thank you,
7 George. Back to Dr. Doucette.

8 **DR. WILLIAM DOUCETTE:** No, I think
9 Sheri covered it. And with George's additional point,
10 it just emphasized that it's really hard to make the
11 justification that there's no sorption to sediments.
12 Thank you.

13 **DR. KENNETH PORTIER:** Thank you. Dr.
14 Kissel?

15 **DR. JOHN KISSEL:** Yeah. I wanted to
16 highlight again Slide 13 that George mentioned. It
17 shows sort of a one-way transport. So you have
18 discharge to surface water, and then the surface water
19 leads to transport into the sediments. And then
20 sediments are an incident sink and anaerobic
21 degradation removes the problem. And that's really a
22 hyper simplified view of the world.

23 And I would, for instance, call
24 people's attention as an example to the experience at

1 the Wells G&H superfund site in Woburn, Massachusetts,
2 which was rather notoriously associated with a
3 leukemia cluster in children. When the wells were
4 riverbank wells and when they were turned on, the
5 water was sucked out of the river, through the
6 sediments, into the groundwater. So flow can go
7 multiple directions, and sediments can be a reservoir
8 from which stuff would slowly be released. And I
9 think we made the point that sorption matters.

10 In one of the comments that Sheri read,
11 there was something that suggested that somehow the
12 sewage sludge data were interesting. I think other
13 people have already noted that there may be an
14 analytical problem there that they didn't even look
15 for TCE in the sewage sludge. But in any case, sewage
16 sludge, generally, by the time you would get to it to
17 analysis it, has probably been at least endogenously
18 heated and perhaps dried out, which would provide a
19 lot of opportunity for volatilization, which would
20 pertain in no way, shape or form to what goes on in
21 sediments and aquifer solids. So I think the
22 references to sewage sludge are ill considered. And
23 that's all I have.

1 **DR. KENNETH PORTIER:** Thank you, John.

2 Dr. Schlenk, did you want to add anything?

3 **DR. DANIEL SCHLENK:** No. I think
4 pretty much Sheri got everything I said. I actually
5 was the one who talked about the sewage sludge and
6 didn't consider the air issue. And I totally agree
7 that any of the biosolid data's probably been heated
8 beyond repair. It was just the fact that, you know, I
9 was mostly focusing on the organic carbon content. If
10 it were present there, then for sure you would see it
11 in sediments I would guess but definitely in an
12 anaerobic situation with heat. So you would probably
13 lose that, so my mistake there.

14 **DR. KENNETH PORTIER:** Thank you. This
15 is Ken Portier. I wanted to make one comment. Sheri
16 read most of my comments in. On the release to lake
17 water, what got me thinking about this was it mentions
18 110 hours as the half-life of TCE in lake waters. And
19 if you start thinking about it, if you're releasing
20 every day, a very small amount will dissipate within a
21 day. And it would build up quickly. So something in
22 the discussion needs to clarify that particular issue.
23 At this point, any additional comments on 1.2 or 1.3?
24 Dr. Morandi?

1 **DR. MARIA MORANDI:** Yes, I have a
2 question, a clarification. And this is for George's
3 comment regarding the data available in terms of
4 concentrations in water. And that data dates back to
5 1977. And there has been a lot of modifications and
6 processes to reduce the amount of TCE used. So how
7 would then -- would you account for the difference in
8 releases from those facilities?

9 And by the way, some of those
10 facilities may no longer exist. I'm thinking like SU
11 Corporation. I would have to check on that. So I
12 would like him to elaborate on how -- it seems to me
13 you cannot use those water concentrations straight
14 without accounting for any decreases over time in the
15 amounts of TCE released because TCE may have been
16 removed from several process.

17 **DR. KENNETH PORTIER:** Dr. Cobb?

18 **DR. GEORGE COBB:** Actually, thank you
19 for that question because it gets to a point I think I
20 was going to bring up in the next question. But this
21 is a good point. If you look at, let's see -- I don't
22 know how to pronounce this name -- Bakke, B-A-K-K-E,
23 et al 2007, which is one of the references in I forget
24 what appendix -- but it's in one of the appendices --

1 talking about U.S. production, that article actually
2 has a tabulated production of TCE or use of TCE in the
3 U.S. And in 1977, that value was 117 million
4 kilograms. And now, we are at 172 divided by 2.2.,
5 whatever that is, 80.

6 **DR. MARIA MORANDI:** It's about half.

7 **DR. GEORGE COBB:** While we're from 117
8 to 80 -- and yeah. That's a 20 or 30 percent
9 decrease, but it's not a 50 or 75 percent decrease.
10 So that's my point is, well, if you want to divide
11 those by 117 over 80, then that's fine. But those
12 data are still much higher than anything that's in
13 these estimates. Does that answer your question?

14 **DR. MARIA MORANDI:** Yes.

15 **DR. KENNETH PORTIER:** Thank you. Dr.
16 Kissel, your hand's still up?

17 **DR. JOHN KISSEL:** My mistake.

18 **DR. KENNETH PORTIER:** Okay. Any
19 additional clarifications or additional comments on
20 Questions 1.1, 1.2, 1.3?

21 **MR. ALAN KAUFMAN:** Ken, this is Al
22 Kaufman. No comments, but I just want to let you know
23 I'm going to have to drop off now for another call.

24 **DR. KENNETH PORTIER:** Okay, Al.

1 **MR. ALAN KAUFMAN:** All right. When do
2 we start tomorrow? 10:00 as well?

3 **DR. KENNETH PORTIER:** Yes.

4 **MR. ALAN KAUFMAN:** Okay. Talk to you
5 then. Thank you.

6 **DR. KENNETH PORTIER:** Okay. Again, I'm
7 finding it's useful to take a short break between
8 these questions just so, if nothing else, we can
9 stretch up and air our ears. So I think we're going
10 to take a -- I have 3:59. Let's reconvene at 4:05,
11 4:06, and we will begin Question 2 at that point.
12 Let's take a six-minute break here.

13 (BREAK)

14 **DR. KENNETH PORTIER:** Okay. I think
15 it's time to reconvene. I should have asked EPA staff
16 at the end of Question 1 whether there were any
17 clarifying questions they had on the comments
18 presented to them by the panel. Hearing none, I'm
19 going to ask Dr. Bethel to read Question 2.1 in.

20 **DR. HEIDI BETHEL:** Can you move the
21 slides forward, please?

22 **DR. KENNETH PORTIER:** Yeah. It's
23 there.

1 **DR. HEIDI BETHEL:** Oh, now I'm on
2 Question 4. Maybe I did that.

3 **DR. KENNETH PORTIER:** We're seeing
4 Questions 2.1 and 2.2.

5
6 **CHARGE QUESTION 2 (2.1)**

7
8 **DR. HEIDI BETHEL:** Okay. I see it now,
9 too. So Question 2, environmental exposure and
10 releases, EPA estimated releases using toxic release
11 inventory and discharge monitoring report data.
12 Environmental exposures were estimated using this data
13 as inputs to EFAST 2014 and compared to monitored
14 surface water values.

15 Question 2.1, please comment on the
16 approaches, models, and data used in the water release
17 assessment, including comparison of model data to
18 monitored data. See Section 2.2.

19 **DR. KENNETH PORTIER:** Good. Now, the
20 lead on this is Dr. Schlenk. Dan?

21 **DR. DANIEL SCHLENK:** Okay. Can you
22 hear?

23 **DR. KENNETH PORTIER:** Yup.

1 **DR. DANIEL SCHLENK:** Okay. Good. So
2 yeah. I'll just stay separately as 2.1, and then we
3 can go through the associates from that. And then
4 we'll do 2.2 afterwards, if that's okay.

5 So modeling estimates were obtained
6 from EFAST using data compiled from TRI, DMR, and CDR.
7 A probabilistic dilution module was then used to
8 estimate surface water concentrations in freshwater
9 streams and still water systems. Some committee
10 members think that this is still unclear on how these
11 data were used in the model. In particular, one
12 committee member thought the MPDS data from DMR was
13 unclear.

14 Based upon the DRE, it seems the only
15 data compiled from DMR was dilution data. It is
16 unclear why monitoring data for TCE in wastewater
17 effluent was not obtained from MPDS. While it appears
18 the tenth percentile value of stream dilution is used
19 as a conservative measure, it is unclear why the upper
20 end conservative value, i.e. 90th percentile of EFAST
21 values, was not used for effluent discharge.

22 Another committee member indicated it
23 was unclear why surface water data across the country
24 was assessed. It was unclear whether the agency was

1 trying to back calculate these to discharge values and
2 then calculate that to uses. This committee member
3 thought it seemed more prudent to confirm model
4 predictions in effluent than use dilution model to
5 predict surface water concentrations at the site. It
6 was also unclear why municipal wastewater was excluded
7 from the WQX data that was used for the comparison.

8 One committee member thought that the
9 approaches followed by EPA to assess water releases
10 seemed adequate. Sections 2.2.2.3, 2.2.6.3., and
11 2.2.6.4 in the report did a good job in highlighting
12 limitations and uncertainties of the assessment. For
13 instance, the TRI data's probably the best source for
14 mass flows. But given its inherent limitations, for
15 example excluding companies with less than ten full-
16 time employees, unknown threshold, potential
17 underreporting, the committee suggested this is likely
18 to be an underestimation of loading.

19 Other points, on the beginning of
20 Section 2.2.6.2.2., it's not clear to the reader what
21 "cleanse datasets" means. I think this was addressed
22 earlier. The committee member suggests enhancing
23 clarity with a quick reminder of the definition given
24 the length of the overall report. The reasons for the

1 filtrate in cleaning are described below, but that is
2 a few paragraphs after the concept of "cleanse
3 dataset" was introduce.

4 In Table 2.10, although not a full
5 uncertainty assessment, this did provide a good sense
6 of potential uncertainty through presenting data
7 ranges and standard deviations. This committee member
8 would recommend using this type of data representation
9 more often through the report when a full uncertainty
10 assessment is not available. The first paragraph in
11 Section 2.2.3 lists advantages of using EPA's EFAST.
12 This committee member thought it would be nice to list
13 at least on disadvantage of using this tool for
14 everything. Are there other models to which EFAST
15 results could be compared?

16 Assumption of just one value for the
17 percent removal from wastewater treatment is based on
18 the specific kind of industrial wastewater treatment
19 facility. Is there any information on the variation
20 of types of industrial wastewater facilities in use,
21 for example, sludge, dewatering, chemical, biological,
22 aerobic, anaerobic, composting, physical screening,
23 sedimentation skimming at facilities that manufacture
24 a processed TCE? On page 89, data filtering and

1 cleansing, again, while placing non-detects with half
2 the detects limit for summary calculation purposes is
3 typical practice, it comes with a cost.

4 If there are few detects, the average
5 concentration becomes close to half the detection
6 limit and is likely an overestimate of the true
7 average concentration. If there are many detects, say
8 greater than 70 percent of observations, than using
9 half the detection limit for non-detects likely has
10 little effect on final average. Since we're often
11 most concerned with higher average concentrations, the
12 overestimation of lower average concentration is not a
13 major issue.

14 Also on page 89, geospatial analysis
15 approach, if the geospatial analysis find a superfund
16 site within one to five miles of the facility, then
17 the DRE indicated that those monitoring sites are
18 excluded. How does this work for DOD facilities that
19 use TCE that are on military bases, and what if the
20 military base also has a superfund site? What if the
21 monitoring site is downstream of the TCE use facility
22 but upstream from the superfund site?

23 On page 90, geographic coordinates, the
24 location of release points is needed rather than the

1 address of the facility or the front door of the
2 superfund site. The geographic analysis sounds quite
3 cursory. The committee member thought that this is a
4 screening analysis, but incorporating land slope,
5 superfund site boundaries, and facility discharge
6 points does not sound like that much extra work.

7 From Table 2.7 to 2.9, the committee
8 member has trouble remember -- has to remember that
9 one part per billion equals one microgram per liter.
10 Since concentrations in the GIS worker reporting
11 micrograms per liter and monitoring concentrations are
12 reported in micrograms per liter, why aren't these
13 tables in micrograms per liter? Also, why are COCs
14 reported in parts per billion instead of micrograms
15 per liter?

16 Page 92 to 93, state of active facility
17 releases and release characteristics should be
18 reported in Sections 2.2.2.2.2 or Section 2.2.2.2.2
19 text moved here or cross-referenced. On Table 2.10,
20 with such a high fraction of non-detects average is
21 likely an overestimate but standard deviation likely
22 an underestimate. Note that in all years the average
23 detection is less than the average of all data,
24 suggesting that there are a lot of non-detects from

1 sites where the detection limit is closer to five than
2 to 0.022.

3 In terms of assumptions and key sources
4 of uncertainty for environmental exposures, EFAST does
5 not estimate stream concentrations based on the
6 potential for downstream transport and dilution. But
7 it is okay for nearfield environmental concentration
8 estimation, poor for downstream concentrations, which
9 are the bulk of environmental measurements. A key
10 admission is the fact that EFAST streamflow data are
11 15 to 30 years old. More recent, last ten years, data
12 needs to be used to significantly decrease
13 uncertainty. GIS work has not been validated through
14 ground shifting.

15 With regard to confidence in aquatic
16 exposure scenarios, the DRE concludes overall moderate
17 confidence. A majority of the committee concludes,
18 despite a lot of work and best intentions, confidence
19 in exposure scenarios is low, primarily due to the
20 higher proportion of uncertainty. More detailed GIS
21 modeling is needed to raise confidence to moderate.
22 And that's all I have for 2.1.

23 **DR. KENNETH PORTIER:** Thank you. Dr.
24 Blystone?

1 **DR. SHERI BLYSTONE:** Sorry. It takes
2 me so long to get everything unmuted. I didn't have
3 anything additional.

4 **DR. KENNETH PORTIER:** All of that work
5 to say, "I don't have anything."

6 **DR. SHERI BLYSTONE:** Exactly.

7 **DR. KENNETH PORTIER:** Dr. Doucette?

8 **DR. WILLIAM DOUCETTE:** Yeah. I think
9 Dan covered everything. I think it still comes down
10 to this, for at least my opinion -- it comes down to
11 old monitoring data versus using modeled data for a
12 model that EPA documentation says is not appropriate
13 for this type of compound. And even in the model,
14 even if we believed it was appropriate, as was just
15 mentioned, the stream data's old. It's about the same
16 age as the monitoring data. So I don't know if I have
17 a solution there. It's just I'm not sure that it was
18 worth a lot of effort in making the comparison between
19 the modeled and the monitoring data when the model's
20 not even appropriate for this sort of compound.

21 **DR. KENNETH PORTIER:** Thank you. Dr.
22 Jimenez-Gonzalez?

1 **DR. CONCEPCION JIMENEZ-GONZALEZ:** Yes.
2 I think all my points were really well covered earlier
3 on, so nothing to add.

4 **DR. KENNETH PORTIER:** Thank you. Dr.
5 Cobb?

6 **DR. GEORGE COBB:** Dan captured the vast
7 majority of my comments very well. I'd maybe like to
8 revisit one topic or tie two topics together. Sheri
9 mentioned my comment I think about spills needing to
10 be used or included because they're part of commerce.
11 I also want to point out it's ironic that EPA has used
12 the Detoro dilution model in streams, which is
13 designed for surface runoff. It's not designed for
14 point source continuous discharge.

15 So while excluding surface runoff and
16 spills, the Agency's used a model that is designed
17 specifically for runoff scenarios. And I'm not sure
18 the extent to which the difference between the pulse
19 released in a surface runoff event versus a continuous
20 discharge would affect the outcome. But I think the
21 Agency should at least evaluate -- somebody that has a
22 better mathematical skill set than me -- how that
23 would potentially affect the outcome of the models.

1 **DR. KENNETH PORTIER:** Thank you,
2 George. Does anyone else on the committee want to
3 comment on Question 2.1? Why don't we go ahead and
4 read in Question 2.2 then?

5
6 **CHARGE QUESTION 2 (2.2)**

7
8 **DR. DANIEL SCHLENK:** Okay. I gathered
9 we already read 2.2. into the record, so I'll just go
10 ahead. So the points here are related, again, to MPDS
11 measurements. Again, if MPDS measurements of TCE
12 could be obtained, a much more robust method of
13 comparison of modeled EFAST data versus measured data
14 could be performed. While measured data was obtained
15 from WQX, this data was primarily surface water
16 measurements that were rarely obtained from discharge
17 sites. Apparently, there were only two where the TRI
18 or other input data was used -- and TRI and other
19 input data was used in EFAST instead. The committee
20 found it concerning that available monitoring data
21 could not be used to corroborate the monitoring
22 approach given the downstream distance, which may
23 represent opportunity for EPA to implement a program

1 monitoring that can provide more data with more
2 confidence.

3 Some other points, on Table 2.3,
4 summary of EPA's estimates for the number of
5 facilities, the estimate of the number of facilities
6 could be enhanced by adding a sense of uncertainty or
7 plus or minus X percent or X facilities. This is
8 evidently needed as one sees the number of facilities
9 for processing as reactant estimated at five to 440,
10 which is quite a range, whereas the rest of the
11 estimations are left without a sense of uncertainty.
12 Ranges across all the estimates may be recommended or
13 a statement of mathematical uncertainty could be
14 added.

15 The report mentions in Section 2.2.5
16 surface water concentration maps, but they were not
17 present. The color coding was provided, but it is not
18 apparent where the maps are. And are those maps in
19 Section 4? If so, this committee member couldn't see
20 the immediate reference.

21 For Figure 2.4, the choice of a tornado
22 graph does not seem to be the best one to promote
23 clarity. One committee member suggested a set of pie
24 charts or section bar graphs may better illustrate the

1 point. Given the uncertainties in medium confidence
2 ranking for the environmental exposure and release
3 aspects, one committee member recommended they do a
4 sensitivity assessment to better understand the impact
5 of key assumptions and limitations in the final
6 conclusion. This committee member noted that there
7 was a sensitivity assessment done in terms of species,
8 i.e. specie sensitivity distribution, which is a good
9 step forward. But there's also the need to evaluate
10 how sensitive the environmental exposure estimates are
11 to assumptions or at least get a semi-qualitative
12 assessment. EPA indicates that where they cannot
13 definitively assign a facility to --

14 **DR. KENNETH PORTIER:** Daniel, it seems
15 they've lost you.

16 **DR. DANIEL SCHLENK:** Oh, okay.

17 **DR. KENNETH PORTIER:** You're back.
18 You're back.

19 **DR. DANIEL SCHLENK:** Am I back now?

20 **DR. KENNETH PORTIER:** Yeah.

21 **DR. DANIEL SCHLENK:** That's weird.

22 **DR. KENNETH PORTIER:** You said, "and it
23 seems that --" And I think that's where we lost you.

1 **DR. DANIEL SCHLENK:** Okay. Given the
2 uncertainties of medium confidence -- oh, yeah. Okay.
3 The choice of a tornado graph does not seem to be the
4 best one to promote clarity. One committee member
5 suggested that a set of pie charts or sectioned bar
6 graph may be better to illustrate the point. Given
7 the uncertainties in medium confidence ranking for
8 environmental exposure and release aspects, one
9 committee member recommended to do a sensitivity
10 assessment to better understand the impact of key
11 assumptions and limitations in the final conclusion.
12 This committee member noted there was a sensitivity
13 assessment done in terms of species, i.e. species
14 sensitivity distribution. And this is a good step
15 forward, but there's also the need to evaluate how
16 sensitive the environmental exposure estimates are to
17 assumptions or at least get a semiquantitative
18 assessment.

19 EPA indicates that where they cannot
20 definitively assign a facility to a COU based on TRI
21 or DMR reporting information, they assigned it to a
22 most likely or primary COU. Depending on the number
23 of sites, it seems like EPA could have asked those
24 facilities for more information on how TCE is used

1 onsite. For manufacturing sites, only three or five,
2 question mark, it seems the EPA could have asked more
3 information on the days of manufacture versus the
4 estimated 350 days per year. And this could have
5 reduced uncertainty. And that's all I got for 2.2.

6 **DR. KENNETH PORTIER:** Sounded like a
7 lot to me, Dan. Dr. Blystone, anything to add?

8 **DR. SHERI BLYSTONE:** Nope. He captured
9 my comments. Thank you.

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

11 **DR. WILLIAM DOUCETTE:** Nothing to add.

12 **DR. KENNETH PORTIER:** Dr. Jimenez-
13 Gonzalez?

14 **DR. CONCEPCION JIMENEZ-GONZALEZ:**
15 Nothing to add.

16 **DR. KENNETH PORTIER:** Dr. Cobb?

17 **DR. GEORGE COBB:** Nothing to add.

18 **DR. KENNETH PORTIER:** Anyone else on
19 the panel wish to comment on Question 2.2? I'm not
20 hearing any additional comments. I'll turn at this
21 point to EPA and ask whether there are -- do you have
22 any follow up questions of the panel on their comments
23 and answers to your questions?

24 **DR. STANLEY BARONE:** Not at this time.

1 **DR. KENNETH PORTIER:** Thank you, Stan.
2 At this point, we're a little ahead of our agenda but
3 not enough that I feel inclined to move forward with
4 Question 3. I did notice that Dr. Matten with EPA has
5 her hand up. I wondered if she had a comment or
6 wanted to address the panel. Dr. Matten?

7 **DR. TODD PETERSON:** Well, Ken, if she
8 doesn't -- this is the DFO. I do have something to
9 read at the close. So if you're close to closing, do
10 what you will to work with the panel to get to that
11 point and then let me know.

12 **DR. KENNETH PORTIER:** Yeah. Okay. Dr.
13 Blystone, your hand's up.

14 **DR. SHERI BLYSTONE:** Yeah. I just
15 wanted to make a comment going back to Question 1 and
16 the exchange between Dr. Cobb and Dr. Morandi. And
17 Dr. Cobb made the point that there wasn't a lot of
18 reduction in production volume over the years from the
19 older data that he was looking at. But I did want to
20 point out that, in that intervening time, there was
21 probably a lot of work done on processing and that
22 would impact releases. So I'm talking about
23 engineering, different processes, whatever. So you
24 can't -- just because production volume's the same,

1 you wouldn't necessarily expect releases to be
2 similar.

3 **DR. KENNETH PORTIER:** I kind of had the
4 same feeling when I looked at it and thought about
5 data that's 35, 37 years old on not just releases but
6 on streamflow with changes in climate and other
7 factors. I just have a hard time thinking that
8 today's environment is that similar to what it was 40
9 years ago. I think with that comment, I'm going to
10 turn the meeting over -- oh, wait. Dr. Bennett, I see
11 your hand's up.

12 **DR. STEVEN BENNETT:** Sorry. I just
13 wanted to add into that. I think the other piece,
14 too, was what I brought up earlier -- was the HFC134
15 production or HFC134A production, which would have
16 been nonexistent. And that was encompassing over 80
17 percent of the production in the cite reported in the
18 risk assessment. So that's another factor that would
19 factor prominently in that, in the amount of TCE
20 produced.

21 **DR. KENNETH PORTIER:** Good point. Dr.
22 Cobb?

23 **DR. GEORGE COBB:** Yup. Can you all
24 hear me?

1 DR. KENNETH PORTIER: Yes.

2 DR. GEORGE COBB: Okay. So I agree
3 with the other two comments. I think the Agency
4 should very seriously look at stream flows, as have
5 been pointed out by others, that are not the same as
6 in the EFAST database. They should also look at uses.
7 One thing, it's difficult to tease out what the actual
8 productions and uses are through all of these
9 datasets. But if the production is going into
10 commerce and the same amount's going in every year,
11 it's got to be coming out somewhere, unless it's a
12 reactant making a polymer somewhere, which is entirely
13 possible. You're going to have material in and
14 material out. Until you can close that mass balance,
15 which is what we've been talking about a lot of times
16 in these events, we're just kind of guessing.

17 And then the last thing I'd like to
18 reiterate is something that Sheri read into the
19 record, but I want to make it -- just circle back to
20 it. Using the EPI Suite models and the actual release
21 data that EPA is using for reporting releases to air,
22 soil, and water, you get a net flux of TCE out of air
23 and into water that increases the concentrations in
24 water substantially. So I will be quiet there.

1 **DR. KENNETH PORTIER:** Thank you, Dr.
2 Cobb. And I know we've had some conversation on this
3 production release mass balance concept, and I think
4 we're going to cover that this time in Question 7. So
5 we're going to have something hopefully substantial to
6 offer there to EPA on that issue. Okay. At this
7 point, I'm going to end the discussion on Question 2,
8 and I'm going to turn the meeting back over to the
9 DFO, Todd Peterson. Todd?

10 **DR. TODD PETERSON:** Yes. Thank you.
11 So during the virtual meeting when all the peer
12 reviewers got together, I made a statement and I
13 called it an understatement. And I was saying, as an
14 understatement, we really appreciate what this panel
15 has been doing. And I just said, simply, thank you.
16 That's the understatement because, except for one new
17 reviewer, the people that have been on this call today
18 with the review, they're working together and have
19 worked well together since our very first SACC peer
20 review back in June of 2019. So it's a good group,
21 and you've been working hard.

22 So there have been some questions about
23 why we went ahead, even under the present
24 circumstances, with the virtual meeting. So I'm going

1 to read to you a statement that I just received, and
2 this is a statement from the EPA Office of Chemical
3 Safety and Pollution Prevention Assistant
4 Administrator Alexandra Dapolito Dunn. And you heard
5 AA Dunn address the meeting earlier this morning.

6 And she's saying, "EPA understands that
7 these are challenging times for everyone and is aware
8 that there were requests to postpone the meeting based
9 on the response to the current unprecedented events
10 related to COVID-19. EPA is working on many fronts to
11 address the COVID-19 pandemic but also continues to
12 have the responsibility to evaluate the risks of
13 chemicals under TSCA. EPA made a decision to proceed
14 with this important peer review meeting after ensuring
15 a majority of SACC members, representing a range of
16 diverse perspectives, were available and interested in
17 participating through a virtual format. We greatly
18 appreciate the SACC reviewers' commitment and response
19 to this call to help us continue our mission." And
20 that's the end of AA Dunn's statement.

21 And I will just say, having been part
22 of all the planning leading up to this virtual meeting
23 and all the people who have contributed to making it a
24 success, today went well. We're still online, and

1 you're still listening. And we're going to continue
2 this process starting tomorrow morning at 10:00 a.m.
3 And with that, I adjourn the meeting as DFO. We'll be
4 talking to you tomorrow. Host, you may end the
5 session.

6 **(MEETING ADJOURNED FOR THE DAY)**
7

OPENING OF MEETING - DAY 2

OPERATOR: Good morning. Welcome to the second day of this meeting series on the U.S. EPA Peer Review of the Draft Risk Evaluation for Trichloroethylene or TCE. Batelle is an EPA contractor providing meeting support for this series. This event is being recorded.

The host may use chat to share announcements with all attendees, but attendees will not be able to respond to the chat. Panelists, please send direct messages to the host or panelists. Do not message all attendees or all participants. I will now introduce Dr. Todd Peterson, the designated federal official.

DR. TODD PETERSON: Good morning. I am Dr. Todd Peterson, and, as the designated federal officer, it is my pleasure to open the second day of the four-day meeting of the Science Advisory Committee on Chemicals -- TSCA SACC is for short -- Peer Review of EPA's Draft Risk Evaluation for Trichloroethylene. I must say

1 yesterday's WebEx hosted meeting went well.

2 However, if you encounter any problems with audio
3 or video transmissions today, again, please go to
4 our web page. And I'll give you the URL. That's
5 <https://www.epa.gov/> -- and it's TSCA. That's T-
6 S-C-A, hyphen, peer, P-E-E-R, hyphen, review, R-E-
7 V-I-E-W. And then on that web page you can click
8 on a link in the side bar that says -- the text of
9 the link says "information on virtual meeting" --
10 peer review meeting for the Draft Risk Evaluation
11 of Trichloroethylene and when that next page comes
12 up, you'll find some helpful hints on what to do
13 next.

14 Today, the agenda as sent out as
15 drafted does not indicate anything but a lunch
16 break. However, we will have the chair announce
17 either 10- or 15-minute breaks that will occur
18 before and after the lunch time. This will only
19 add a modest amount of time to today. We should
20 easily meet the federal register's notice of
21 announcement of meetings ending at 5:00 p.m.
22 Eastern Daylight Time, so that will help. And

1 he'll announce those breaks, and we will post on
2 the screen when the return time is for those
3 coming into the meeting.

4 Also, as noted in my opening
5 comments yesterday, a reminder that peer reviewers
6 please send a note to myself and the chair
7 indicating if you must step away for a short time,
8 and then also let us know when you've come back.
9 In a minute, we'll do the check-in roll call and
10 then start today's meeting. And therefore, I turn
11 the meeting over to Dr. Portier.

12 **DR. KENNETH PORTIER:** Good morning,
13 everyone. Welcome to Day 2 of this Science
14 Advisory Committee on Chemicals review of
15 trichloroethylene. We're going to begin this
16 morning by just calling the role to ensure -- to
17 at least ensure to the public that the committee
18 is here and ready to work. I'm Ken Portier,
19 chair, biostatistician. And I'll start with --
20 Dr. Anderson is here, but he's been called away
21 first thing this morning. So we'll skip him. Dr.
22 Bennett?

1 **DR. STEVEN BENNETT:** Good morning.

2 I am here. Steve Bennett with the Household &
3 Commercial Products Association. I'm a chemist by
4 training, and I'll bring expertise on consumer use
5 and exposure to the panel.

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

7 Dr. Barton.

8 **DR. CHARLES BARTON:** Hello, my name
9 is Chuck Barton. I'm an independent consultant in
10 toxicology. My expertise is toxicology and risk
11 assessment.

12 **DR. KENNETH PORTIER:** Dr. Blystone.

13 **DR. SHERI BLYSTONE:** Yes, hi. Sheri
14 Blystone, chemist with SNF Holding Company,
15 product safety and compliance.

16 **DR. KENNETH PORTIER:** Dr. Bruckner.

17 **DR. JAMES BRUCKNER:** Jim Bruckner,
18 pharmacologist, toxicologist, pharmacokineticist,
19 University of Georgia, emeritus professor.

20 **DR. KENNETH PORTIER:** Dr. Cory-
21 Slechta.

1 **DR. DEBORAH CORY-SLECHTA:** This is
2 Deborah Cory-Slechta, Department of Environmental
3 Medicine, University of Rochester Medical School.
4 I am a neurotoxicologist by research.

5 **DR. KENNETH PORTIER:** Thank you.
6 Dr. Davies.

7 **DR. HOLLY DAVIES:** Hi, this is Holly
8 Davies. I'm a toxicologist at the Washington
9 State Department of Health. I have a background
10 in developmental and reproductive genetics, and I
11 have expertise in consumer exposure.

12 **DR. KENNETH PORTIER:** Dr. Doucette.

13 **DR. WILLIAM DOUCETTE:** Yeah. I'm
14 Bill Doucette, an environmental chemist and
15 professor at Utah State University.

16 **DR. KENNETH PORTIER:** Thank you.
17 Dr. Jimenez-Gonzalez is going to be joining us at
18 10:30. She had an early morning meeting. Dr.
19 Gilbert.

20 **DR. KATHLEEN GILBERT:** Good morning.
21 I'm an immunotoxicologist retired from the
22 Universities of Arkansas for Medical Sciences.

1 DR. KENNETH PORTIER: Dr. Johnson.

2 DR. MARK JOHNSON: Good morning.

3 Mark Johnson, director of toxicology for the
4 Army's Public Health Center. My background's in
5 environmental toxicology and risk assessment.

6 DR. KENNETH PORTIER: Dr. Kaufman.
7 Dr. Kaufman. Dr. Kissel.

8 MR. ALAN KAUFMAN: Sorry, Ken, this
9 is Al Kaufman. It muted me again. Can you hear
10 me?

11 DR. KENNETH PORTIER: Yes.

12 MR. ALAN KAUFMAN: Okay. Hi, Al
13 Kaufman. I'm with the Toy Association handling
14 technical affairs; biologist and chemist by
15 training; and expertise is manufacturing
16 operations, downstream uses, and consumer
17 exposure.

18 DR. KENNETH PORTIER: Thank you.
19 Dr. Kissel.

20 DR. JOHN KISSEL: John Kissel,
21 professor emeritus of Environmental and
22 Occupational Health Sciences at the University of

1 Washington in Seattle, engineer by training and
2 human exposure scientist by practice.

3 **DR. KENNETH PORTIER:** Dr. Rowlands.

4 **DR. CRAIG ROWLANDS:** Good morning,
5 Craig Rowlands. I'm a toxicologist and a risk
6 assessor with Underwriters Laboratories corporate
7 research and development.

8 **DR. KENNETH PORTIER:** Dr. Schlenk.

9 **DR. DANIEL SCHLENK:** Dan Schlenk,
10 professor of aquatic hematoxicology, University of
11 California, Riverside.

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

13 That's the committee members. The ad hoc members
14 -- Dr. Apte.

15 **DR. UDAYAN APTE:** This is Udayan
16 Apte. I'm an associate professor of toxicology at
17 University of Kansas Medical Center. My expertise
18 is in drug-induced liver injury, toxicology,
19 chemical carcinogenesis, and liver pathobiology.

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

21 Dr. Cobb.

1 **DR. GEORGE COBB:** Hi, this is George
2 Cobb. I'm the chair of the Environmental Science
3 Department at Baylor University. I'm an
4 analytical environmental chemist by training and
5 have done a bit of exposure assessment work for
6 ecological risk assessments.

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

8 **DR. STEPHEN GRANT:** Yes, I'm Stephen
9 Grant. I'm a professor of public health at Nova
10 Southeastern University. My background is in
11 genetics, but I've been working on cancer for the
12 last 30 years from both a genetic and
13 toxicological side.

14 **DR. KENNETH PORTIER:** Dr. Hossain.

15 **DR. MUHAMMAD HOSSAIN:** Hi, I am
16 Muhammad Hossain, assistant professor in the
17 Department of Environmental Health Sciences and
18 Florida International University. By training,
19 I'm a veterinarian, and I have expertise in
20 neurotoxicology and molecular and neuroscience.

21 **DR. KENNETH PORTIER:** Dr. Jenkins.

1 **MS. ALLISON JENKINS:** This is
2 Allison Jenkins. I'm a toxicologist and risk
3 assessor at the Texas Commission on Environmental
4 Quality.

5 **DR. KENNETH PORTIER:** Dr. Lash.

6 **DR. LAWRENCE LASH:** Hi, this is
7 Larry Lash. I'm a professor in pharmacology at
8 Wayne State University in Detroit, and my work
9 involves drug metabolism, mechanisms of cell
10 injury primarily focusing on the kidneys as a
11 target organ.

12 **DR. KENNETH PORTIER:** Dr. Morandi.

13 **DR. MARIA MORANDI:** Good morning, my
14 name is Maria Morandi. I am retired from the
15 University of Texas and University of Montana, and
16 my areas of interest and expertise and exposure
17 assessment and industrial hygiene.

18 **DR. KENNETH PORTIER:** Dr. Morris.

19 **DR. JOHN MORRIS:** Hi, this is John
20 Morris. I'm an emeritus professor at the
21 University of Connecticut with expertise in
22 inhalation toxicology and PBPK modeling.

1 **DR. KENNETH PORTIER:** Dr. Isaac
2 Pessah is on the committee, but he has been called
3 away today. Dr. Rosol?

4 **DR. THOMAS ROSOL:** Hi, this is Tom
5 Rosol. I'm a veterinary and toxicologic
6 pathologist and chair of Biomedical Sciences at
7 the Heritage College of Osteopathic Medicine in
8 Ohio.

9 **DR. KENNETH PORTIER:** Dr. Vorhees.

10 **DR. CHARLES VORHEES:** Chip Vorhees,
11 professor of pediatric neurology at the University
12 of Cincinnati and Cincinnati Children's Hospital.
13 My areas are developmental neuroscience and
14 neurotoxicology.

15 **DR. KENNETH PORTIER:** And I think
16 that's everyone. I don't think I missed anyone.
17 At this time I will turn to Dr. Bethel with EPA to
18 kind of introduce who's on the line from EPA and
19 that will be interacting with the committee. Dr.
20 Bethel.

21 **DR. HEIDI BETHEL:** Hi, can everyone
22 hear me?

1 DR. KENNETH PORTIER: Yes.

2 DR. HEIDI BETHEL: This is Heidi
3 Bethel of the U.S. EPA Risk Assessment Division.
4 I am the co-team lead of the trichloroethylene
5 assessment, and I'll be reading the questions this
6 morning. We have our second -- our primary lead,
7 Keith Jacobs. Is Keith on the line?

8 DR. KEITH JACOBS: I'm here.

9 DR. HEIDI BETHEL: Hi, Keith. You
10 want to say anything?

11 DR. KEITH JACOBS: No, you got it.

12 DR. HEIDI BETHEL: Okay. We have
13 Stan Barone, who is one of our management leads,
14 and Nhan Nguyen, who is our primary management
15 lead for the trichloroethylene assessment. We
16 have Franklyn Hall, who is our engineer; Kara
17 Koehrn, who is our eco assessor; Xiah Kragie, who
18 is one of consumer assessors; Wen Lee, who is our
19 fate assessor; Sue Makris, human health assessor;
20 Stephanie Sarraino is another one of our consumer
21 exposure assessors. Did we miss anybody today?
22 Okay. I think I got them all, Ken.

1 **DR. KENNETH PORTIER:** Thank you, and
2 for the public who may be listening in,
3 occasionally you may hear Martin Alvarado from
4 Battelle who's the host of this WebEx session. He
5 may be popping in every once in a while. And
6 there are other Battelle staff online to support
7 this WebEx, and I want to express my appreciation
8 for them for technically keeping un on the line.

9
10 **FOLLOW-UP ON PREVIOUS DAY DISCUSSION**

11
12 At this point we're going to move on
13 with the meeting, first up, to see if there are
14 any follow up comments by the panel on yesterday's
15 discussion on Questions 1 and 2. Does anybody
16 want to add anything or clarify something from the
17 day before? I'm not seeing any hands or any
18 voices jumping in. I think it was pretty clear
19 yesterday. I wanted to ask EPA if there were
20 questions or clarifying questions or issues that
21 they felt the panel should have addressed in

1 Questions 1 and 2 that we didn't, now that you've
2 had time to think about it?

3 **DR. TODD PETERSON:** Scroll down,
4 Ken. Dr. Hossain has his hand up.

5 **DR. KENNETH PORTIER:** Yeah. Okay.
6 Dr. Hossain, remember to unmute yourself.

7 **DR. MUHAMMAD HOSSAIN:** Yeah. Thank
8 you. I have just little question about the half-
9 life of TCE in river water and lake water. In the
10 draft report, page number 259, Section 4.--

11 **DR. KENNETH PORTIER:** I think we're
12 going to get into TP -- you said TPE? I'm sorry,
13 you're a little bit loud for me.

14 **DR. MUHAMMAD HOSSAIN:** TCE,
15 trichloroethylene, half-life of --

16 **DR. KENNETH PORTIER:** Oh, right.
17 I'm sorry.

18 **DR. MUHAMMAD HOSSAIN:** --
19 trichloroethylene in river water and lake water.

20 **MR. WEN-HSIUNG LEE:** This is Wen
21 Lee, fate assessor. We used EPI Suite to do
22 estimation. For half-life in water, half-life is

1 1.238 hours. Half-life in lake is 109.6 hours, so
2 it means 4.5 days. That's from our EPI Suite
3 information.

4 **DR. MUHAMMAD HOSSAIN:** Yeah. I saw
5 that the available half-life for the river water
6 is 1.2 hours and lake water is 110 hours. But my
7 concern is this product -- this chemical is highly
8 volatile and would be effected by the temperature
9 used and volatilization. So is there any
10 differences of half-life in the summer and winter?
11 So if so, so how you are just get at that issue?

12 **MR. WEN-HSIUNG LEE:** Yeah. We do
13 not -- the change temperature to do estimation.
14 But I think because we did this, 80 percent will
15 be either in wastewater treatment plant or in the
16 source water where it vaporize very fast. So we
17 still think this will not change that much because
18 we think the fate will be mostly as evaporation.
19 So we do not do the calculation based on the
20 temperature.

21 **DR. MUHAMMAD HOSSAIN:** Okay. Thank
22 you.

1 **DR. KENNETH PORTIER:** Yeah. Dr.

2 Cobb, you wanted to join in on this?

3 **DR. GEORGE COBB:** Ken, this is
4 actually a little bit different. I was wondering
5 if the Agency could do one of two things: point us
6 to where in the reports the inputs and outputs
7 from the EPI Suite information may be or if they
8 could just provide that EPI Suite report that is
9 generated so that I can look through that a little
10 bit and make sure that my comments are synchronous
11 with exactly what EPA did; because I didn't find
12 that in the report, but I could possibly have
13 missed it.

14 **MR. WEN-HSIUNG LEE:** I had put the
15 (inaudible) what's the number I use it and what's
16 the five different -- from study we use. Table 1-
17 1 as the input, and also all the output as in the
18 appendix. So you should find out in the appendix
19 for all the EPI Suite outputs.

20 **DR. GEORGE COBB:** In which appendix
21 is that?

22 **MR. WEN-HSIUNG LEE:** Appendix --

1 **DR. GEORGE COBB:** And we can do this
2 offline or just save it after a break or
3 something.

4 **MR. WEN-HSIUNG LEE:** Okay.

5 **DR. GEORGE COBB:** Thank you.

6 **MR. WEN-HSIUNG LEE:** Thank you.

7 **DR. KENNETH PORTIER:** Yeah. Thank
8 you. George, I thought you were going to say
9 something about the water and volatility. I was
10 trying to remember the comments from methylene
11 chloride and the modeling but --

12 **DR. GEORGE COBB:** Ken, that's
13 exactly the point is that the -- depending on what
14 the concentrations are in the air and the water
15 and sediment, that determines which way the
16 equilibrium pushes the compound or forces the
17 compound in. You can actually force back in the
18 water if the concentrations in water are assumed
19 to be low and the concentration in air is high.

20 **MR. WEN-HSIUNG LEE:** This is Wen
21 Lee. We have EPI Suite have viscosity, the Level
22 3 model. And we're doing the model and find out a

1 partition between air, water, soil is 35, 54 and
2 10. But we've -- from the half-life water in lake
3 we still think this is mostly with occasion into
4 air. And also, we think that there's a lot of in
5 wastewater disturbance. And also, it does appear
6 either facility they, through the MPPS per mean,
7 they usually will be into have certain dilution in
8 through water. So we think it's in more in the
9 mixing, the kind of running water environment, so
10 we feel more comfortable then that would be
11 getting to air.

12 However, that as some my internal
13 data showed, the ppb -- EC -- ppb -- as I say,
14 more ppb, the higher concentration that we believe
15 that because it has 1.4, the 1.3 gram per liter is
16 considered high -- moderate and high solubility,
17 so you still have some in the water.

18 **DR. GEORGE COBB:** Yeah. Look, if
19 you're basing your -- if you're basing your
20 assessment on a model, the model says that 54
21 percent -- that's what I computed. I wanted to
22 use it in EPI Suite. I wanted to make sure I was

1 not using input data that was different than yours
2 and getting different results. If you're
3 predicting 54 percent in water and 30-something
4 percent in air, then 54 percent in water, you
5 can't undo that.

6 The bigger point is, when you input
7 the actual releases, at least the ones that are in
8 a problem formulation because I can't find actual
9 releases in the main document, you get a ten-fold
10 increase in TCE concentration in the water over
11 what is said to be released into water. And
12 depending on the way you run the model you can get
13 up to 100-fold increase. So that's what I'm
14 asking is I want to see what your inputs. And,
15 for instance, in the Level 3, as Dr. Doucette
16 pointed out several meetings ago, it's a thousand
17 kilograms per hour released into each compartment:
18 sediment, water, and air -- and just to see if
19 those are what your default runs work because it
20 seems that's what you did.

21 **MR. WEN-HSIUNG LEE:** Yes, we
22 understand that, but just like we said, the half-

1 life in river in the running water is 1.2, so we
2 are just about high, very, very fast. So we don't
3 believe that 50 percent -- 54 percent TCE will
4 remain in water because after a couple of days I
5 think it all will vaporize. And we assume the
6 OITI, the exposure assessment that we think this
7 is more like that it will vaporize. So we use a
8 80 percent of wastewater treatment as a
9 calculation to remove 80 percent of TCE through
10 the prior evaporation, so that's our rationale.

11 **DR. GEORGE COBB:** Yeah. But
12 wastewater treatment plants' water is aerated, and
13 so it's in essence sparged. And river water is
14 not in essence sparged nor is lake water. So your
15 equilibrium model is at equilibrium not at --
16 you're not -- once everything settles out if it
17 partitions into the air and partitions back into
18 water, that's what your equilibrium is.

19 So again, the model you're using
20 right now suggests that the majority of the TCE is
21 in water, not in air. And the model also, if you
22 put in the release data that you have in your

1 documents, suggest at least a ten-fold, if not a
2 hundred-fold, increase of TCE concentration in
3 water compared to what you're using for your
4 release estimates.

5 **MR. WEN-HSIUNG LEE:** Because the
6 model is assume this is still water but however,
7 we use the kind of half-life, we know that in the
8 discharge through the river -- discharge through
9 the water body they should have the -- predominate
10 by the evaporation, so that's the reason we have
11 half-life in water is only 1.2 hours. So I
12 believe you cannot say the total TCE is all in
13 water where they are controlled by viscosity they
14 kind of partition because that's another major
15 factor is evaporation. So that's a reason, and
16 actually for my certain data we didn't show
17 there's not such a high TCE concentration.

18 Most of them are in PPB level,
19 unless there's some kind of spill or some kind of
20 the -- the super fund side, they have higher level
21 evaporated concentration, so we still think that a

1 half-life create the major role for this kind of -
2 - our calculation.

3 **DR. KENNETH PORTIER:** This is Ken
4 Portier. I only want to allow about five more
5 minutes for this discussion. Dr. Doucette, did
6 you want to jump in?

7 **DR. WILLIAM DOUCETTE:** Yes, just
8 quickly and to follow up on George's comment, I
9 think it would really be helpful -- there are
10 several models within the EPI Suite program.
11 There's the wastewater treatment or STP model. It
12 would be nice to see what EPA -- if they just used
13 the default assumptions within that model or if
14 they made changes. There's also the fugacity
15 level 3 model and, again, that also has default
16 inputs that may or not be realistic or appropriate
17 for TCE. And I think a brief description of
18 essentially the input and output of those models
19 in appendices with some sort of a unifying
20 discussion would really clarify things.

21 **MR. WEN-HSIUNG LEE:** Sure. We will
22 put more effort to trying to fine tune the model

1 in the -- however, that the current estimation we
2 use STP model.

3 **DR. KENNETH PORTIER:** So I'm
4 informed that the release ranges are in Table 2-2.
5 The full release information is provided in
6 Appendix P of the DRE, and the full details are in
7 the engineering release and occupational exposure
8 supplemental file. So I'm going to request that
9 Dr. Cobb and Dr. Doucette kind of look at those
10 during whatever breaks we have today, and you can
11 come -- I'll give you an opportunity tomorrow
12 morning to come back and see if that satisfied the
13 need.

14 At this point I think I'd like to
15 move on to Question 3 and begin our new
16 discussions for the day. Dr. Cobb, Dr. Doucette,
17 lower your hands, thank you. Dr. Bethel, I think
18 we're ready to read Questions 3.1 and 3.2, if you
19 can, if you please.

20
21 **CHARGE QUESTION 3 (3.1 AND 3.2)**
22

1 **DR. HEIDI BETHEL:** Thank you. Thank
2 you Dr. Portier. This is Heidi. Question number
3 3 relates to the Environmental Hazards section of
4 the document. Question 3.1, please comment on
5 EPA'S approach for characterizing environmental
6 hazard for each risk scenario, such as acute
7 aquatic, chronic aquatic. What other additional
8 information, if any, should be considered? And
9 this is from Section 3.1 of the document.

10 Question 3.2, please comment on the
11 use and interpretation of Species Sensitivity
12 Distributions and hazardous concentrations for
13 ecological risk characterization and provide any
14 specific suggestions or recommendations for how
15 this information could inform EPA's risk
16 assessment for TCE or other solvents from Section
17 3.1 of the document.

18 **DR. KENNETH PORTIER:** Thank you.
19 Dr. Johnson, you have the lead on this. I
20 recommend we just take Question 3.1 first, kind of
21 discuss that, and then let's do 3.2 because
22 they're kind of separate ideas. Dr. Johnson.

1 **DR. MARK JOHNSON:** Okay. Good
2 morning. So far, I've received comments from Dr.
3 Portier, Jiminez-Gonzalez, Schlenk, and Cobb.
4 And, team, please let me know if I don't hit on
5 your points. I've tried my best to harmonize what
6 I've received so far. I will separate the 3.2 as
7 you have recommended, Dr. Portier, so we'll talk
8 about the Species Sensitivity Distribution in just
9 a bit.

10 But just briefly, all of us were
11 very encouraged that you did include those with
12 TCE. We thought that was a great thing to do, and
13 so we'll talk a little more in detail. It was
14 also encouraging the sub-lethal endpoints of
15 growth reproduction were also used to develop the
16 chronic value for aquatic invertebrates.

17 Even though there was a 32-day
18 growth value used for the COC determination of
19 approximately 8 milligrams per liter, it's not
20 clear why a lower 4 milligram per liter tadpole
21 survival NOEC was not used. And so you may want
22 to try and rationalize that. Since they're about

1 the same order of magnitude and there was an AF
2 used, it doesn't seem to affect the overall COC
3 estimates that much.

4 The lack of an aquatic vertebrate
5 reproduction endpoint may suggest that additional
6 uncertainty factor of maybe of 100, but we were
7 all not in agreement on that particular comment.
8 Some thought that the assessment factors that you
9 used were appropriate. In fact, there's a
10 reference I'm going to pass on, Belanger and Carr,
11 2019, "Practical considerations in development and
12 use of application factors applied to species
13 sensitivity distributions," so we'll include that
14 as well.

15 Reproductive endpoints seem very
16 important for several type of organisms, so you
17 may want to discuss for the ones you do have data
18 for and the ones you do not. It appears that a
19 EC₂₀ was used for fish growth, and that a NOEC was
20 available for amphibians but was not used. But
21 the NOEC is still valuable to help corroborate the

1 EC₂₀ value for fish growth, so you probably want
2 to consider both.

3 There's a difference between data
4 quality and data relevance, and so when I talk
5 about data relevance, what I'm really thinking
6 about is how relevant are the data in developing a
7 COC? That's a little bit different than
8 biological relevance, so you may want to think
9 about exactly what you mean by data relevance
10 through your systematic review process and how
11 that may provide coherence in developing a COC.
12 Some other data still have relevance though,
13 addressing biological plausibility in terms of
14 mechanistic information and mode of action.

15 One comment was the COCs for acute
16 algal effects. We have one that's, oh,
17 approximately four orders of magnitude different
18 than the other. And so typically when you see
19 things like that, you wonder about outliers, and
20 the big thing I think that's incumbent upon the
21 EPA in this particular case is to take a critical
22 review of that study. I believe that's a -- let

1 me see -- Lauder (phonetic) study for the EC --
2 for the 0.003 ppm value geometric mean between a
3 LOEC and NOEC for algae to see if there's an
4 explanation for that.

5 Data tables in Appendix C contain
6 COC exceedance information. It seems to be in
7 there. This has, I think, more to do with the
8 previous question, but it's one I received. It
9 says, when a surface concentration, for example,
10 is 23.04 micrograms per liter for 20-day discharge
11 per year, how can there be only four values that
12 exceed three parts per billion? If the mean
13 represents central tendency, then half the data or
14 none of that ten value should be over megagrams
15 per liter.

16 Additionally, the data for the NASA
17 facility in Louisiana far exceed the COCs, but
18 estimated number of exceedance for algae and
19 animals are about the same even though the COCs
20 are listed as 3 and 7-8-8 respectively. Same
21 problem exists for the site where too few
22 exceedances are predicted. I'm happy to send that

1 comment on to others because I'm not quite sure if
2 it fits in this section or not regarding that
3 question.

4 Risk characterization, I guess when
5 it comes to some of the hazard -- and so I'm not
6 sure if this goes in the Risk Characterization
7 section -- but when EPA considers volatilization
8 rates not to contribute to exposures to
9 terrestrial organisms, the investigator wonders
10 about soil invertebrates and burrowing mammals in
11 functionally confined spaces to TCE through vapor
12 intrusion from contaminated underground sources.
13 Certainly this is a concern for human health.
14 Maybe it fits under other EPA regulations like
15 CERCLA or superfund.

16 I know there have been toxicity
17 reference values developed for mammals in
18 functionally confined spaces like burrows, but
19 it's something you may want to think about since
20 the compound does volatilize. I think the
21 rationale that the EPA provided probably isn't
22 sufficient to just say we're not going to do it.

1 Using the EC₂₀ for fish growth,
2 again, divided by a diversity factor of ten was
3 thought to be reasonable by some other reviewers.
4 And also a reference from Kienzler et al was also
5 cited to help support your use of uncertainty
6 factors. And this reference is "Waiving chronic
7 fish tests: possible use of acute-to-chronic
8 relationships and interspecies correlations." And
9 that's a 2017 reference that we'll pass on.

10 And it's not clear why the Labra
11 study -- this is the one for the very low value
12 for algae. The quality metric was downgraded to
13 medium while most of the individual quality
14 components were rated high. So we didn't quite
15 understand why that was a discrepancy.

16 The other thing you may want to
17 think about too -- and this is something that's
18 been under debate, and I know the Society of
19 Environmental Toxicology and Chemistry for decades
20 now -- that the mantra that the only toxic
21 endpoints that are populationally relevant of
22 mortality, growth, and reproduction is, in my

1 view, fundamentally flawed since we really don't
2 have any direct knowledge of what criteria are
3 important to maintaining populations in a lot of
4 these areas. Sometimes it's predation. Sometimes
5 it's food. Sometimes it's other things.

6 I can come up with many
7 circumstances where not even mortality is
8 important in some areas where population
9 maintenance is sustained by, by example,
10 immigrants in sink populations. Sometimes growth
11 isn't that important, depending on the organism.
12 In certain circumstances it's good to be small. I
13 think of white-tailed deer in Texas, for example.

14 In some cases, reproduction isn't
15 even that important in maintaining population
16 numbers or densities where some organisms they
17 call -- are selected where they dump a lot of
18 eggs, and maybe only 10 percent or 20 percent of
19 those eggs are actually expected to get to
20 reproductive age under really good conditions. I
21 often question where you look at -- and an example
22 for birds, you look at egg production. If you see

1 a ten percent decrease in the egg production when
2 you look at the ecological data and see that 60
3 percent of the nests are hit by predation, what
4 does that really mean?

5 And so what I would recommend is
6 that the EPA really think about any adverse effect
7 and just assuming, because we don't know, that
8 that could have population relevance. And really,
9 when we say population, we're talking about meta-
10 population, the population at that site where the
11 release occurs, not the whole species population,
12 which may span most of North America. That kind
13 of gets to be a moot issue.

14 So I would just think about any
15 adverse effect that has potential of being
16 populationally relevant, not just mortality,
17 growth and reproduction, particularly sublethal
18 effects for sure. And if you have any mechanistic
19 information to help support that, that's important
20 as well. Don't consider adaptive response, things
21 like enzyme induction. Typically, that's
22 adaptive; that's a good thing. That's not a bad

1 thing. It's an indicator of exposure but maybe
2 not an indicator of adverse effect. And that's
3 all I have, if anyone else on the team has
4 anything to add.

5 **DR. KENNETH PORTIER:** This is Ken
6 Portier. I'll go through the list of the
7 associates to see if anyone has anything to add.
8 Dr. Blystone.

9 **DR. SHERI BLYSTONE:** Yeah. Just
10 reacting to what Dr. Johnson was just talking
11 about, I mean, he alluded to an argument or a
12 discussion within the ecotox community for however
13 many decades it's been going on. So while I
14 appreciate his opinion, I think it's also
15 important that, especially for the regulated
16 community, that they know what standard that
17 they're looking at. So if the standard for risk
18 assessment is to look at mortality, then that's
19 what it is. Other than that, I have no other
20 comment.

21 **DR. KENNETH PORTIER:** Thank you. I
22 think Dr. Jimenez-Gonzalez may have joined us at

1 this time. Oh, she's probably still delayed. Dr.
2 Schlenk.

3 **DR. DANIEL SCHLENK:** Yeah. I think
4 Mark got my comments early on. One thing that I
5 did think about actually yesterday and started
6 thinking about the volatility issues in terms of
7 the fate -- again, this is more uncertainty, and I
8 agree with Sheri in terms of we kind of have to
9 stick with what's relevant and what can be used in
10 a regulatory capacity now. But one thing, at
11 least from an uncertainty perspective, that should
12 also be thought about are aquatic birds,
13 particularly at wastewater discharge locations or
14 in wastewater dominated streams where you actually
15 see full effluent. And I see this a lot in
16 southern California and the Southwest for sure.

17 I just think these are worst-case
18 scenarios that should at least be addressed at
19 least in uncertainty aspects, not, obviously, in
20 the numbers that you have but something I think
21 that should be considered. Particularly if we're
22 thinking about volatility from the water, if

1 you're looking at shore birds or aquatic fowl or
2 any other mammal, for that instance, just to
3 disregard those receptors just because you don't
4 think it's -- you don't have the data, that's one
5 thing. And I think that should be stated. But
6 the fact that those are potential receptors should
7 be addressed, at least in the uncertainty
8 analysis, and maybe that's something that should
9 go in Question 6 later on but just something that
10 came out yesterday when I was thinking about this.

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

12 Dr. Cobb, did you have anything to add?

13 **DR. GEORGE COBB:** I think Dr.

14 Johnson got all of my comments in. The one thing
15 I'd like to point out is the Kienzler reference
16 that he cited. It also has data in distributions
17 for many studies, and they actually look at
18 interspecies uncertainty factor, so using one
19 species to estimate toxicity across populations.
20 So it not only does acute to chronic for fish, but
21 it does chronic to chronic for various types of
22 organisms. And that's all.

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

2 And this is Ken Portier, and Dr. Johnson fairly
3 included my comments as well. So I don't have
4 anything to add. Does anyone else on the
5 committee wish to comment on Question -- a
6 response to Question 3.1? I'm not seeing any
7 hands up, so why don't we move on, Dr. Johnson, to
8 Question 3.2?

9 **DR. MARK JOHNSON:** All right. It's
10 fair to say that all of us were in agreement that
11 the Species Sensitivity Distributions was
12 encouraging, and it was great to see that they are
13 put together. This visual display of toxicity
14 helps us to understand how the COCs were derived.

15 It was a little bit unclear -- is
16 that -- and I think we talked about, Kara, this
17 earlier at least in regard to my question
18 regarding the use of lethal and sublethal values,
19 EC and LC50s and mixing those together. But I
20 think in this case it makes a lot of sense. We
21 talked about, at least for aquatic invertebrates,
22 maybe narcosis is the mode of action here. And

1 from an ecological perspective, they would result
2 in the same outcomes. So that's encouraging. We
3 may want to go a little bit further and try to
4 explicitly explain what the EC₀₅ value really
5 represents, and so that would be one comment I
6 would add.

7 Let me see, just going down a list
8 here. Precisely why the HC₀₅ wasn't used as a POD
9 for acute exposures to aquatic vertebrates should
10 probably be better supported. I mean it's very
11 close the value used. Rather than using eight, it
12 was 10, roughly, milligrams per liter, but you may
13 want to explain that maybe just because it's a
14 lower value to be additionally protective.

15 Let me see here, benefit of -- mode
16 of action, we talked briefly about this. I would
17 also add that any kind of graphical display of the
18 relative toxicity information between species is a
19 good idea to present. The idea of a Species
20 Sensitivity Distribution is to really focus on
21 what the variation is in a toxic endpoint between

1 species. And for a lot of aquatic organisms, the
2 methods are pretty standard.

3 However, I just would exercise
4 caution if there's an intent to do this, and this
5 would not be my recommendation to do it for
6 terrestrial vertebrates, only because there's so
7 much difference in the methods. There's feeding
8 studies. There's drinking studies. There's
9 gavage studies. The kinetics really affect it.
10 And so a lot of times, you've just got to be
11 careful that the results that you're showing are
12 really truly due to differences between species
13 and not due to methodological differences.

14 Let me see. There's one comment on
15 line 348 to -55, aqueous concentrations should be
16 expressed uniformly either the microgram per liter
17 or milligram per liter in some cases is part per
18 million. And so we want to just be consistent as
19 much as we possibly can. There's some comments on
20 Figure 3-1. We have some taxonomic differences.
21 There's -- I hope I don't -- I hope I get this
22 correct -- *Raphidocelis subcapitata* and

1 *Pseudokirchneriella subcapitata*, it seems that
2 there was some differences in the taxonomic. We
3 probably should use with the most recent taxonomic
4 nomenclature as for the green algae.

5 There are some values that don't
6 seem to be correct. If we look at the figure, the
7 one for green algae log 10 is 2.61. That's from
8 the Loeber (phonetic) study. In Figure 1, it's
9 shown as two. It's close, but I think if you look
10 better at that figure to see if some of these
11 values match up. And I'll send you all the
12 specifics later on. The same for the diatom
13 *Skeletonerma costatum*. It's the log is 2, a
14 little bit over that. We may also want to look at
15 the 1.39 for the green algae in Figure 3-1 as
16 well. Also, the genus that was previous *Rana* is
17 now *Lithobates*. That's frog.

18 It's also of note that developmental
19 effects could result in premature mortality as
20 well to aquatic organisms, so that comment we
21 discussed yesterday about the developmental
22 endpoint for amphibians would probably be

1 appropriately listed in the Species Sensitivity
2 Distribution. And on page 192, line 144, I would
3 be specific on the term "mild intoxication." I'm
4 assuming that's narcosis lethargy, but, if that's
5 the case, I would just state that. And I believe
6 that's all I had for that comment, unless there's
7 any others from the team.

8 **DR. KENNETH PORTIER:** I'll go
9 through the list. Dr. Blystone.

10 **DR. SHERI BLYSTONE:** No further
11 comment.

12 **DR. KENNETH PORTIER:** Dr. Jimenez-
13 Gonzalez, we're on 3.2. Dr. Schlenk.

14 **DR. DANIEL SCHLENK:** Yeah. Just one
15 thing to add on just the benefit of SSDs. Mark
16 kind of addressed this, but I just wanted to
17 include the word "probabilistic." That's really
18 the benefit of doing these estimates. Everything
19 that we've seen beforehand, at least all the
20 panels that I've been on or committees I've been
21 on, have basically used a deterministic method.
22 And you've got so much uncertainty there,

1 particularly when using acute mortality,
2 primarily, as the endpoint.

3 One way, again, to address the
4 probabilistic assessment -- and, again, this is
5 where the HC₅ comes in. It's a probabilistic
6 estimate of the five percentile, which I think is
7 a very strong number. But, again, because it's an
8 acute value, I think it's really important to
9 include the most sensitive species as well, and I
10 totally agree with the way the agency has done
11 that analysis, again, primarily because we don't
12 have enough data to do a Species Sensitivity
13 Distribution for some of the sublethal endpoints,
14 such as growth and reproduction.

15 And I totally agree with using the
16 EC₅₀ and the LC₅₀ from vertebrates. That's pretty
17 standard practice these days, at least in most of
18 the studies that I've seen anyway looking at
19 invertebrate toxicity. So yeah. That's my just
20 add-on comments for that.

21 **DR. KENNETH PORTIER:** Dr. Cobb, do
22 you have anything to add?

1 **DR. GEORGE COBB:** One real quick
2 thing just so that we can write to it more than
3 anything, depending on how you use uncertainty
4 factors, if at all, and how you use the different
5 distributions in selecting from the different
6 distributions for that HC₅, you can get vastly
7 different exceedance, frequencies of exceedance
8 and different risk quotients. So I wanted to just
9 get that out there, and then that's all.

10 **DR. KENNETH PORTIER:** Thank you.
11 Back to you, Dr. Johnson.

12 **DR. MARK JOHNSON:** Oh, yeah. Just
13 quickly, one alibi, part of my participation in
14 the previous EPA effort, the eco soil screening
15 level effort, I know from the folks who are
16 working with soil invertebrates there was
17 consensus within that group that they focus on an
18 EC₂₀. And so I'd like to hear what Dan thinks
19 about that for aquatic, but I think, if you do
20 decide to look at soil invertebrates, EC₂₀ would
21 probably be the benchmark to look for.

22 **DR. KENNETH PORTIER:** Dr. Schlenk.

1 **DR. DANIEL SCHLENK:** Yeah. This is
2 Dan. I had not heard that as a recommendation. I
3 guess it would depend on the distribution of the
4 data and whether or not you had enough data to get
5 down that low. Generally, I mean, statically, we
6 use the 50 percentile just because it generally
7 has the least amount of uncertainty in a
8 population. At least, that's the dogma that we
9 use in toxicology anyway.

10 So the further the dose response
11 curve you go, the more uncertainty that you have.
12 So I guess that would be dependent upon the data
13 that you had for that endpoint, whatever endpoint
14 you're looking at, whether or not you went to the
15 20th percentile. I know, for example, in the
16 fathead minnow study that they used an EC₂₀ -- and
17 that's, again, primarily because I think the data
18 was fairly strong in that case to go down to the
19 20th percentile. But generally, I think that the
20 safer bet is usually the 50th, unless the data is
21 strong enough to go to the 20th. But that's my
22 take on that.

1 **DR. MARK JOHNSON:** That makes sense.

2 Thanks, Dan.

3 **DR. KENNETH PORTIER:** Are there any
4 -- anyone else on the committee want to comment on
5 Question 3.1 or 3.2? I'm not seeing any hands
6 raised. At this time, I'll turn to EPA and ask
7 whether EPA has any clarifying questions of the
8 panel's comments. If somebody's commenting,
9 they're muted.

10 **MS. KARA KOEHRN:** This is Kara. No
11 comments, just thank you for your feedback.

12 **DR. KENNETH PORTIER:** Okay. And
13 certainly, you'll get a written report on this.
14 Okay. Well, at that point, I think we're about 50
15 minutes into this meeting. Let's go ahead and
16 begin what is probably going to be the remaining
17 work for the committee today, which is the set of
18 questions on occupational exposure. Let's begin
19 by reading in the introduction material for Charge
20 Question 4 and at least 4.1, please, 4.1 and 4.2.

21

1 **CHARGE QUESTION 4 (4.1 AND 4.2)**

2

3 **DR. HEIDI BETHEL:** Okay. Question 4

4 is regarding occupational and consumer exposure.

5 For inhalation exposure, EPA quantified

6 occupational exposures for both workers and

7 occupational non-users, or ONUs, based on a

8 combination of monitoring data and modeled

9 exposure concentration. EPA modeled dermal

10 exposure for workers only, accounting for the

11 effect of volatilization. EPA assumed that

12 workers and ONUs would include adolescents greater

13 or equal to 16 years old and adults of both sexes.

14 Question 4.1 states please comment

15 on the approaches and estimation methods, models,

16 and data used in the occupational exposure

17 assessment (Section 2.3.1).

18 Question 4.2, please provide any

19 specific suggestions or recommendations for

20 alternative data (modeling or monitoring) or

21 estimation methods that could be considered by the

22 Agency for conducting the occupational exposure

1 assessment. If so, please provide specific
2 literature, reports, or data that would help us
3 refine the exposure assessment (Section 2.3.1).

4 **DR. KENNETH PORTIER:** Thank you, Dr.
5 Bethel. I'm going to turn to Dr. Kaufman who we
6 asked to lead the discussions on this section.
7 Dr. Kaufman. You're on mute.

8 **MR. ALAN KAUFMAN:** Yeah. I had to
9 double mute there or double unmute I should say.
10 Yeah. We got plenty of comments here, so this may
11 take a few minutes as I go through it. Comments
12 that I got back from the group, in general, the
13 estimation methods, the models, and the data are
14 similar to the approaches that have been used in
15 the past, but there are some problems that persist
16 to more specifically define any occupational
17 exposure pathways that were not included because
18 there are competing areas of other regulations
19 that cover them.

20 Sometimes those are not explicit,
21 and they should be. And there are obviously some
22 cases that are recognized because they're clearly

1 cosmetics. One thing that seemed to throw
2 everybody was hoof polish. Is that a cosmetic, or
3 is that something else?

4 And then next comment, a detailed
5 explanation about the impact of regrouping
6 subcategories into different categories and so
7 providing some data demonstrating that there
8 really isn't any impact on the exposure estimates.
9 One comment that was very positive was Tables 2-12
10 to 2-16 were very useful for following the results
11 of the occupational exposure evaluations. I think
12 the level of confidence for dermal exposures has
13 to be added.

14 And it would be useful to link the
15 cell entries internally. I think we've talked
16 about this on past reviews where, if you had links
17 in the cell entries, you could go immediately to
18 the section where those estimates are derived so
19 that, if you wanted some more detail, you could
20 click on it and go. And there should be specific
21 links between that section and the corresponding
22 section in the appendices.

1 One comment was an application of --
2 I'm not sure how to pronounce it -- NCHS, or NICUS
3 2009, the box model for estimating inhalation
4 exposures. Were there other models that were
5 explored for vapor generation? It isn't clear
6 whether the literature was explored on liquid
7 aerosol modeling to see if it was possible to
8 estimate vapor-phased fraction in a different way.

9 It would be useful to provide a
10 table summarizing recommended gloves for TCE from
11 OSHA, NIOSH and others, both for neat and mixtures
12 of TCE, maybe as part of an appendix. The
13 exposure control hierarchy, the discussion should
14 be more complete. And I think there's --
15 something that has come up over and over again in
16 these reviews is taking into account more fully
17 poor adherence to guidelines and recommendations.

18 And in fact -- hang on one second --
19 I'm bouncing back and forth here between comments,
20 so bear with me for a second. There was some --
21 the NIOSH HHEs give you some alternative data that
22 doesn't seem to have been fully considered. In

1 other words, there's data for exposure assessment,
2 but then there are -- one of the reference to HHEs
3 states that it was observed that no safety glasses
4 or protective gloves were used during degreasing
5 operations. Respiratory protection is provided.
6 Half-face piece respirator with organic vapor
7 cartridge is not approved, but it's not being used
8 by the operators.

9 So I think some of the assumptions
10 around PPE, as we've talked about before, need to
11 be reexamined. It seems that adherence to the PPE
12 recommendations are probably, if anything, less
13 robust here than they have been in some of the
14 other reviews that we've done.

15 Let's see here -- for aerosol and
16 non-aerosol products and for repacking, EPA used a
17 surrogate condition unloading and repacking and
18 monitoring daily from a semi-closed production
19 manufacturing facility in Germany. It's the same
20 source that was used for degreasing. The OEL for
21 Germany may have been 30 ppm TWA, although it's
22 likely that EU Commission of 10 ppm TWA was

1 already adopted at the time the data were
2 collected.

3 And they're both lower than OSHA's
4 100 ppm time-weighted average. So there's
5 potential for exposures in Germany to be lower
6 because of tighter controls. So that may not be
7 applicable to manufacturing operations here in the
8 States.

9 There should be additional
10 discussion about differences between model- and
11 measurement-based exposures and a presentation of
12 the reasons for the differences and why they were
13 chosen. And two sets of estimates show the
14 classical pattern that central tendency estimates
15 tend to match better than the upper or lower
16 estimates. Should be more discussion about NIOSH
17 monitoring data used for metalworking fluids. It
18 dates back to the second half of the 1970s about
19 the composition of these fluids. And the
20 attention paid to exposure controls are likely
21 improved compared to the present. I'm sorry,
22 that's the present compared to the past, it should

1 be. Should be better discussed in terms of
2 relevance of these data for current exposures.

3 One thing that did come up in a
4 number of the comments was the fact that there's
5 non-consideration of aggregate exposures. In
6 other words, you have workers who are dermally
7 exposed who may also be exposed by inhalation.
8 And I think there was a little disagreement among
9 the group here. I think some people felt they
10 should always be aggregated.

11 I think in some cases, for instance,
12 if someone is dermally exposed, they're probably
13 almost always going to be exposed by inhalation
14 but not necessarily the converse. So you need to
15 be careful about doing that. But what is clear is
16 that all of these occupational users are also
17 consumers and the potential aggregate of, let's
18 say, drinking water when they go home, especially
19 if their house is on a well where there may not be
20 adequate or robust testing for TCE -- I think
21 might change some of the considerations in terms
22 of aggregate exposure here.

1 And let's see here. I think that's
2 it for 4.1. Although, as there as has been in the
3 past, there's some overlap here between some of
4 these questions. So I'm going to turn it over to
5 the rest of the group, see if anybody wants to add
6 anything that I might have missed.

7 **DR. KENNETH PORTIER:** Thank you, Al.
8 Dr. Anderson has joined us. Dr. Anderson, do you
9 have anything to add on Question 4.1?

10 **DR. HENRY ANDERSON:** I did submit a
11 lot of written comments I'm assuming also become
12 part of the record. Again, I'm still concerned
13 about the use of the PPE as a factor. And looking
14 at all the various factors, the impact, the
15 ultimate risk determination, the adjustment for
16 assuming the use of PPE really is the number 1
17 factor there. I think that was pointed out in
18 some of the public comments.

19 And I also saw there was a nice
20 analysis of that in the EDF submission that just
21 went up Friday or so, and I quickly looked at
22 that, so I think that's a good summary of what

1 those reductions are and what those impacts are.
2 And for this particular chemical, the estimated
3 exposures are sufficiently elevated, that even
4 with the high use of PPE or the 50-fold reduction
5 factor of exposure, it's still the MOEs are in the
6 hazardous range. But it does tend to not really
7 express the full risk that's there.

8 One of the issues that I had on the
9 PPE -- and I'm trying to understand the rationale
10 for this. And it seems to me that it probably
11 would be helpful if that would be stated in the
12 various documents that what's being done is EPA is
13 using the same rationale that's used for the
14 general population. Others saying that there's
15 another regulations in place that have been
16 assessed and that effectively control exposures.

17 Of course, on the general population
18 side, if you look, I can't find any evaluations or
19 published documents saying that the existing
20 regulations have effectively controlled the
21 general population exposure. So I'm assuming that
22 that's probably the same argument that's used for

1 the occupational component that there are
2 standards in place, and those are being adhered
3 to. What's kind of unusual for TCE is that the
4 standard that OSHA is using does not require the
5 use of respiratory protection unless the PEL is
6 exceeded. And that PEL is the original PEL that
7 was established 1971. So there is really no
8 requirement to put in place a respiratory
9 protection program unless the exposure exceeds the
10 100-ppm standard.

11 And for many of these, at least, the
12 average or the exposure that they're using, the
13 first general figure tends to be below what the
14 standard would be and, therefore, a respirator
15 program would be voluntary. And one of the
16 disincentives for industry to provide respirators
17 if they're not required is that they also have to
18 have a full respiratory protection program, which
19 involves doing inner monitoring in the workplace
20 as well as having a medical monitoring program in
21 place. So all of those features that would have

1 to be done for the company to even offer voluntary
2 use is very expensive so tends not to be done.

3 It would seem to me that one thing
4 that would be -- one could argue is reasonably
5 available information, especially since this is an
6 issue that has come up in every one of our
7 evaluations over the last nine months and knowing
8 EPA must have an idea what the next ten chemicals
9 are going to be, they could quite easily ask OSHA
10 or NIOSH to survey the various producers and users
11 to see what, in fact, the programs are and what's
12 available there. And then if they don't get much
13 of a response, at least in the document they could
14 say we contacted all of the companies, asked them
15 to complete a very simple survey on what they're
16 doing, and here's what we found. Because also I
17 think it's problematic when you look at that the
18 ultimate decision on what data to use -- in some
19 of these it's from one company and there's six
20 samples.

21 Well, that's hardly (inaudible) if
22 there's a large (inaudible) OSHA there isn't even

1 described. And if it's there, they would use the
2 argument that from my perspective of trying to
3 find it, it wasn't reasonably available
4 information in the document what the actual
5 exposure measurements are. So I would think it
6 would be helpful to expand on the rationale for a
7 factor that really does -- has a significant
8 impact on the risk determination that's ultimately
9 there. As I say, we saw that when you apply those
10 in for some of the compounds that we've already
11 done, then there doesn't seem to be a need to
12 declare it to be a hazardous exposure.

13 Another thing I would say to be
14 added is, this is somewhat unique to TCE, it has a
15 quite -- on the workers, it's quite an impact if
16 the workers also consume alcohol on a regular
17 basis or before or after they're exposed. This
18 leads to exacerbation of symptoms. So I would say
19 that a proportion of the workforce that may well
20 be alcoholic or at least are heavy consumers of
21 alcohol should be considered a vulnerable
22 population.

1 So there's a number of other
2 comments I made there in my written things, but,
3 again, for me the most important issue is doing a
4 better job of defining on the PPE issue. It's
5 used as a categorical figure assuming that
6 everybody is using it when everybody knows that's
7 not the case and as the example of the one HHE.
8 And you could go through all the NIOSH HHEs, and
9 they will all describe what's being done in the
10 facility where they were doing their
11 investigation. And most of them had exposures
12 below the standard and therefore had sparse use of
13 the respirators.

14 So I think in this instance the
15 application of the factor for assuming everybody
16 is wearing a respirator really is not appropriate
17 unless they have better rationale that there is a
18 requirement to do that, which would follow on the
19 assessed and effectively controlled regulatory
20 approach that's used to eliminate the inclusion of
21 some exposures. In this instance, there really
22 isn't a regulatory requirement for the

1 establishment of respiratory protection program in
2 all of the industries involved here. So that's
3 just a quick summary.

4 As I say, there's a -- I would say
5 my comments pretty much parallel what I had --
6 what we've put into many of the previous
7 chemicals. But I think this one is especially
8 egregious because there really isn't a regulatory
9 requirement there. And in the data that's
10 presented, it's very hard to find a table that
11 actually gives what is the respiratory ppm
12 exposure. Most of the tables use the ratios of
13 MOEs. And that's interesting from the perspective
14 of the methodology that declare a significant
15 hazard or not but really doesn't help understand
16 what the actual exposures are to the workers,
17 average basis or even on their 90th percentile
18 exposure factor.

19 So there's other things I had there,
20 but that really is the crux of what my major
21 concerns are and where I think the documentation
22 needs to be enhanced in the document so that it's

1 easily understood what's going on and the
2 comparisons can be made, as this instance it's
3 especially problematic.

4 **DR. KENNETH PORTIER:** Thank you, Dr.
5 Anderson. Dr. Bennett.

6 **DR. STEVEN BENNETT:** Sorry, this
7 thing -- it's way too many buttons to push. I
8 think overall we've covered a pretty good comments
9 here, and certainly Dr. Kaufman captured most of
10 mine. I noticed one thing with the spot cleaning
11 model in particular where it's relying a particle
12 of the ERDA study from 2007 for the use rate. And
13 that predates a ban of TCE in the state of
14 California, and I'm not sure that's the best proxy
15 for that because the product is no longer allowed
16 in California.

17 I recognize that may be the only
18 data that they have. But both there and with a
19 couple of them, I notice that this -- unclear if
20 that's a proxy for other state -- or it's a proxy
21 and unclear if the distribution of the use pattern
22 is representative of other geographical locations.

1 And I think it'd be useful for the Agency do a
2 better description of what efforts they did to
3 have a better understanding of that distribution.

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

5 Dr. Kissel, did you want to comment on inhalation
6 exposure?

7 **DR. JOHN KISSEL:** Well, are we
8 speaking only of inhalation exposure or is this
9 exposure generally?

10 **DR. KENNETH PORTIER:** I think this
11 is Question 4.1. I guess it's exposure in
12 general. I'm sorry. I had to reread the whole
13 statement. Please proceed.

14 **DR. JOHN KISSEL:** Yeah. It's more
15 general. Yeah. So I do want to comment. I would
16 just reiterate a couple of the comments that have
17 already been made regarding, well, just to make it
18 clear to confirm that more than one member thinks
19 that the APF and GPF numbers that EPA -- the PPE
20 protective factors that EPA is using are overly
21 optimistic. So I think we have a trouble reaching

1 consensus, but I think that's one for which many
2 of the people that have an opinion would agree.

3 And I want to reiterate the
4 aggregate exposure notion. I would like to see
5 inhalation and dermal exposures aggregated, and I
6 would like to see -- although in the case of
7 trichloroethylene, it's probably not mostly
8 important -- but most of the time it's not going
9 to be important -- I would like to see dermal
10 vapor considered. And even if it turns out to not
11 be a significant contributor, having the
12 calculations in black and white in front of people
13 to show the justification for ignoring dermal
14 vapor would be valuable as a matter of course. It
15 should just be a routine component of these risk
16 assessments.

17 With respect to the aggregate
18 exposure question, on page 137 of the document,
19 there's a citation of the NIOSH skin notation
20 documents for TCE which concludes that inhalation
21 dominates dermal. And the DRE says we agree with
22 that, so we don't think dermal is very important.

1 But we will do dermal calculations in a few cases
2 anyway.

3 The caveat that needs to be added is
4 that the NIOSH skin notation assumes that
5 inhalation dominates dermal for a specific
6 scenario which is somewhat arbitrary. And the
7 specific scenario assumes 50 parts per million,
8 which it describes as the NIOSH REL for TCE. That
9 NIOSH REL is actually now 25 and not 50, so the
10 scenario that the skin notation is using is
11 already out of date.

12 And it compares it to a specific
13 dermal liquid exposure which assumes 360 square
14 centimeters of skin is exposed, which might be
15 true but also might not be true. So it's not hard
16 and fast that the result that NIOSH got, which is
17 an SI of 0.02, only holds for their set of
18 assumptions and it doesn't hold for all possible
19 assumptions that one might make. And in fact, for
20 the worker scenarios shown in the air
21 concentrations shown in 213, the vast majority of
22 them are air concentrations less than 50 parts per

1 million. And it would be -- if you keep the
2 liquid exposure assumptions constant and reduce
3 the air concentration, you get a proportional
4 decrease in the importance of inhalation and the
5 proportional increase in the importance of dermal
6 exposure.

7 So I don't think blanket assumptions
8 or conclusions should be drawn from that NIOSH
9 document. I think it's over interpreted, and it
10 would be much better to see the aggregate
11 exposures and then decide whether one is bigger
12 than the other than to just announce in advance
13 that inhalation is more important. I also have
14 argued for inclusion in the physical-chemical
15 parameters a bunch of dermal parameters, which are
16 still somewhat mysterious to most people because
17 Bill Doucette's seen them. But most people have
18 not.

19 But in there I would like to see
20 things like the maximum flux calculation for this
21 particular compound, for each particular compound
22 as they come up. And the value of that is you

1 could take, if EPA was actually doing it -- so you
2 were using a percent absorbed approach here, which
3 means that you're getting to a dose without ever
4 explicitly stating what the flux through skin is.
5 And it would be very useful to have side-by-side a
6 maximum flux number and an implied flux number
7 associated with the fraction absorbed so that you
8 can compare the things. And if you're -- one of
9 the rubs here is that if you put large masses of
10 material on skin and then assume the fixed
11 fractional absorption, you may get to an
12 implausible flux through skin.

13 And a check on that would be to have
14 those numbers next to each other so that you could
15 look at them. And then that is hidden here, which
16 is not a good thing. So if my recommendations for
17 physical-chemical parameters was adopted --
18 interpret and if EPA would report the implied flux
19 associated with their fractional absorption, then
20 it would be easier to check those things against
21 each other.

1 Now, one caveat I just said or about
2 what I just said is that there's no mention -- so
3 we're using the Frasch interpretation of the
4 Kasting work to estimate fraction absorbed versus
5 fraction evaporated, and there is no correction in
6 there for corrosion of the skin. Most of the
7 exposures we're talking about here are to neat TCE
8 -- and TCE's a degreaser. And routine exposure to
9 degreasers can damage the barrier function of the
10 skin, so standard estimates of uptake through skin
11 could turn out to be underestimates to people who
12 have skin damage from chronic exposure to
13 degreasers.

14 And let's see if there was anything
15 else. No, I think I've covered the stuff that I
16 wanted to say for 4.1.

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

18 Dr. Morandi.

19 **DR. MARIA MORANDI:** Yes, just a
20 couple of things just to be on the record. I
21 agree with everything that has been said. And
22 with respect to a description of the exposure

1 control hierarchy personal protection equipment, I
2 was kind of surprised because in the prior
3 document that we reviewed for -- that was carbon
4 tet -- there was a more extensive description
5 including the data from NIOSH, which is actually -
6 - the memorandum from NIOSH which is actually
7 part of the documentation we have in the docket.
8 However, because the main document doesn't mention
9 any of that data from NIOSH, it seems to be an
10 afterthought.

11 And I think this is a big issue, as
12 prior members of the committee have talked about.
13 And we also heard yesterday the very eloquent
14 presentation from Dr. Michaels addressing the
15 issue of difference between what is expected to be
16 done and what is actually done in many industries.
17 And I think in this case, it may be also
18 differential in terms of its size and how big the
19 companies they are, so what big companies may
20 actually be adapting recommended PPE and, of
21 course, following the hierarchy of exposures
22 because they can afford to do so. And they are

1 more afraid of litigation issues, but the smaller
2 companies cannot.

3 And in addition, I wanted to add
4 that, and I was planning to add this when we got
5 to risk characterization evaluation that to assume
6 that PPE is used in small commercial enterprises
7 like dry cleaners -- I think this is a completely
8 unsupported assumption. I have never seen anybody
9 in a dry cleaner facility using any kind of PPE,
10 either respirators or gloves. So I'll come back
11 to that issue when we go to the discussion in
12 Question 6.

13 I also wanted to add that for
14 manufacturing, for processing -- sorry, if EPA
15 uses monitoring data from a surrogate and thus
16 they have provided from HSIA -- and I couldn't get
17 the data. I informed Todd to see that the link --
18 the data provided in HERO has the document where
19 HSIA discusses the Johnson study and the Charles
20 River study in terms of developmental heart
21 defects. But it doesn't provide the data that was
22 used for these occupational exposure scenarios.

1 But my assumption is, is that data
2 in some facilities that are fairly well
3 controlled. I doubt that they would be strictly
4 applicable to all manufacturing processing as a
5 reactant. And therefore, that that source of
6 uncertainty should be added into the use of this
7 particular surrogate data for other categories.

8 I also wanted to add, with respect
9 to Dr. Kissel mentioned that there should be some
10 discussion about the vapor to the skin route
11 pathway, that there should also be some discussion
12 about the possibility of vapor penetration through
13 clothing since most clothing is not impermeable
14 and there is a probability or a potential for
15 vapor to go through clothing and then be deposited
16 on the skin. So I think that was pretty much what
17 I had on this question.

18 **DR. KENNETH PORTIER:** Thank you, Dr.
19 Morandi. Does anyone else want to chime in on
20 Question 4.1? Dr. Morandi, I see your hand is up.

21 **DR. MARIA MORANDI:** Oh, sorry.

1 **DR. KENNETH PORTIER:** I'm not seeing
2 any hands go up. What I think I'm going to do at
3 this point is call a 15-minute break, Dr. Kaufman,
4 and we'll come back and continue to see if anybody
5 had any additional comments on 4.1, and then we'll
6 move on to 4.2. I have 11:25. Let's return at
7 11:40 so 15-minute break. Thank you.

8 **MR. ALAN KAUFMAN:** Thanks.

9
10 **(BREAK)**

11
12 **DR. STANLEY BARONE:** Hello, can you
13 hear me? This is Stan Barone.

14 **UNIDENTIFIED MALE:** I can hear you,
15 Stan.

16 **DR. STANLEY BARONE:** Okay. Thank
17 you. I did raise my hand. When the committee
18 comes back, I wanted to make some clarifications.

19 **UNIDENTIFIED MALE:** Okay. That'd be
20 great. Yeah. Just be careful. The system has a
21 tendency to have a mind of its own and decide to
22 mute you at random.

1 (BREAK)

2
3 DR. KENNETH PORTIER: This is Ken
4 Portier. Are we ready to return? Can anyone hear
5 me?

6 DR. TODD PETERSON: We can hear you
7 just fine, Ken.

8 DR. STANLEY BARONE: Yes, Dr.
9 Portier.

10 DR. KENNETH PORTIER: Thank you.

11 DR. STANLEY BARONE: This is Stan
12 Barone and I raised my hand.

13 DR. KENNETH PORTIER: So I have a --
14 yeah, Stan. Yeah, Stan. I was going to call you
15 next. Dr. Barone, do you have a comment?

16 DR. STANLEY BARONE: Yes, Dr.
17 Portier, I wanted to make a clarification. Dr.
18 Morandi and others made mention of PPE usage for
19 many of the commercial conditions of use. And I
20 wanted to make the clarification that we did not
21 assume PPE would be used for many of the
22 commercial uses that have already been mentioned,

1 including spot and wipe cleaning, commercial
2 printing and copying, the other commercial uses
3 category, and dry cleaning. So those do not
4 presume that PPE would be employed in any
5 consistent fashion. That's also reflected in the
6 risk tables in the Risk Characterization section,
7 too.

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

9 Dr. Grant, your hand's up.

10 **DR. STEPHEN GRANT:** Hello, yeah.

11 The issue of PPE is one that we've wrestled with
12 for a couple of panels as far as I can see. And I
13 thought when we got the tables that had no PPE and
14 then PPE of various protection factors that we had
15 made a significant impact. But we keep hearing
16 the words "hierarchy of control." And having a
17 line in a table that says no PPE and then going
18 straight to PPE ignores that structure, that
19 hierarchy of control. For example, the first
20 issue if you have a problem is structural control,
21 and that may be redesigning the workplace.

1 And I don't think because
2 redesigning the workplace is, one, expensive and
3 somewhat ambiguous -- how do you anticipate the
4 protection factor for that? -- that you're
5 justified in jumping over it and going to
6 something that's somewhat easier to quantify,
7 which is PPE. And we've already skipped another
8 step, which are the administrative controls. And
9 that would be do you need -- among other things,
10 do you need to use this chemical, or can you
11 redesign the process so that you're using a
12 substitute which is of lower hazard?

13 I think we are missing all of this.
14 Several times it's been pointed out that perhaps
15 we need an OSHA representative on the panel, and
16 maybe now I'm the best thing that -- next best
17 thing. I think everyone has been thinking of this
18 but wrestling about those are ambiguous things
19 because in each condition of use and in fact in
20 each condition each exposure scenario and site
21 those things may be different.

1 But I think at the moment we are
2 giving up on them and skipping them over or paying
3 lip service to them. And I don't think we should
4 do that. I think we should require, if we have an
5 unreasonable risk, no, you can't just slap a pair
6 of gloves on. You have to go through the
7 hierarchy of control. That's it.

8 **DR. KENNETH PORTIER:** Stephen, this
9 is Ken Portier, but I thought that was the whole
10 point of providing with and without. A lot of the
11 tables show without PPE, and then it shows with
12 PPE. So at least EPA is showing these two
13 conditions. I think the part of the discussion is
14 more in the text than in the tables. The tables
15 give you those options. And then there is the
16 issue of how much PPE, how much protection do you
17 assume --

18 **DR. STEPHEN GRANT:** Oh, no, I've
19 been on many of these panels.

20 **DR. KENNETH PORTIER:** -- under
21 certain glove use.

1 **DR. STEPHEN GRANT:** The issue is not
2 whether or not PPE work or not. The issue is that
3 it seems that we are leaping over other control
4 levels and saying, well, if you're over, you can
5 handle it with PPE. And that's not supposed to be
6 the approach. Okay? I know that the other, the
7 intermediate approaches, which are structural and
8 administrative controls, are difficult to
9 quantify. But they need to be brought up and say,
10 if you have an unreasonable risk, the first thing
11 you do is redesign the interface between the
12 workers and the agent, not, again, slap some PPE
13 on. That is the last resort. And I'll leave it
14 there.

15 **DR. KENNETH PORTIER:** But I think
16 that --

17 **DR. STEPHEN GRANT:** I was actually
18 bring this up. It's Question 6, but it seemed to
19 already come up here. So I thought I'd throw it
20 in now.

21 **DR. KENNETH PORTIER:** Well, it will
22 come up in 6 again. I thought there was at least

1 acknowledgement of that in this report, that
2 engineering controls is -- in the discussion I
3 read, I thought I saw some of that. My question
4 to you and the rest of you on this question is
5 what's our recommendation for EPA to how to
6 present this in a way that satisfies our concerns
7 but also informs the risk mitigation community
8 that this is kind of step 1 or risk without PPE in
9 this case, clearly. And in this case, there were
10 risk with the simple PPE, implying that you're
11 going to have consider other mitigation.

12 So I guess we read this Draft Risk
13 Evaluation, I see that in there, but I'm feeling
14 that the committee still feels that these draft
15 risk evaluations have not coached that discussion
16 in a way that you feel comfortable with it. And I
17 think what -- we owe them some comments and
18 recommendations that help them to drive that text
19 in the direction we'd like to see it go. And so I
20 get the feeling that Dr. Morandi, Dr. Anderson,
21 and yourself, Dr. Grant, kind of see in your minds
22 how you'd like that conversation to be written

1 down. And I think we need to come up with
2 suggestions for EPA on how to present that.

3 And then the other thing is the
4 expectation of the industry for chemicals to come,
5 they need to be able to see this is what EPA needs
6 to be able to fairly assess risk, especially in
7 manufacturing or in processing plants. And
8 they're going to systematically go through no PPE,
9 engineering controls, added PPE or whatever. Do
10 you understand what I'm saying, Dr. Grant, Dr.
11 Morandi? Am I disconnected?

12 **DR. STEPHEN GRANT:** We hear you. We
13 hear you.

14 **DR. MARIA MORANDI:** Ken, I just
15 don't --

16 **DR. STEPHEN GRANT:** It's just it
17 seems like we've been wrestling with the PPE, and
18 now that we've resolved it somewhat, it's time to
19 wrestle with the entire hierarchy of control.

20 **DR. KENNETH PORTIER:** Okay. And so
21 I guess I'm saying we need to kind of help EPA get
22 that conversation right in this document.

1 **DR. HENRY ANDERSON:** Ken, this is
2 Andy.

3 **DR. KENNETH PORTIER:** Yeah, Andy.
4 Dr. Anderson, please, join the conversation.

5 **DR. HENRY ANDERSON:** I was going to
6 say I think on the some of the other chemicals I
7 think one of the things that was raised is to have
8 a separate mitigation section in the report.
9 Here, it's all lumped together. And I think if
10 you would pull those out and then discuss the
11 mitigation, then you could have the whole
12 hierarchy of control and then show if you use the
13 protective equipment, this is the level of
14 reduction one could get. That might be a better
15 place to put that than have it in the overall
16 hazard assessment.

17 I think that might be a better way,
18 and you could have more text along with it. It's
19 almost moving to what EPA would recommend doing or
20 will decide to do once they get the final document
21 out. But that would be one way to put greater
22 space between the description of what's going on

1 out there now and then what approaches can be used
2 or should be used. And that would then allow one
3 to, in a fairly short section, work through the
4 various hierarchy of control issues, which would
5 end then with a --

6 **DR. KENNETH PORTIER:** But --

7 **DR. HENRY ANDERSON:** Yeah, go ahead.

8 **DR. KENNETH PORTIER:** Dr. Anderson,
9 what I was hearing you say is maybe in whatever it
10 is, Section 2.3.1 on Occupational Exposures,
11 there's no discussion of PPE and no discussion of
12 environmental controls. It's just here's the
13 exposure data and here's the estimated exposure,
14 if you like, right outside the face of the worker.
15 But then in maybe risk characterization, you're
16 saying, well, the risk is here and the
17 implications for risk mitigation -- because this
18 document isn't about risk mitigation. And this
19 particular group in OPP is not going to -- OPP is
20 not going to want to go there.

21 But what I thought I heard you say
22 is that maybe in the discussion in the risk

1 characterization there can be some discussion of,
2 well, the risk is such and such. We characterize
3 the risk under this exposure scenario. If you
4 implement engineering controls and can lower
5 levels -- ambient levels this way, you can reduce
6 risk proportionately. Dr. Morandi?

7 **DR. MARIA MORANDI:** Yeah. I want to
8 finish on this issue, and then I have a question
9 for Dr. Barone with respect to one of his answers.

10 **DR. KENNETH PORTIER:** Dr. Morandi,
11 you keep breaking up a little bit. You need to
12 talk right into your microphone.

13 **DR. MARIA MORANDI:** Yeah. And I'm
14 sorry. I'm looking at two different screens. On
15 the issue of PPE, I have -- and I want to mention
16 this about EPA. From the first chemical where I
17 was a member of the panel, the evaluation that was
18 1-4 Dioxane to the last one, carbon tetrachloride,
19 I mean, there was an enormous difference in terms
20 of -- relative difference in terms of the
21 attention paid to the issue of PPE.

1 I thought this in particular for
2 carbon tet was a sizeable improvement because it
3 was actually data showing there were adherence to
4 use of personal protective equipment. The
5 document -- actually, not only carbon tet, this
6 one too -- emphasizes that personal protective
7 equipment is the last thing you should do after
8 everything else, meaning, you know, engineering
9 and following the hierarchy of controls after you
10 do that. And you still you may have a risk of
11 excessive exposure, that then as less before you
12 go to use of PPE. For some occupational
13 situations, like working in enclosed spaces, you
14 may not have options for control, so PPE is the
15 only thing you may have.

16 So the document actually mentions
17 that. But it's a matter of how much emphasis is
18 done on this issue across the various documents
19 and also how EPA incorporates this issue in terms
20 of confidence about their risk estimate. And I
21 think I have made this point in the past that if
22 EPA does not have a specific information for any

1 scenario about the adequacy of having met all the
2 control recommendations and actually have
3 appropriate programs for use of PPE that that
4 would be included as a source of uncertainty. So
5 you cannot have the estimate with the no use of
6 PPE and use of PPE have the same level of
7 confidence in both cases because certainly you
8 have far less confidence for the estimate with use
9 of PPE. So that would be a way of also addressing
10 this issue.

11 But I think both in the Exposure
12 section of the panel -- of the document and also
13 in the Risk Characterization, there should be more
14 explanation and more emphasis on the issue of
15 appropriate use of controls and then use PPE as a
16 last resort. Because for people who are somewhat
17 familiar with it and they look at the previous
18 editions from EPA, they kind of say it's okay.
19 Most of the public is not aware of any of this, so
20 EPA has to be very, very clear in acknowledging
21 the fact that the estimates assuming PPE are not

1 very reliable at all because of all the issues
2 that we are aware about.

3 So I don't know if this contributed
4 anything to the discussion before I move to my
5 question to Dr. Barone.

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

7 Dr. Kaufman?

8 **MR. ALAN KAUFMAN:** Yes, thanks.

9 Let's see. Am I -- yeah. I'm unmuted here.

10 Yeah. I think you said it real
11 well, Dr. Portier. I think this is a risk
12 evaluation document. It's not a risk mitigation
13 document. But maybe the way to make this a little
14 clearer would be to think about it in terms of
15 instead of a single use case maybe the, let's say,
16 metal vapor degreasing with PPE and without PPE --
17 treat those as separate use cases and outline
18 whatever we know about likelihood of use of PPE
19 and the uncertainty surrounding each of those
20 separately.

21 I think that might make it a little
22 clearer. And that way you can say, okay, there is

1 a risk with PPE. There's not a risk -- or sorry -
2 - without PPE, and there's not a risk with PPE and
3 kind of treat each of those use cases separately.
4 Is that something that EPA -- and also recognizing
5 EPA doesn't have any statutory authority to make
6 people use PPE other than to make recommendations
7 in this document. Is that something has appeal
8 for anyone?

9 **DR. KENNETH PORTIER:** I think that's
10 a good point that it's not far from what they're
11 attempting to do right now. And I guess my
12 questions were where in what they're doing is
13 unclear? And I like -- now, I like this idea of
14 calling it another condition of use. So vapor
15 degreasing without gloves, vapor degreasing with
16 gloves, it's in the table, but it's not identified
17 as another condition of use. It's more focused on
18 the PPE and less on the condition of use.

19 And that may be a good kind of
20 comment to make back to EPA that focusing it that
21 way or, as Dr. Morandi said, focusing it as a
22 bigger part of the uncertainty discussion that the

1 condition of use without gloves is a more likely
2 scenario than the condition of use with gloves.
3 So I don't want to belabor this, and I think at
4 this point I'd like to move on. But Dr. Jimenez-
5 Gonzalez, you have your hand up.

6 **DR. CONCEPCION JIMENEZ-GONZALEZ:**

7 Yeah. I had my hand down, and I put it down as
8 you --

9 **DR. KENNETH PORTIER:** I see you

10 unmuted --

11 **DR. CONCEPCION JIMENEZ-GONZALEZ:**

12 Yeah. Can you hear me?

13 **DR. KENNETH PORTIER:** Yes, I can.

14 **DR. CONCEPCION JIMENEZ-GONZALEZ:**

15 Hello? Yes. Yeah. I put it down after you said
16 you didn't want to belabor the point. I guess the
17 one thing I will add to what you were saying is
18 that that's assuming proper use of PPE, which, as
19 Dr. Morandi was saying, well, it's part of the
20 uncertainty as well, because they -- as we are
21 seeing right now with the pandemic, not all the
22 PPE is used properly. Maybe some companies will

1 go into great lengths to ensure the fit testing
2 but might not happen everywhere. So it's just
3 that's a distinction that will make this proper
4 use.

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

6 Dr. Kissel?

7 **DR. JOHN KISSEL:** Yeah. That was my
8 point that the conversation was going in a way
9 that was just a little too much with and without
10 gloves. It should be with the appropriate gloves
11 and with a trained and conscientious user. Then
12 you get the protective effect. Without all those
13 things, you get maybe nothing or worse than
14 nothing.

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

16 Dr. Anderson, I see your hand's up again.

17 **DR. HENRY ANDERSON:** Yeah. I would
18 think having a condition of use as a separate one
19 that certainly would address the issue. The other
20 would be adding a condition of use dealing with
21 spills. A lot of the PPE, if you look at the
22 literature at what's being used, it's more what

1 they call emergencies or emergency response
2 issues, which deals with spills. So that might be
3 another way to do it because I think most
4 everybody, or their response teams, use
5 respiratory protection.

6 And I think if we have high
7 measurements, those are often the circumstance
8 where they occur. It's not that that atmosphere
9 in that facility is at those high levels
10 continuously for eight hours a day, forty hours a
11 week. It's all variable. So that might be
12 another condition of use one could look at that
13 would begin to address the high-end exposure
14 issues.

15 **DR. KENNETH PORTIER:** Thank you, Dr.
16 Anderson. Dr. Morandi, your hand's still up.

17 **DR. MARIA MORANDI:** Yes, and I was
18 wondering if I can ask the question to Dr. Barone
19 that I hadn't asked before. But it's not related
20 to the -- well, it is related to the PPE issue but
21 not what we are discussing right now.

1 **DR. KENNETH PORTIER:** Okay. Let's
2 finish off this conversation. I think Dr. Cobb
3 and then Dr. Barone wants to jump in with some
4 comments. Dr. Cobb.

5 **DR. GEORGE COBB:** Thank you, Ken.
6 Just real quick in a past panel I had suggested
7 that the uncertainties that are being discussed in
8 this section and the uncertainties that are being
9 discussed in the exposure assessment be included
10 as uncertainty factors in computing the risk
11 quotients, not simply in the discussion section
12 about uncertainties. That's all.

13 **DR. KENNETH PORTIER:** Thank you.
14 Dr. Barone, did you want to comment?

15 **DR. STANLEY BARONE:** Sure. A couple
16 of things, the PPE issue does come up under later
17 charge questions. And some of this discussion
18 actually gets at the risk characterization and the
19 risk characterization questions. We are trying to
20 make it clear in the Exposure section -- and I
21 think you've identified a couple of ambiguities
22 where we can provide more clarity about the

1 hierarchy of controls and what we considered and
2 didn't consider in the hierarchy of controls and
3 PPE.

4 We are not presuming that PPE is
5 uniformly applied or utilized. And we are
6 actually looking at the conditions of use and
7 determining if the conditions of use would be
8 appropriate for using and implementing the PPE
9 because, as several of the panel members have
10 indicated, in order to get that 50 APF protection
11 factor, you have to have a monitoring program, you
12 have to have inspections, you have to have
13 training, you have to have fit testing, all of
14 that. When we get to the risk characterization, I
15 think it will be important to revisit this.

16 I think the suggestions about
17 uncertainty and the discussions of the uncertainty
18 is important. We should come back to that. I
19 think the issue of separate conditions of use is
20 basically a non-starter. The way we have to
21 legally evaluate conditions of use it's the
22 conditions of use for that. It's not about PPE or

1 no PPE. It's all the different factors within
2 that condition of use. And again, that comes back
3 to the holistic evaluation of the hierarchy of
4 controls.

5 So we're trying to do that in the
6 risk evaluation. Dr. Portier, you've already
7 pointed out this is not a risk mitigation
8 document. This is the not the rule making. We
9 are trying to determine if we have unreasonable
10 risk under the appropriate conditions for that
11 condition of use. Once we find that we have
12 unreasonable risk, then we move into that risk
13 mitigation phase.

14 There was also a question or a
15 comment about spills as a condition of use. We've
16 talked about this before. Spills are not a normal
17 part of the condition of use and would be handled
18 outside of the TSCA context currently. So that's
19 -- spills are not part of the normal practices.
20 Again, we take comments under consideration, but
21 that's not part -- there's not a condition of use
22 for spills. I hope that clarified.

1 **DR. KENNETH PORTIER:** I think all of
2 that's pretty clear. What I'd like to do at this
3 point is end this discussion and go on to Question
4 4.2 with the understanding that we're probably
5 going to come back to this later on. Dr. Morandi,
6 you wanted the last word.

7 **DR. MARIA MORANDI:** No, that's okay.
8 I'll ask -- well, I wanted to ask a question of
9 clarification from Dr. Barone because I went
10 through Appendix C, which is where all the
11 exposure estimates are actually better explained.
12 And in those tables, there are estimates for
13 things like -- I'm looking at one of them -- spot
14 cleaning and one wipe cleaning and other
15 commercial uses. And it does provide estimates
16 for this with and without PPE with a caveat in
17 that section about the fact that EPA does not
18 believe that this is actually used in many of the
19 commercial uses.

20 So I'm a little bit confused about
21 his answer with respect to what I saw in the

1 document, but I agree that perhaps we can look at
2 this when we get to the risk evaluation question.

3 **DR. STANLEY BARONE:** Sure. So can
4 you hear me and respond?

5 **DR. KENNETH PORTIER:** Dr. Barone.

6 **DR. MARIA MORANDI:** Yes.

7 **DR. STANLEY BARONE:** Yeah. So part
8 of this is based upon our past practices. When we
9 -- in our previous risk assessments for TSCA, when
10 we moved to Section 6 Rule Making, the comments
11 arose of, oh, you're including additional analysis
12 with and without PPE, with and without engineering
13 controls. You should have had that peer reviewed
14 -- those additional calculations and estimates.

15 So to basically address that in the
16 risk evaluation, we provided that kind of
17 calculations, those kinds of approaches and,
18 specifically, to get your comments about those
19 because when we go to developing options for rule,
20 we want to know -- we want to be able to say with
21 some veracity what we think is the uncertainty for
22 options with different kinds of approaches. So

1 that's the reason for including that kind of
2 information. Your feedback on those additional
3 calculations and approaches is critically
4 important for us to move forward with the
5 finalization of our risk determination and will be
6 part and parcel of our considerations as we move
7 into developing options in the subsequent
8 activities if unreasonable risk is determined. I
9 hope that clarifies.

10 **DR. MARIA MORANDI:** Yeah. It does
11 except that, aside from this information you
12 provided, obviously, the general public that reads
13 this document is not aware of that. And -- unless
14 they were to go through all documents related to
15 how these methods were developed so -- but we can
16 go we can get back to this again when we discuss
17 the risk evaluation.

18 **DR. KENNETH PORTIER:** And, Dr.
19 Barone, this is Ken Portier. When I listen to
20 that, I think that this becomes a topic for maybe
21 a special consultation with the committee where we
22 focus specifically on that and do a deeper dive

1 into those methodologies to be able to give you
2 back that confidence and that veracity assumption
3 that -- a veracity assessment that you're looking
4 for.

5 **DR. STANLEY BARONE:** Thank you.

6 Thank you, Dr. Portier. And that's definitely
7 something I think our assistant administrator
8 brought up with you in the last meeting in her
9 opening remarks about follow ups. And on cross-
10 cutting issues it will be helpful to have those
11 conversations as we move into the future and our
12 risk evaluation for the next 20 and what we do to
13 retool following our lessons learned from the
14 first 10.

15 **DR. KENNETH PORTIER:** Yep. So I

16 think this has been a good conversation, a good
17 discussion. And I think it continues to clarify
18 in my mind the issues around with and without PPE
19 and engineering controls and how that gets
20 discussed and the different sections of the Draft
21 Risk Evaluation so that the communication -- I'm
22 more interested in the communication. I know a

1 lot of calculations are here. And I have some
2 confidence in those calculations, but I think we
3 still have a communication issue of how all of
4 that gets communicated in a logical way that the
5 exposure information is clear and then the risk
6 characterization information is clear.

7 At this point, though, I want to
8 turn to Dr. Kaufman and say let's start on
9 Question 4.2, which is suggestions and
10 recommendations for ultimate data models,
11 estimation methods that we should be looking at.
12 Dr. Kaufman.

13 **MR. ALAN KAUFMAN:** Thanks, Dr.
14 Portier. The comments that we've got -- and do
15 you want me to read the question first -- provide
16 any specific suggestions or recommendations for
17 alternative data?

18 **DR. KENNETH PORTIER:** You can re-
19 read the question. Most everybody sees it in
20 front of them.

21 **MR. ALAN KAUFMAN:** Okay, that's
22 fine. I'll dispense with that. I think one of

1 the questions that's come up -- and this is
2 something that we're going to have to grapple with
3 when it comes to consumer exposure as well -- is
4 did EPA attempt to get information on the use of
5 products directly from distributors and retailers?
6 For some uses like dry cleaning or metalworking
7 fluids, I can't believe that the number of
8 suppliers is going to be overwhelming.

9 It would seem to make sense to maybe
10 contact them and see if, A, how are these used
11 and, B, the more important thing is I think some
12 of the data may be outdated. This -- TCE has been
13 on the California Proposition 65 list since 1988.
14 And I know for some uses there's been some
15 reformulation, particularly on the consumer side.
16 That may also be the case in terms of industrial
17 uses. And so making sure we've got up to date
18 information I think is something that we need to
19 strive for, so I think there's a question about
20 that.

21 In other words, A, how robust is the
22 data we have and how up to date is it? I think

1 there were -- maybe we'd like to see some
2 discussion about potential alternatives to the
3 model in NCHS 2009. And there are some references
4 to AIHI publications, and we can provide those.

5 Third, identifying the drivers for
6 the model exposure estimates from the *Monte Carlo*
7 simulations, how does changing the values in those
8 drivers affect the CT and HE model-based exposure
9 estimates in comparison to estimates based on
10 measurements? And that exercise provides an
11 insight into the assumptions that might need
12 refinement or additional data that EPA could then
13 go out and get.

14 The other point was EPA had
15 indicated that there's a wealth of OSHA data, and
16 EPA indicated that it might be not representative.
17 But it seems to some of us that the data's at
18 least as representative as the single plant data
19 with small numbers that were used. And so a
20 composite approach to understanding exposure would
21 make some sense. We're back to the central
22 tendency and high-end descriptors. So if you

1 compile all of that data, you might have a broader
2 base. It's a little concerning that -- were you
3 looking for one study to use?

4 Most of the data tables provide MOE
5 ratios, but it's difficult to -- again, I think
6 this goes to the question of links. It's
7 difficult to get back to the actual data
8 measurement descriptors so you can compare that to
9 the regulatory numbers. That I think is
10 everything I've got. I'm going to turn it over to
11 the associate assessors and ask them if they've
12 got anything to add.

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

14 Dr. Anderson, do you have anything to add?

15 **DR. HENRY ANDERSON:** Just briefly, I
16 think the issue of using the OSHA data -- it'd be
17 helpful to have that described in the actual text
18 in the report rather than have to rely on looking
19 at that elsewhere in the document. That I think
20 whether you use that or not as your primary
21 modeling data is not as important as it is to see
22 how does that compare to the data that you're

1 actually using, that, while the assumption is that
2 there may be a bias in that data, it's still
3 useful to see is the single 16 samples from one
4 facility -- how representative is that?

5 You can get a sense of that by
6 looking at what OSHA found or NIOSH found in the
7 facilities they've been to, so that gives you a
8 confidence that this isn't a outlier one way or
9 the other. I would say putting the data together
10 and doing a composite, I think that is a good --
11 gives you further confidence that really what
12 you're after is what is the actual likelihood of
13 exposures and what are they across the spectrum of
14 various industries. Otherwise, I think now
15 summarize the points. A lot of these overlap with
16 what I said before.

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

18 Dr. Bennett?

19 **DR. STEVEN BENNETT:** I don't have
20 anything more to add at this point.

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

22 Dr. Kissel?

1 **DR. JOHN KISSEL:** I don't have much
2 to add. I would say that we potentially have a
3 problem here with the fact that the conventional
4 methods for estimating dermal absorption don't
5 work if you have damaged skin. And there is no
6 methodology for damaged skin, so all you can do is
7 look for empirical evidence. And I can provide a
8 couple of references, but in vivo in rats neat
9 trichloroethylene is apparently absorbed based
10 upon blood levels at two hours after exposure.

11 It's about a 25-fold increase over
12 saturated solution, so thermodynamically you would
13 expect those to be the same. But the fact that
14 it's 25 times bigger from the neat compound
15 suggests that it's actually damaging the skin.
16 And this is relevant to the consumer stuff later
17 also, but I'll provide a reference.

18 **DR. KENNETH PORTIER:** Thank you.
19 Dr. Morandi?

20 **DR. MARIA MORANDI:** Nothing to add.

21 **DR. KENNETH PORTIER:** Dr. Cobb, I
22 see your hand up. I'm not sure if it's for this?

1 **DR. STEPHEN GRANT:** So, Ken, yeah.
2 What Dr. Kissel just mentioned the damaged skin,
3 is there any data in the literature for
4 occupational use about the extent to which skin
5 might be damaged by TCE or related compounds, and,
6 if so, would that help at all?

7 **DR. JOHN KISSEL:** No. This is John
8 Kissel again. I'm not aware of such literature.
9 But it's not -- I haven't searched for it, so I
10 can't say definitively that it's not there. But I
11 would be surprised if anybody had done any
12 systematic test. It's the sort of thing you can't
13 actually do in a live human being for human
14 subjects reasons, and so you would only kind of by
15 happenstance find data. And it's probably not
16 available.

17 So surrogate data in rat of the type
18 that I just mentioned, which is not really --
19 people have done cadaver skin experiments and
20 animal experiments where they deliberately damage
21 skin. I don't know that there are any of them
22 that been done with TCE. Again, I'd have to

1 search on that. I think it would be sheer dumb
2 luck if there actually was any directly applicable
3 data.

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

5 Dr. Barone, your hand's up. You have a comment,
6 clarifying question?

7 **DR. STANLEY BARONE:** Yes, this is
8 also a follow on to the issue of damaged skin. If
9 we're -- different approaches -- if we're taking
10 the permeability approach, I see where that's
11 relevant. But if we're taking the absorption
12 approach, which we did include, and assuming 100
13 percent permeability damaged skin, it seems Dr.
14 Kissel's recommendation damaged skin is not really
15 so much of a factor. So it would be helpful to
16 get your feedback on that.

17 **DR. KENNETH PORTIER:** Dr. Kissel?

18 **DR. JOHN KISSEL:** So I'm not sure
19 where 100 percent absorption comes into play here.
20 In the occupational scenarios, you're using the
21 Kasting, Miller, Frasch approach and assuming
22 either 8 percent or 13 percent absorbed. The 8 or

1 13 percent absorbed is basically an estimate of
2 the consequence of a competition. The material is
3 either absorbed or it volatilizes.

4 And if you up the speed at which
5 material is absorbed, then less volatilizes in the
6 same window because some of that material's
7 already made it to the blood. Some of the
8 material that would have otherwise been
9 volatilized will get to the bloodstream before the
10 volatilization occurs. So if the skin is more
11 permeable, the fraction absorbed should go up.

12 **DR. STANLEY BARONE:** So just so I
13 understand, basically you're saying damaged skin
14 we would have a higher penetration of either eight
15 or a higher percentage?

16 **DR. JOHN KISSEL:** Correct.

17 **DR. STANLEY BARONE:** And you don't
18 know of any data that's existing that would help
19 inform us for different assumptions of the 8 or 13
20 percent?

21 **DR. JOHN KISSEL:** I don't know of
22 any human data for TCE that would help with that.

1 I think there's either rat data with TCE or
2 perhaps human cadaver skin data with other
3 solvents that could be at least somewhat
4 informative but not definitive.

5 **DR. STANLEY BARONE:** Okay. We'll
6 look. Thank you.

7 **DR. KENNETH PORTIER:** This is Ken
8 Portier. You might also want to look in the
9 cosmetics industry research because I know of a
10 lot that's been done with things like sunscreen,
11 chemicals and absorption. But Dr. Kissel, one of
12 the things I thought I heard you say is it's not
13 just the fraction absorbed but it's the rate of
14 absorption. You're saying, with damaged skin,
15 it's going to get into the bloodstream maybe
16 faster than it can volatilize. Is that what I
17 heard?

18 **DR. JOHN KISSEL:** Well, that's the -
19 - where this fraction absorbed is coming from for
20 VOCs is it's basically the calculation involves
21 estimation of how fast it's evaporating and
22 estimation of how fast it's absorbing. And you

1 have direct competition between those two
2 processes. So if one of them happens faster, then
3 that's why there's a -- the 8 and 13 percent
4 difference is a reflection of the different
5 assumptions about wind speed.

6 So when wind speed goes up,
7 evaporation happens faster and absorption goes
8 down. The 8 percent is the higher wind speed and
9 the 13 percent is the lower wind speed. So you
10 can work with variable rates on the other side
11 also on the absorption side. So if the absorption
12 rate goes up, then the fraction that's going to be
13 absorbed goes up.

14 **DR. KENNETH PORTIER:** Thank you.
15 Are there any other comments on Question 4.2?
16 Somebody's typing and not muted. Dr. Barone, I
17 think you're typing not muted.

18 **DR. STANLEY BARONE:** I'm sorry.

19 **DR. KENNETH PORTIER:** So I think at
20 this point if it's good, that we'll go and move on
21 to Question 4.3. I'd like to at least get that
22 done before we break for lunch. Dr. Bethel, would

1 you read Question 4.3 and 4.4 into the record?

2 You're not unmuted. We're not hearing anything
3 here. We may have lost Dr. Bethel.

4 **MR. ALAN KAUFMAN:** Ken, do you want
5 me to read it?

6 **DR. KENNETH PORTIER:** Yes, please.
7 Keith?

8
9 ***CHARGE QUESTION 4 (4.3)***
10

11 **MR. ALAN KAUFMAN:** Yeah, I'll just
12 go ahead and read it. That's probably the fastest
13 thing to do. 4.3, please comment on assumptions
14 used in the absence of specific exposure
15 information inferens, e.g., dermal surface area
16 assumptions [high-end values, which represents two
17 full hands in contact with a liquid: 890
18 centimeters squared (mean for females), 1070
19 centimeters squared (mean for males)] and [central
20 tendency values, which is half of two full hands
21 (equivalent to one full hand) in contact with a
22 liquid and represents only the palm-side of both

1 hands exposed to a liquid: 445 centimeters squared
2 for females and 535 centimeters squared for
3 males]. Please also consider these values in the
4 context of different life stages and body weights
5 (Section 2.3.1.2).

6 Yeah. You may want to reword that
7 slightly, by the way, before I get started on the
8 comment. It talks about high-end values, but then
9 it talks about mean for females and males, which
10 might be a little confusing to readers even though
11 I know exactly what you're getting at. Okay.
12 Comments.

13 **DR. KENNETH PORTIER:** So --

14 **MR. ALAN KAUFMAN:** Sorry, go ahead.

15 **DR. KENNETH PORTIER:** I was just
16 going to say go ahead, and let's go ahead and
17 start with the comments on 4.3.

18 **DR. ALAN KAUFMAN:** Okay. The
19 comments were that there were not significant
20 problems with the assumption. The mean surface
21 areas as described in the *Exposure Factors*
22 *Handbook*, which comes from NHANES -- the handbook

1 also presents estimates for males and females over
2 21, children 11 to 16 years, and children 16 to 21
3 years, as they represent a percentage of body
4 surface. Body surface area can be calculated from
5 body weight, so it's possible to include a
6 distribution of surface areas was one comment.

7 And then the other comment that we
8 had was -- and this is something that's going to
9 come again I think when we get to the consumer
10 exposures -- the issue of aggregate exposure
11 combining inhalation and dermal is inadequately
12 discussed and ignored. It's clear that
13 individuals will be exposed via both routes, and
14 the combined exposure will certainly be greater
15 than each individually. Simply begin by simply
16 adding the exposures.

17 We talked already about spills, so I
18 won't talk about that. I think we have a similar
19 conversation when we get to consumer exposures
20 when it comes to activities like huffing of TCE.
21 And I think that is essentially it.

1 I did receive one comment from
2 someone who was not on the panel -- let me get to
3 my email here -- or not one of the associates.
4 But there was a question about paints possibly
5 being a condition of use that might expose both
6 occupational and consumer users, and that did not
7 seem to be one of the conditions of use. I'm
8 assuming -- excuse me, I'm assuming it's because
9 we were able to confirm that TCE is not used as a
10 solvent in paints, but that's something that
11 probably needs to be mentioned because it's a
12 question that has come up.

13 And that is it. I'm going to turn
14 it over to the associates to add anything they'd
15 like.

16 **DR. KENNETH PORTIER:** Okay. Dr.
17 Anderson, anything to add?

18 **DR. HENRY ANDERSON:** No, I don't
19 have anything to add.

20 **DR. KENNETH PORTIER:** Dr. Bennet?

21 **DR. STEVEN BENNETT:** I don't
22 anything additional to add.

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

2 **DR. JOHN KISSEL:** I would say that
3 we've been using these assumptions for a while
4 now, and I don't think you could justify --
5 they're not really chemical specific, and you
6 couldn't justify changing them at this point. I
7 think that EPA needs to take a look to try to find
8 data to proof these assumption. The only data
9 that I know of that might be useful are not really
10 VOC data. They're pesticide data.

11 But I think it would be worthwhile
12 to do an exercise. And I'm not so much worried
13 about the surface area assumptions. It's the load
14 numbers that EPA is using that are kind of gross,
15 and I wonder at how well those would stand up
16 against empirical data. And I think that an
17 overall analysis not just for TCE but for dermal
18 exposure, generally, needs to be conducted to try
19 to put the loads that EPA is using into some kind
20 of context.

21 **DR. KENNETH PORTIER:** Dr. Kissel,
22 when you say gross, you mean not fine-tuned, I

1 guess is -- I was trying to figure out what there

2 --

3 **DR. JOHN KISSEL:** Yeah. "Not fine-
4 tuned" is better language.

5 **DR. KENNETH PORTIER:** I was just
6 trying to figure out what does he really mean by
7 kind of gross? And I came up with that thinking.
8 Dr. Morandi.

9 **DR. MARIA MORANDI:** Nothing to add.
10 I call this the OMB question, Office of Management
11 and Budget question.

12 **DR. KENNETH PORTIER:** Yeah. Anyone
13 else have comments on Question 4.3? This is Ken
14 Portier. Interesting that the idea of replacing
15 these with distributions and some kind of
16 sensitivity or *Monte Carlo* analysis. I guess the
17 results would probably be pretty straightforward.
18 If the loading is constant and the hand is bigger,
19 then you would expect lower internal doses and
20 vice versa, so maybe that's not particularly
21 useful. EPA, do you have any follow up clarifying
22 questions or comments on the panel's response?

1 **DR. STANLEY BARONE:** Not at this
2 point.

3 **DR. KENNETH PORTIER:** Good. Let's
4 see if Dr. Bethel joined us again? She may be
5 able to read Question 4.4?

6 **DR. KEITH JACOBS:** This is Keith
7 Jacobs. Heidi, are you --

8 **DR. KENNETH PORTIER:** I was
9 concerned -- Yes, Keith?

10 **DR. KEITH JACOBS:** Heidi, are you
11 on? If not, I can read. It looks like Heidi's
12 on.

13 **DR. KENNETH PORTIER:** She's there
14 and she's unmuted. But we're not hearing her.
15 Your phone might be muted.

16 **DR. KEITH JACOBS:** But she was --
17 she was having connection problems. I'll read 4.4
18 for now.

19 **DR. KENNETH PORTIER:** Yeah.

20

21 *CHARGE QUESTION 4 (4.4)*

22

1 **DR. KEITH JACOBS:** Please comment on

2 --

3 **DR. KENNETH PORTIER:** Keith Jacobs
4 with EPA.

5 **DR. KEITH JACOBS:** Sorry, yes, Keith
6 Jacobs, EPA. Please comment on EPA's approach to
7 characterizing the strengths, limitations and
8 overall confidence for each occupational exposure
9 scenario presented in Section 2.3.1. Please
10 comment on the appropriateness of these confidence
11 ratings for each scenario. Please also comment on
12 EPA's approach to characterizing the uncertainties
13 summarized in Section 2.3.1.3.

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

15 **MR. ALAN KAUFMAN:** Yes. Okay. Just
16 essentially two comments, one general and one
17 specific. Specific one is when you're estimating
18 occupational non-user inhalation exposure, there
19 was -- EPA reviewed the personal monitoring data,
20 area monitoring data and did some modeling on far-
21 field exposure concentrations. When the Agency
22 wasn't able to identify personal or area data or

1 parameters for modeling those ONU inhalation
2 exposures, we've gone back to the same assumption,
3 which I think we've talked about on past chemical
4 evaluations, where the assumption is that ONU
5 inhalation exposure would always be lower than
6 occupational users, which is probably valid.

7 The question, of course, is what's
8 the relative exposure? And I think the central
9 tendency from occupational exposure personal
10 breathing zones, using that to estimate ONU
11 exposures I think is -- there are certainly some
12 issues with that approach. But I don't have a
13 suggestion. I don't anybody has a suggestion for
14 doing anything better than that in the absence of
15 more data. And that might be an area where, if
16 you're trying to get some additional data either
17 from OSHA or from some of the companies involved,
18 might be helpful.

19 And the general comment was that EPA
20 has done a pretty good job of describing some of
21 the assumptions, the limitations, the
22 uncertainties. But where I think there's a

1 communication issue, to your point, Dr. Portier,
2 it was the lack of connecting that to a clear and
3 transparent link to the overall confidence levels.
4 And maybe a detailed map of all the assumptions
5 and uncertainties inherent in each of the step --
6 each step of the derivation when you're modeling
7 or coming up with estimates, either by modeling or
8 measurements. Trying to connect all of those
9 individual uncertainties to an overall uncertainty
10 remains unclear.

11 And that is all I've got, so I'm
12 going to turn it over to the rest of the group to
13 add anything they'd like.

14 **DR. KENNETH PORTIER:** And, Dr.
15 Kaufman, I just want to make sure these were
16 comments for 4.4 because you mentioned ONUs, and
17 that's the focus of Question 4.5. So this was
18 4.4?

19 **MR. ALAN KAUFMAN:** Sorry, that was a
20 comment that I received under 4.4. So okay.
21 We'll pause the ONU exposure to 4.5, but the
22 general comment still applies.

1 DR. KENNETH PORTIER: Applies, yeah.

2 Thank you. Dr. Anderson?

3 DR. HENRY ANDERSON: Yeah. Just a
4 quick comment. I don't know where this fits in
5 but again, just kind of thinking back over all the
6 chemicals we've worked on and then looking at
7 those various sections, the uncertainties and the
8 characterization -- the view is often quite
9 similar between them. It would seem to me going
10 forward it would be useful to identify which of
11 those seem to be the most critical and then begin
12 to develop a strategy for how are we going to fill
13 in that.

14 It's easy just to characterize it
15 and discuss the uncertainties because they are
16 what they are. But how do we go about reducing
17 those uncertainties so we have greater confidence
18 in the exposure scenarios and their descriptors?
19 I think in some of these we could probably --
20 given a year to begin to develop some of that
21 since it's kind of categorical for a lot of the
22 chemicals, it might be worth then EPA considering

1 proposing gathering additional information would
2 help reduce the uncertainties.

3 **DR. KENNETH PORTIER:** Dr. Anderson,
4 this is Ken Portier. This is a -- that's actually
5 a very good point because from a quality
6 improvement perspective, we'd like to know which
7 are the greatest uncertainties. And we know that
8 we improve the quality by tackling the greatest
9 uncertainty first. So that was a good point. Dr.
10 Bennett?

11 **DR. STEVEN BENNETT:** This is Dr.
12 Bennet. I don't have anything additional to add
13 to the uncertainty conversation.

14 **DR. KENNETH PORTIER:** Thank you.
15 Dr. Kissel?

16 **DR. JOHN KISSEL:** No additional
17 comment.

18 **DR. KENNETH PORTIER:** Dr. Morandi.

19 **DR. MARIA MORANDI:** Yes, actually I
20 had this comment in the consumer exposures that
21 Table 2.71, I guess, and 2.72 for consumer
22 exposure is kind of goes in the direction of

1 trying to be more explicit about the various
2 confidence levels -- in this case it's for
3 modeling -- is considering exposure modeling
4 scenarios -- and provide the level of confidence
5 for the model full values and so forth. So I
6 think the idea of trying to develop a map of all
7 the uncertainties in detail including the issue
8 of, well, if I use data from a surrogate type of
9 variable, like a different exposure scenario or a
10 different chemical and so forth and having help go
11 through it in detail and very, very specifically
12 and very, very transparently and then in the end
13 then come up with the overall confidence level.

14 And that's what is difficult to
15 assess in all these documents unless one were to
16 go through in detail doing that kind of work. And
17 what I was going to suggest is perhaps this is
18 another issue that EPA may want to consult the
19 committee about, in other words how to be more
20 clear in portraying and communicating all the
21 uncertainties and the overall confidence level.
22 That's all.

1 **DR. KENNETH PORTIER:** Thank you, Dr.
2 Morandi. That's a good idea -- adding it to my
3 list and the list keeps growing. Does anyone else
4 want to comment on Question 4.4? I don't see any
5 hands going up. I'll turn to EPA. Do you have
6 any clarifying questions or comments on the
7 panel's response?

8 **DR. STANLEY BARONE:** No. I do
9 appreciate Dr. Morandi's last comment. That is
10 one of the focus areas we plan to engage the
11 Academy on with regard to our systematic review
12 evidence integration approaches in the weight of
13 the scientific evidence and how we get to a
14 strength of evidence call. So again, I think
15 between the NAS and with the committee in a follow
16 up, I think we want to engage and get further
17 input.

18 **DR. KENNETH PORTIER:** Okay. I see
19 by the clock that we're at 12:45. We're planning
20 to break at 1:00. I'm kind of reluctant to go on
21 to the next set of questions, so I think what
22 we'll do is we'll break for lunch at this point

1 and reconvene at 1:30. So at that point I
2 recommend that the panel try to remain connected,
3 at least your WebEx connection remain up. Your
4 phone may hang up, but you can always use WebEx to
5 dial back in again. So we'll reconvene at 1:30.

6 Thank you.

7 (LUNCH BREAK)

8
9 **DR. KENNETH PORTIER:** Hi. Ken
10 Portier here.

11 **DR. TODD PETERSON:** We can hear you.

12 **DR. KENNETH PORTIER:** Yeah, I can
13 hear you just fine.

14 **DR. HEIDI BETHEL:** Terrific. Thank
15 you.

16 **DR. TODD PETERSON:** This is Heidi, I
17 take it?

18 **DR. HEIDI BETHEL:** Yeah. This is
19 Heidi.

20 **DR. TODD PETERSON:** Okay. This is
21 Todd. And --

22 **DR. HEIDI BETHEL:** Hi, Todd.

1 **DR. TODD PETERSON:** -- we're about a
2 minute from starting.

3 **DR. HEIDI BETHEL:** Oh.

4 **DR. TODD PETERSON:** So Ken, usually,
5 I'm at the table asking everybody to sit down.
6 But at 1:30, I welcome you to just go ahead and
7 announce that we're starting and go from there.
8 We are doing the roll call at this point after
9 lunch; is that correct?

10 **DR. KENNETH PORTIER:** Yes. Thanks
11 for reminding me. I'm just going to call names,
12 and I'm going to want a yes/no.

13 **DR. TODD PETERSON:** Yeah. In fact,
14 we can do that on Thursday and Friday. They don't
15 have to reintroduce themselves. I think we just
16 didn't tell them. But yes/no is great. Thank
17 you.

18 **DR. KENNETH PORTIER:** Yeah. Okay.
19 I see by my clock it's 1:30. And I'd like to
20 continue with this SACC meeting of the Science
21 Advisory Committee on Chemicals, review of the
22 Draft Risk Evaluation for TCE. At this point, I'm

1 going to call the roll, just to ensure that all of
2 the committee has returned. And I'm just going to
3 ask each member to indicate present or yes, so
4 that we know you're here.

5 **DR. TODD PETERSON:** And we have some
6 background noise.

7 **DR. KENNETH PORTIER:** Dr. Anderson?

8 **DR. TODD PETERSON:** There are a
9 couple people that are unmuted. Could they mute
10 themselves? I'm sorry for interrupting.

11 **DR. KENNETH PORTIER:** Yeah.

12 **DR. TODD PETERSON:** Go ahead with
13 the roll.

14 **DR. KENNETH PORTIER:** Dr. Slechta, I
15 think it's coming from hers.

16 **DR. TODD PETERSON:** No, I see --

17 **DR. KENNETH PORTIER:** There we go.
18 Thank you.

19 **DR. TODD PETERSON:** -- from OPPT as
20 well.

21 **DR. KENNETH PORTIER:** Yeah. Okay.
22 Let's continue with the roll. Dr. Anderson?

1 **DR. HENRY ANDERSON:** Yeah. Sorry, I
2 got back a little late here.

3 **DR. KENNETH PORTIER:** No, just fine.
4 We're starting. Dr. Bennett?

5 **DR. BENNETT:** I am here.

6 **DR. KENNETH PORTIER:** Dr. Barton?
7 Dr. Blystone?

8 **DR. SHERI BLYSTONE:** I'm here.

9 **DR. KENNETH PORTIER:** Dr. Bruckner?
10 Dr. Cory-Slechta?

11 **DR. DEBORAH CORY-SLECHTA:** Here.

12 **DR. KENNETH PORTIER:** Dr. Davies?

13 **DR. HOLLY DAVIES:** Here.

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

15 **DR. WILLIAM DOUCETTE:** Present.

16 **DR. KENNETH PORTIER:** Dr. Jimenez-
17 Gonzalez?

18 **DR. CONCEPCION JIMENEZ-GONZALEZ:**
19 Here.

20 **DR. KENNETH PORTIER:** Dr. Gilbert?
21 Dr. Johnson?

22 **DR. MARK JOHNSON:** I'm here.

1 DR. KENNETH PORTIER: Dr. Kaufman?

2 MR. ALAN KAUFMAN: I'm here.

3 DR. KENNETH PORTIER: Dr. Kissel?

4 DR. JOHN KISSEL: Here.

5 DR. KENNETH PORTIER: Dr. Rowlands?

6 Dr. Schlenk?

7 DR. DANIEL SCHLENK: Here.

8 DR. KENNETH PORTIER: Let me go

9 back. Dr. Bennett?

10 DR. STEVEN BENNETT: I am here.

11 DR. KENNETH PORTIER: Dr. Bruckner?

12 Good. Thanks, Dr. Bennett. Dr. Bruckner? Dr.

13 Rowlands? Okay, Dr. Jimenez-Gonzalez?

14 DR. TODD PETERSON: She responded

15 yes.

16 DR. KENNETH PORTIER: Dr. Apte?

17 DR. CONCEPTION JIMENEZ-GONZALEZ:

18 Yeah. I responded yes.

19 DR. KENNETH PORTIER: Oh, okay. Who

20 was it I missed?

21 DR. TODD PETERSON: Barton.

1 **DR. KENNETH PORTIER:** I think I
2 missed Dr. Rowlands. And Dr. Barton? We'll come
3 back. Dr. Apte? Dr. Cobb?

4 **DR. GEORGE COBB:** I am here.

5 **DR. KENNETH PORTIER:** Dr. Grant?

6 **DR. STEPHEN GRANT:** I'm here.

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

8 **DR. MUHAMMAD HOSSAIN:** I am here.

9 **DR. KENNETH PORTIER:** Dr. Jenkins?

10 **MS. ALLISON JENKINS:** Here.

11 **DR. KENNETH PORTIER:** Dr. Lash?

12 **DR. LAWRENCE LASH:** I'm here.

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

14 **DR. MARIA MORANDI:** Here.

15 **DR. KENNETH PORTIER:** Dr. Morris?

16 **DR. JOHN MORRIS:** Here.

17 **DR. KENNETH PORTIER:** Dr. Rosol?

18 Dr. Vorhees? Dr. Rosol? Todd, do we have a
19 quorum?

20 **DR. TODD PETERSON:** Yes, we have
21 quorum. And I'm sure that a couple of people are

1 just a little late getting back. So we're good to
2 go.

3 **DR. KENNETH PORTIER:** Yeah. It's
4 not unusual for a few people to come dragging five
5 minutes after lunch.

6 **DR. TODD PETERSON:** Yeah. They're
7 the ones that keep repeating that they need to --

8 **DR. KENNETH PORTIER:** Okay.

9 **DR. TODD PETERSON:** -- come to the
10 table.

11 **DR. KENNETH PORTIER:** Any final
12 comments on Question 4.4 or 4.3 that the Committee
13 members may have had before we move on to Question
14 4.5? And I think Dr. Bethel had joined us again.
15 She took care of her technical issues. Would you
16 please read Question 4.5 and 4.6 in?

17
18 ***CHARGE QUESTION 4 (4.5 AND 4.6)***
19

20 **DR. HEIDI BETHEL:** Yes. Thank you.
21 Question 4 related to occupational and consumer
22 exposures (continued): to estimate occupational
23 nonuser inhalation exposure, EPA reviewed personal

1 monitoring data, area monitoring data, and modeled
2 far-field exposure concentration. When exposures
3 to ONUs could not be quantified, EPA considered
4 the central tendency from worker personal
5 breathing zones to estimate ONU exposures.

6 Question 4.5: Please comment on the
7 adequacy, appropriateness, and transparency of
8 EPA's approach and the assumptions EPA used to
9 characterize ONU exposure via this approach from
10 Section 2.3.1.

11 Question 4.6: Are there other
12 approaches or methods for assessing ONU exposure
13 for the specific condition of use? (Section
14 2.3.1).

15 **DR. KENNETH PORTIER:** Thank you.
16 Dr. Kaufman, you have the lead on 4.5?

17 **MR. ALAN KAUFMAN:** Yes. And
18 actually, I think I have the lead on 4.6 because
19 that's where it breaks. I think there was a
20 little confusion because I think that the quick
21 reference guide that was put together indicated it
22 was 4.1 to 4.5. But I think it should be 4.6

1 because that's where occupational exposure sort of
2 breaks from consumer exposure. But the comments
3 that I've got --

4 **DR. KENNETH PORTIER:** Okay.

5 **MR. ALAN KAUFMAN:** -- sort of apply
6 to both. So I'm not going to separate the two
7 because they really are part of the same
8 discussion.

9 The comments that we had, first of
10 all, it's not clear why ONU exposures were not
11 estimated for all of the conditions where there
12 are estimates for worker exposure. In other
13 words, if we're going to use that traditional
14 approach, which we talked about a little earlier,
15 of using the occupational user central tendency,
16 the ONU exposures should be pretty easy to
17 calculate. But they apparently weren't estimated
18 for all conditions of use. So that's one
19 question.

20 Another comment was that EPA
21 probably needs to consider breathing rates in
22 inhalation assessments. The rate that's being

1 used is basically a resting rate. There should be
2 a calculation also using a strenuous rate of
3 exercised breathing or at least something sort of
4 in between the two that would indicate, if
5 somebody is working, they're probably breathing a
6 little harder than their resting respiration rate.

7 And then the other question is heavy
8 alcohol consumption is known to interact and
9 aggravate some of the symptoms of TCE exposure.
10 And that group of workers probably needs to be
11 considered a vulnerable subpopulation. It may be
12 a bigger group than some of the illness groups.

13 And sort of a general comment, given
14 the fact that we've reviewed a number of compounds
15 over the last nine months, some of the same issues
16 keep coming up. At this point, there's probably
17 ample time for the next 20 to implement programs
18 to fill the data gaps that can't be met because of
19 the time between the draft release and the review
20 limits. There are limits on what's reasonably
21 available information based on some of the
22 statutory limitations that have been put in place

1 by Congress. Certainly, at the very least,
2 working with NIOSH and OSHA to gather information
3 from facilities, I think that would be very
4 helpful in sort of flushing out some of these
5 data.

6 To estimate occupational nonuser
7 inhalation exposure, the EPA reviewed personal
8 monitoring data, area monitoring data, and then
9 modeled far-field exposure concentrations. So I
10 think we talked about this a little earlier. We
11 didn't -- the Agency didn't identify personal area
12 data or parameters for modeling potential ONU
13 inhalation exposures. So we just kind of made
14 that assumption.

15 I guess the upshot is that in the
16 absence of other available information, using that
17 central tendency makes sense. On the other hand,
18 I think that this is the same thing we've talked
19 about since almost the beginning. It seems like
20 there could be some outreach to NIOSH and OSHA to
21 see if we can get some additional information that

1 might be available by the time we look at the next
2 20.

3 And then I've got a bunch of general
4 stuff. I don't think I need to go through it.
5 There are things about citations, number of
6 significant figures, et cetera. And I'll just put
7 those in the notes. I don't think we need to
8 belabor that at this point. So I'll put it up to
9 the associate assessors to see what their
10 additional comments are. Thanks.

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

12 Dr. Anderson, do you have anything to add?

13 **DR. HENRY ANDERSON:** No, I don't
14 think so. The only -- and it might have been
15 better under 4.4. It just wasn't clear to me how
16 does EPA use the confidence grading. I mean, it's
17 helpful to know is it just a descriptive thing
18 when you say medium, or low, or high confidence in
19 some of the databases, especially as it relates to
20 the ONU exposures.

21 It would be nice if, where you have
22 medium or low confidence, that that would suggest

1 that EPA is going to pursue how to improve the
2 confidence in their estimates and the data that's
3 provided. But otherwise, it's just sort of
4 hanging out there that okay, so they've considered
5 it to be low or high. It's unclear as to how that
6 characterization is used going forward.

7 **DR. KENNETH PORTIER:** Point taken.

8 Dr. Bennett?

9 **DR. STEVEN BENNETT:** This is Dr.
10 Bennett. I don't have any additional pieces to
11 add to the ONU discussion.

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

13 Dr. Kissel?

14 **DR. JOHN KISSEL:** No additional
15 comments.

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

17 Dr. Morandi?

18 **DR. MARIA MORANDI:** Yes. I wanted
19 to add, for 4.3, the response that was sent to me,
20 probably because the associate interpreted that
21 all the questions in this section would go to 4.6.
22 And the issues that were raised were relevant to

1 if there are analyses for other compounds that are
2 perhaps kind of similar in terms of physical-
3 chemical properties where there could be data for
4 workers and ONUs and if EPA could find those and
5 use that to get a sense of how far or how close
6 their estimates for ONUs are with respect to
7 workers.

8 And then this reviewer also have
9 some questions related to issues having to do with
10 the model assumptions, in terms of if the size of
11 the room, if doors could be opened or not in a
12 typical workplace, releases to outside air, or if
13 assumptions of the far-field is that it's infinite
14 or it's equivalent to outside. So I call on this
15 associate that probably recognize his comments, I
16 hope, to chime in if I have misrepresented what he
17 said. And I'll forward this to Dr. Kaufman.

18 And the only thing I want to do in
19 addition was to emphasize the potential use of
20 area samples. Sometimes these are called study
21 samples. But the idea is that these are samples
22 that are taken for different reasons at different

1 locations with respect to a source. And
2 understanding that the distance from the source
3 and other relevant information would not be
4 available, it could provide, at the minimum, some
5 data or some information with regards to what kind
6 of average concentrations you could expect, or
7 average or medium concentrations you could expect,
8 in a location that was not within the one meter or
9 less envelope for the worker.

10 And again, understanding that this
11 approach could have a lot of limitations, and
12 still, you could get some sort of information to
13 compare with estimates that lacking data on ONUs
14 you derived from with other means -- from some
15 other types of approaches. And so that was all.

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

17 Does anyone else have comments on Question 4.5 and
18 4.6? I noticed on 4.6 that Dr. Grant and Dr.
19 Davies are kind of listed as part of the second
20 half. And I didn't know if either one of them had
21 developed comments for 4.6.

1 **DR. MARIA MORANDI:** Dr. Portier,
2 those are when I was mentioning that I had
3 received those answers sent to me in error. So
4 they were not sent to Dr. Kaufman, so --

5 **MR. ALAN KAUFMAN:** And if you could

6 --

7 **DR. KENNETH PORTIER:** Okay. So you

8 --

9 **MR. ALAN KAUFMAN:** -- forward those
10 to me --

11 **DR. KENNETH PORTIER:** -- captured
12 their comments?

13 **DR. MARIA MORANDI:** Yeah, I will.

14 **MR. TODD PETERSON:** Yeah. If you
15 could send them to me, I'll include them in the
16 writeup. Thank you.

17 **DR. MARIA MORANDI:** Of course.

18 **DR. HOLLY DAVIES:** And I -- this is
19 Dr. Davies -- I didn't send anything for 4.6. I
20 assumed that that was a mistake, and I just did
21 4.7 to 4.10.

1 **DR. KENNETH PORTIER:** Okay. Thank
2 you. This is Ken Portier. I kind of have a
3 question for Dr. Morandi and Dr. Kaufman. And
4 it's a combination of a comment from Dr. Anderson
5 and then Dr. Kaufman.

6 When you're looking at that estimate
7 of half of -- or the median or average
8 occupational exposure being the estimate for the
9 occupational nonuser, I mean, I would've assumed
10 when they run these models, the near-field, far-
11 field models, they validated them at some point.
12 So we have some estimate of confidence in those
13 models. So does that confidence, do you think,
14 carry over into the estimates for the ONU?

15 I was trying to figure out -- I see
16 in the report where we have confidence statements
17 on the occupational exposure estimates for each
18 condition of use. But there's a large number of
19 occupational nonusers, and I'm not sure we have
20 much confidence or we have an assessment of
21 confidence on ONU estimates.

1 **MR. ALAN KAUFMAN:** I think you're
2 right, Ken.

3 **DR. KENNETH PORTIER:** Do either one
4 of you want to comment on that?

5 **MR. ALAN KAUFMAN:** Yeah. This is Al
6 Kaufman. I think you're right. I think that
7 there's reasonable confidence for the occupational
8 users. I think, when you get to the ONUs, I think
9 there's an assumption there that we really don't
10 have any confidence bounds around or any
11 uncertainty idea.

12 I think it's probably as good an
13 estimate of any in the absence of better data.
14 But I think that's one of the points is we believe
15 that there probably are better data out there that
16 could be gotten with relatively -- I don't want to
17 say little effort -- but maybe relatively little
18 effort.

19 **DR. MARIA MORANDI:** This is Maria
20 Morandi. I would agree. I'm not sure if they
21 would be better data, but at least it would be
22 data, like in the case of the static samples, that

1 will give you maybe sort of a bounding estimate,
2 more on the lower side than the higher side. Let
3 me rephrase.

4 So if you assume that the ONUs'
5 exposure is half the exposure of the -- is the --
6 corresponds to the central tendency estimate of
7 exposure for workers, that's a very high value;
8 okay? So it's very conservative, which actually
9 is not a bad idea. If you don't have any other
10 data, you are better off in these cases by
11 assuming very conservative values, even if you
12 know they are not -- they are overestimate, which
13 is okay.

14 With respect to the use of area
15 samples, if they are available, or model estimates
16 for the far-field, they should be -- obviously,
17 you don't know exactly where the ONU was located,
18 for example, with respect to the source. So there
19 are a larger number of uncertainties, too. But it
20 would give you a sense, I think, of how far off
21 you could be, even if it's not an exact number.

1 And so these static samples or the
2 exposures estimates using modeling for the far-
3 field are not ideal. But there is an additional
4 piece of information that, in the lack of data, it
5 would be useful to kind of give a sense of how far
6 the number -- the exposure estimates for ONUs
7 could be from the very conservative estimate to
8 estimates that are likely to be far less
9 conservative.

10 **DR. KENNETH PORTIER:** Thank you, Dr.
11 Morandi. I'd like to have that kind of added in
12 as a little bit of an uncertainty discussion in
13 the ONUs, even though they don't have any -- they
14 don't mention that in the question. I think it's
15 nice to point that out. Dr. Grant, you wanted to
16 comment on these questions?

17 **DR. STEPHEN GRANT:** Yeah. The issue
18 I have is when does an ONU become a user simply by
19 proximity? And yes, we have the near-field and
20 the far-field, but I'm not sure there's enough --
21 I'm not sure that we are looking at the individual
22 cases well enough to know whether or not a steady

1 state is achieved in the area where the work is
2 being done, such that simply being in the room
3 makes you a user or equivalent dose to a user.
4 This comes back from the point of view that we
5 have a statement that's often made. EPA expects
6 ONU exposure to be less than worker exposure. And
7 that, quote/unquote, makes sense.

8 But one of the first things I teach
9 in my class is that common sense isn't common or
10 sense. So one of the things we need to know is
11 how is this venting? And the active venting was
12 mentioned as part of the model. But the question
13 is, if it's not active venting, is it sufficient
14 to cause a flow-through and not expose everyone to
15 about the same amount? And even in that case, the
16 question would be, if we're relying on doors open
17 to the outside, is that going to be compromised
18 depending on the weather and the season.

19 **DR. KENNETH PORTIER:** Thank you, Dr.
20 Grant. I think in one of the previous committee
21 meetings, we also talked about the fact that EPA
22 tries to be conservative if an individual who

1 might be classified as an ONU is commonly in the
2 use area and may be required to use PPE as part of
3 their job. They're kind of reclassified as an
4 occupation user. So that's another level of
5 conservativeness that I think is built into these
6 draft risk evaluations. Any additional -- anybody
7 want to comment on these questions? Dr. Anderson?

8 **DR. HENRY ANDERSON:** Yeah. I was
9 just going to add one data source that might be
10 helpful here would be the OSHA inspection data or
11 the NIOSH. They often describe the circumstances
12 in other workers that may be around. And that
13 might be helpful to understand where ONUs are and
14 in what kind of facility.

15 So that might help with the near-
16 field/far-field sort of issue or is there some
17 that could be two lines. One is doing product
18 with TCE, and just behind them is somebody who's
19 doing some kind of a powder material. And they're
20 all wearing respirators, but one wears just a dusk
21 mask.

1 So you may find some additional
2 information that would help qualitatively
3 understand ONU versus occupational or those
4 datasets or the specific ones. Or again, going
5 forward, you could ask OSHA, when they're in a
6 facility, to look for these things and record it,
7 and then going forward over the course of the next
8 two years, you'd have quite a bit of data on some
9 facilities.

10 **DR. KENNETH PORTIER:** Thank you, Dr.
11 Anderson. Please send that along to Dr. Kaufman,
12 so it can be included in our report. Any
13 additional comments on Questions 4.5, 4.6? I'm
14 not seeing any hands come up. I'll turn to EPA.
15 Do you have any clarifying questions or comments
16 on the committee's response?

17 **DR. STANLEY BARONE:** Not at this
18 time. This is Stan Barone.

19 **DR. KENNETH PORTIER:** Okay. Well, I
20 guess what we're going to do is move on to the
21 more challenging question of consumer exposures.
22 Dr. Bethel, please read 4.7, 4.8, I guess.

1 DR. HEIDI BETHEL: Hello. Can
2 everyone hear me?

3 DR. KENNETH PORTIER: Yes.

4

5 *CHARGE QUESTION 4 (4.7 AND 4.8)*

6 DR. HEIDI BETHEL: Question 4, again
7
8 on the occupational and consumer exposure.
9 Consumer exposure, EPA collected data from
10 available sources and conducted modeling for
11 estimating consumer inhalation and dermal
12 exposures using the Consumer Exposure Model or
13 CEM. Product-specific consumer monitoring
14 information was not identified in literature.
15 Therefore model inputs related to consumer use
16 patterns are based on data from a comprehensive
17 national survey, Westat 1987, as described and
18 referenced within the TCE Draft Risk Evaluation.
19 Weight fractions of chemical within product are
20 based on safety data sheets. Default model values
21 are based on literature reviewed as part of model
22 development as well as EPA's Exposure Factors
23 Handbook.

1 Question 4.7: please comment on the
2 appropriateness of the approaches, models,
3 exposure or use information and overall
4 characterization of consumer inhalation and dermal
5 exposures for users and bystanders for each of the
6 identified conditions of use. What other
7 additional information or approaches, if any,
8 should be considered? (Section 2.3.2).

9 Question 4.8: please recommend any
10 additional data sources or studies that may be
11 more reflective of current consumer use patterns
12 for specific conditions of use. (Section 2.3.2).

13 **DR. KENNETH PORTIER:** Thank you.
14 And we've asked Dr. Morandi to lead the discussion
15 on these questions. Dr. Morandi?

16 **DR. MARIA MORANDI:** Yes. So we
17 received -- I received comments from members of
18 the panel, quite a few comments. So I split them
19 between those comments that seem to be consistent
20 across all the associates that sent comments from
21 those where there was not such a strong level of
22 agreement. So one issue in which everybody agree

1 was that EPA should have performed chronic
2 inhalation -- should have estimated chronic
3 inhalation exposures for non-consumers. The
4 reason being that TCE is very frequently present
5 in many consumer drugs.

6 Consumers also are more likely to
7 use more than one product, not just one, through a
8 typical year. So the actual exposures of TCE may
9 be more frequent than EPA has assumed in the
10 model, just based on one type of product and
11 exposure scenario at the time. So with respect to
12 this point, again, everybody seemed to agree, and
13 the other associates may want to expound on their
14 response to the question.

15 The other issue where everybody
16 agrees is that there was a lack of clarity in
17 terms of how EPA actually obtained all the
18 consumer product information because the
19 description in the document is not sufficiently
20 detailed to ascertain that. For example, there
21 are comments, well, a search was done without
22 being very specific about it. And in addition, in

1 other cases, some things didn't seem to make quite
2 sense.

3 For example, for two uses, which is
4 film cleaner and toner A, a surrogate product was
5 used instead of the actual product. And I
6 actually went online very quickly. And right off
7 the bat, Amazon, of course, gave me the source of
8 these two brands for paint thinner by -- one is
9 called EDWAL, The other one's Ethanol. And for
10 Toner A, apparently a very popular one is Stay
11 Away. So I couldn't understand why a surrogate
12 had to be used for products available. And
13 actually, at least for one of them, I could find
14 it INDS online.

15 The third issue where everybody
16 seems to agree also was that the Westat surrogate
17 data is a little bit old, and that it may be
18 dated. At least some of the information they
19 collected may be dated, because of changes in
20 products and changes in use patterns among
21 consumers. And in the past, the committee has

1 recommended that there should be an attempt to
2 update the data.

3 There was a little bit of less
4 consensus I terms of the face of the model. Some
5 members of the panel expressed doubt about the
6 model estimates. Although, it wasn't clear upon
7 first reading if the doubts were about the inputs
8 to the model or the model itself. I think
9 personally, I have a relatively decent level of
10 confidence, not to say high confidence, for the
11 basics of the CNE model. The question of
12 confidence about the input, that's a separate
13 issue.

14 Members of the panel also considered
15 that there should be an aggregation of exposures,
16 including the indoor concentrations, where I can
17 recall, again, that is emitted by water
18 frequently. And some contaminated water is
19 present in many compounds. And in addition, once
20 they compound it, and it feels like carpet
21 cleaner, for example, the chemicals will keep on
22 emitting, even after they were used, contributing

1 to indoor concentrations and the exposures of the
2 residents of the households.

3 Let me see if I have anything else
4 on this. Then there were some issues that, again,
5 have come up with respect to the CME exposure
6 model, in particular, the assumption of the
7 bystander always being in the far-field, meaning
8 away from the room where the product is being
9 used. And this is problematic because one can see
10 many of these applications where actually a
11 bystander could be in the same room very close to
12 the locations where the product is made.

13 So I think that's about it in terms
14 of the summary. And I would let the other
15 associates discuss more of the details because
16 then this will promote some discussion of the
17 issues.

18 **DR. KENNETH PORTIER:** Thank you, Dr.
19 Morandi. I'll run down the names of the five
20 associates and see if they have anything to add.
21 Dr. Bennett?

1 **DR. STEVEN BENNETT:** This is Dr.
2 Bennett. I think she captured most of them. I
3 do, at one point, want to touch a little bit on
4 the pepper spray modeling. But I think I'll let
5 the discussion go a little bit before we talk
6 about that.

7 And I do want to add one piece. The
8 hoof polish product, I don't have any issues per
9 say with the model. But I did some looking into
10 all the products. In fact, I looked at all of the
11 products that are referenced in the market in the
12 issue report.

13 And a good number of those, I'll say
14 about half of them still continue to appear to be
15 available. A couple are no longer available. And
16 quite a few, it's really unclear what they're
17 status is. And so I think that would be a really
18 good exercise for the Agency to verify which of
19 those -- for the completeness, because I think
20 certainly, some of these have to pull off the
21 market.

1 I think in particular, hoof Polish
2 product certainly appears to be reformulated
3 because the labeling information indicates that
4 it's now extremely flammable, which would be
5 inconsistent with a TCE-containing product. But
6 it doesn't have an SDS available. But that would
7 be what I look from, but I do want to touch on the
8 pepper spray at some point.

9 **DR. KENNETH PORTIER:** Thank you.
10 We'll hold pepper spray in reserve. Dr. Davies?
11 Dr. Davies?

12 **DR. TODD PETERSON:** Are you on mute?

13 **DR. KENNETH PORTIER:** She -- yeah.

14 **DR. HOLLY DAVIES:** I thought I --

15 **DR. KENNETH PORTIER:** There we go.

16 **DR. HOLLY DAVIES:** -- had clicked
17 mute, but apparently, I didn't. So now I'm here.
18 So Dr. Morandi did a good job of summarizing the
19 comments I sent in. I just wanted to highlight
20 verifying the products.

21 We had a discussion about this in
22 the ATSDR document. I can't remember the year of

1 ATSDR. But there was a lot of different products,
2 and again, not just verifying them and explaining
3 where they came from. She mentioned the Westat
4 survey being old. The specific recommendation I
5 was thinking is that for the future, the EPA
6 should consider updating that.

7 Oh, and one other thing. There's
8 some -- between the consumer products and the
9 occupational products, I wasn't sure why paint was
10 in occupational but not in consumer. And there's
11 some consumer exposure for these occupational uses
12 such as spot cleaners because that would be like a
13 dry cleaner using a spot cleaner. There would
14 still be residual TCE on the fabric that was then
15 brought into the household. So that should also
16 be at least acknowledged.

17 **DR. KENNETH PORTIER:** Is that it,
18 Dr. Davies?

19 **DR. HOLLY DAVIES:** Yes. I re-muted
20 myself. I had to unmute.

21 **DR. KENNETH PORTIER:** We'll move on
22 to -- okay.

1 DR. HOLLY DAVIES: Yeah.

2 DR. KENNETH PORTIER: Sorry. Move
3 on to Dr. Kaufman then.

4 MR. ALAN KAUFMAN: Hi. Yeah, I
5 think Dr. Morandi did a great job of summarizing
6 my comments. The only thing I would mention is, I
7 think there's a -- I mentioned it when we were
8 talking about occupational exposures. The
9 question -- I think particularly with consumer
10 exposures as to whether you aggregate dermal and
11 inhalation exposure in all cases -- I think if
12 there's dermal exposure, then there's almost
13 certainly going to be inhalation exposure. And
14 there should be some way of aggregating those.

15 However, the converse isn't always
16 true. In other words, you could have inhalation
17 exposure without any dermal exposure. So I think
18 we just need to use a little care there in terms
19 of each condition of use.

20 And I would just emphasize what a
21 couple of the commenters have said already. I
22 think there does need to be additional research as

1 to the status of some of these products. I think
2 some of them are still available, some of them are
3 no longer available, and others may be available
4 but have been reformulated to eliminate TCE.

5 So I think especially what's been
6 driving that is the Proposition 65. It's been
7 there since 1988. I know a lot of products have,
8 if they're able to, substituted alternative
9 solvents for TCE, for just that reason, so they
10 don't have to label. And that, I think covers it.
11 I think Marie did a great job summarizing
12 everything. Thank you.

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

14 Dr. Kissel?

15 **DR. JOHN KISSEL:** My comments are
16 better directed at 4.9, so I'll pass at this
17 point.

18 **DR. KENNETH PORTIER:** Okay. Dr.

19 Grant?

20 **DR. STEPHEN GRANT:** No additional
21 comments.

1 **DR. KENNETH PORTIER:** Okay. Does
2 anyone else have any comments on 4.7 and 4.8
3 before we go back to the pepper spray issue? I
4 haven't forgotten that one -- Dr. Morandi? I see
5 Dr. Morandi's hand up, but she's still muted.

6 **DR. MARIA MORANDI:** You are correct,
7 Dr. Portier; I forgot to click. What I was saying
8 is that I'm going to add something that puts me
9 out a little bit on a limb, with respect to EPA
10 TSCA approaches. And I know the consistently,
11 they are not considering the residential
12 concentrations or the personal exposure
13 concentrations, if they are available, to add to
14 their estimates of exposures related specifically
15 to product users.

16 On the other hand, it could be worth
17 it for them in this case to run a little exercise
18 to see how much of an effect that could have in
19 terms of a final risk estimate. There is a
20 sizeable amount of data in terms of indoor
21 concentrations for TCE, as well as personal
22 exposures of the residents to see at the same time

1 that those indoor concentrations were being
2 monitored. And the CNE model has an option where
3 you can enter a background concentration when you
4 do the calculations.

5 So as I was thinking about this, a
6 decision that keeps on coming up of, well, how
7 much risk is this exposure compared to what
8 already is contributing to risk from this indoor
9 environment, why not just enter as the background
10 concentration, instead of zero, the upper
11 concentrations of either the residential
12 monitoring data, the indoor residential monitoring
13 data, or perhaps the indoor personal exposure
14 monitoring data? Maybe collection, I think that
15 that, in terms of personal exposure is higher --

16 **DR. KENNETH PORTIER:** Dr. Morandi, I
17 can see you talking, but we don't hear you, for
18 some reason.

19 **DR. MARIA MORANDI:** When did you
20 stop hearing me? Hello? Can you hear me?

1 **DR. TODD PETERSON:** Hi, Maria. I can
2 hear you just fine. I didn't -- I don't mean to -
3 -

4 **DR. KENNETH PORTIER:** I don't hear
5 you, but I don't --

6 **DR. GEORGE COBB:** I can, too.

7 **DR. HOLLY DAVIES:** I heard her the
8 whole time.

9 **MR. ALAN KAUFMAN:** I think it's you,
10 Ken.

11 **DR. MARIA MORANDI:** Okay.

12 **DR. KENNETH PORTIER:** That's
13 interesting.

14 **DR. MARIA MORANDI:** To make it --
15 once we select those, we'll be able to say we are
16 not sure where they go. Okay. I'm joking.

17 So what I was suggesting that EPA
18 could do as an exercise is -- or they may have
19 done it already without telling us -- is one, if
20 you were to replace the assumption for zero
21 background concentration into the CNE model
22 estimates for inhalation with either, let's say

1 the upper five percent LSO of indoor air
2 concentrations that are available for all
3 different sites or even the maximum personal
4 exposure concentration measurements, which I think
5 was about 300 micrograms per cubic meter -- and
6 just enter that into the model and see if it makes
7 a significant difference in terms of exposure, and
8 also eventually, I think in terms of risk.

9 And this will be a way of getting
10 around first of all the issue, well, you know, EPA
11 has really the responsibility in this area or some
12 other organization. But I'm not saying EPA would
13 provide these as an estimate of risk but perhaps
14 as a way of providing context for their estimates
15 of exposure and risk for -- due to the use of
16 their specific type. So I just wanted to put that
17 on the table.

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

19 Does anyone else want to comment? Dr. Davies?

20 **DR. HOLLY DAVIES:** Yes. Hi. I
21 wanted to add one other thing that hadn't come up
22 before, which is the intentional TCE inhalations

1 by consumers, as something that should be at least
2 mentioned. And this is something that there is,
3 as Marie said, not agreement on with everyone on
4 the question. And that was it.

5 **MR. ALAN KAUFMAN:** Yeah. This is Al
6 Kaufman. If I can kind of follow up on that, I'm
7 one of the ones who kind of disagrees. I think it
8 probably falls into the same category as spills.
9 If you're intentionally huffing chlorinated
10 solvents, I don't know that there's a lot that we
11 can do here that's going to be helpful. But I
12 know there are others who disagree with that.

13 **DR. HOLLY DAVIES:** This is Dr.
14 Davies. I --

15 **DR. KENNETH PORTIER:** I think Dr.
16 Blystone --

17 **DR. HOLLY DAVIES:** Could I just
18 follow up on Al's, unless --

19 **DR. KENNETH PORTIER:** Oh, go ahead.

20 **DR. HOLLY DAVIES:** -- Sheri had some
21 more questions? I just wanted to say that I also
22 thought it was similar to spills. That was

1 something that was in my head, too. But of
2 course, if the products weren't for sale, then we
3 wouldn't have to worry about it.

4 **DR. KENNETH PORTIER:** That was Dr.
5 Blystone, right?

6 **DR. SHERI BLYSTONE:** No, that was --

7 **DR. HOLLY DAVIES:** No --

8 **DR. SHERI BLYSTONE:** -- Dr. Davies.

9 **DR. HOLLY DAVIES:** -- that was Dr.
10 Davies.

11 **DR. SHERI BLYSTONE:** This is Dr.
12 Blystone.

13 **DR. HOLLY DAVIES:** I was following
14 up on Al.

15 **DR. KENNETH PORTIER:** Oh, that was
16 Davies.

17 **DR. HOLLY DAVIES:** Yeah. Sorry.

18 **DR. KENNETH PORTIER:** Okay.

19 **DR. HOLLY DAVIES:** That was Dr.
20 Blystone.

21 **DR. KENNETH PORTIER:** Yeah. Sorry.
22 Dr. Blystone?

1 DR. SHERI BLYSTONE: Yeah --

2 DR. KENNETH PORTIER: I'll get it.

3 DR. SHERI BLYSTONE: I have to chime
4 in here -- is that intentional misuse of a product
5 is not a condition of use under TSCA.

6 DR. KENNETH PORTIER: I think we've
7 heard that before. Dr. Bennett?

8 DR. STEVEN BENNETT: This is Steve
9 Bennett. I'll just add on to that. I think that
10 those who intentionally misuse products,
11 inhalants, et cetera, they tend to go to the
12 lowest hanging fruit. And so chlorinate products
13 would probably not be their first choice because
14 there's other products that they be more likely to
15 abuse in those types of situations, unfortunately.
16 So that's just what I'll add into that.

17 MR. ALAN KAUFMAN: Yeah. Hi. This
18 is Al again. I missed part of the conversation
19 because, for some reason, my connection dropped.
20 But it sounds like we're talking about the huffing
21 still.

1 **DR. KENNETH PORTIER:** Yeah. I think
2 we've ended that conversation. I think we've
3 decided this is not necessarily covered under TSCA
4 and would be very difficult to handle in any other
5 way.

6 **MR. ALAN KAUFMAN:** Yeah.

7 **DR. KENNETH PORTIER:** Let's see. I
8 still see Dr. Davies' hand up and Dr. Morandi's
9 hand up. Dr. Davies? Hand went down. Dr.
10 Morandi?

11 **DR. MARIA MORANDI:** Yeah. I
12 neglected to mention another issue that is related
13 to the dermal exposures. And I couldn't find in
14 the document the justification for this. And the
15 model assumes that only 10 percent of the total
16 hand surface area is exposed to the liquid. This
17 would be with -- assuming that, for example, a
18 cleaning rag was being used, so the rag with the
19 liquid would be in contact with the skin directly.
20 And I didn't see -- I looked through the whole
21 document and didn't find a 10 percent -- this

1 explanation of the 10 percent. So this needs to
2 be clarified by EPA. That was all.

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

4 Dr. Barone, you want to comment?

5 **DR. STANLEY BARONE:** Yeah. I just
6 wanted to provide a follow up and clarification on
7 consumer paints. There's actually a SNUR, which
8 is a significant new use rule, that prohibits TCE
9 being included in paint and coatings for consumer
10 products. So that link will be sent along to the
11 DFO for consideration by the panel.

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

13 Dr. Bennett, I still see your hand up.

14 **DR. STEVEN BENNETT:** Dr. Bennett.
15 Yeah. I was still holding off for the pepper
16 spray. But just clarification to Dr. Barone, is
17 that the 2016 SNUR, or is that an earlier SNUR
18 with respect to TCE?

19 **DR. STANLEY BARONE:** I believe it is
20 the 2016 SNUR, Dr. Bennett.

21 **DR. STEVEN BENNETT:** Okay. Thank
22 you.

1 DR. STANLEY BARONE: Yeah.

2 DR. KENNETH PORTIER: Steve, let's
3 go ahead and do the pepper spray now.

4 DR. STEVEN BENNETT: Okay. Sorry.
5 I want to talk a little bit about the pepper
6 spray. I realize that we'll talk again about this
7 in the later portion when we get you looking at
8 the risk piece. But I wanted to make sure that we
9 have a good understanding around the conditions of
10 use itself. So when we get to the risk piece, we
11 can address that more adequately because this is -
12 - the use of pepper spray in the consumer space
13 was the only identified risk that did not present
14 unreasonable risk. So I wanted to make sure that
15 we have a good understanding of that.

16 That was one that I looked at in
17 particular tried to identify the products. And
18 there's certainly pepper spray products out there.
19 But it's unclear -- I could not verify, the
20 concentrations that are cited in the Risk
21 Evaluation. And there only appears to be one of
22 the products that are cited for that particular

1 concentration. Granted, it was a 91.5 percent
2 concentration, so it was effectively pure TCE.

3 So I want to make that -- and then
4 with the risk assessment, the Agency notes that
5 they did some research on to it, and the most
6 popular product, the website indicated these are
7 the particular use scenario. And then they used
8 another source for the spray duration. I just
9 want to make sure you get an understanding of
10 whether there's other research or other
11 information that are reforming that particular
12 scenario.

13 This is more directed towards EPA
14 staff than anything. But I certainly want to make
15 sure that the Agency has exhausted all available
16 opportunities, make sure that they have a good
17 understanding of that particular product because
18 of those circumstances.

19 **DR. KENNETH PORTIER:** Dr. Barone,
20 did you want to address this now or --?

1 **DR. STANLEY BARONE:** I think we'll
2 have to follow up. I don't have direct feedback
3 right at the moment.

4 **DR. KENNETH PORTIER:** Okay. Thank
5 you, Dr. Bennett. That's an excellent point. Any
6 additional comments on Questions 4.7, 4.8? Very
7 good. We're a good 45 minutes ahead of schedule
8 at this point. I think I'll go ahead and take a
9 10-minute break, just to get up and get the blood
10 flowing before we finish with the last two
11 questions.

12 It's my intent that we will complete
13 all the subparts of Question 4 today and
14 potentially break early and start bright and early
15 tomorrow morning with Question 5. So let's take a
16 10-minute break. We'll reconvene at 2:35. Thank
17 you.

18 (BREAK)

19
20 **DR. KENNETH PORTIER:** Okay. Let's
21 reconvene. I've asked the host to create a slide
22 for display to the public of the link to the 2016

1 TCE significant new use rule that we were just
2 talking about. And we'll leave it on the screen
3 for a minute, giving the public the opportunity to
4 copy that link if they need to. Can we have that
5 slide? There we go.

6 While people are copying this slide,
7 do we have any additional comments on Questions
8 4.7 and 4.8? And I guess I can turn to EPA and
9 ask, do you have any -- EPA, do you have any
10 questions, clarifying questions or comments on the
11 panel response? Not hearing anything.

12 **MR. ALAN KAUFMAN:** All right. Dr.
13 Portier --

14 **DR. KENNETH PORTIER:** Dr. Kaufman, I
15 see your hand's up.

16 **MR. ALAN KAUFMAN:** I'm sorry. Who
17 were you calling on?

18 **DR. KENNETH PORTIER:** Well, I think
19 that was Dr. Barone saying, we don't have any
20 comments. And then Dr. Kaufman, I saw your hand's
21 up.

1 **MR. ALAN KAUFMAN:** Yes. We've been
2 going back and forth after -- and this question is
3 for Dr. Barone. You had mentioned that there is a
4 SNUR, and paint is not listed among the existing
5 uses. So presumably, the inclusion of TCE in
6 paint, at least for consumer use, would be
7 considered subject to an application to EPA under
8 the SNUR.

9 But my question is, if that's the
10 case, is there a reason that paint is included in
11 the occupational exposures? Because presumably,
12 that would be an issue as well.

13 **DR. STANLEY BARONE:** Well, so the
14 issue there is the SNUR applied to consumer
15 products only in 2016. And that was based upon
16 our previous risk evaluation for consumer
17 products, in those conditions of use. And we did
18 not get to do a broader application.

19 **MR. ALAN KAUFMAN:** Okay. That makes
20 sense. Thank you.

21 **DR. KENNETH PORTIER:** Okay. I think
22 we're ready -- oh, Dr. Morandi, I see your hand's

1 up, and Dr. Davies. Dr. Morandi? You're still
2 muted. Dr. Davies, why don't you go ahead?

3 **DR. MARIA MORANDI:** I'm unmuted now.
4 Sorry.

5 **DR. KENNETH PORTIER:** Oh, okay.
6 Okay, Dr. Morandi.

7 **DR. MARIA MORANDI:** I'm delayed in
8 pushing -- on clicking. I was saying that thought
9 we were addressing 4.7 and 4.8 separately,
10 although some of the responses for 4.7 were
11 actually more relevant than 4.8, particularly the
12 use of the ATSDR profile list of sources. But I
13 also wanted to add that I don't know any
14 additional database that could provide data on
15 patterns of use of consumer products.

16 So clearly, this is an area where
17 EPA needs to do more research. There could be
18 some additional information in the population
19 studies on personal indoor and outdoor
20 concentrations that are cited in an appendix the
21 document. Many of those studies included
22 questions in terms of activity patterns. And some

1 of them also have questions in terms of product
2 use. Not specific to for, how long do you use
3 this product or exactly the brand of the product,
4 but there could be a general question like, did
5 you use any adhesives during the time that you
6 were monitored? So there could be some sort of --
7 some additional information is not perhaps --
8 actually, it's not qualitative -- I'm sorry,
9 quantitative -- at least qualitative with a sense.
10 Some use patterns have changed over time since
11 Westat.

12 In addition, I wanted to mention
13 that there is a wealth of information on the
14 internet. And this is for all the do-it-yourself
15 crafts, et cetera, videos that typically show what
16 products are being used. Now, mind you, these are
17 not necessarily representative, but it can give
18 you some idea if you are missing any type of
19 products that could contain TCE or whether the
20 patterns of use of some of these products may have
21 changed with respect to the databases --
22 information from databases I've already explored.

1 And I wanted to also emphasize my
2 concern in this sense with the fact that perhaps
3 exposures related to hobbies and use of materials
4 for hobbies, and also, for do-it-yourself and for
5 small-scale -- some businesses, those could be
6 underestimated because the uses could be more
7 intensive and more frequent than what EPA appears
8 to assume. So I just wanted that to be on the
9 record too. That's all.

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

11 Dr. Davies?

12 **DR. HOLLY DAVIES:** Hi. I'm still
13 questioning the paint. So it sounds like --
14 because paint is included in industrial exposure.
15 So it sounds like what EPA is saying is that we
16 have TCE in industrial paint but not in consumer
17 paint. And I guess I'm trying to figure out what
18 paint there would be, if it's like a technical
19 paint that's not available for consumer purchase,
20 or how that would be that there would be
21 occupational exposure but not in consumer paints.

1 I didn't know if the paint data was old and if
2 it's still actually in industrial paints.

3 **DR. KENNETH PORTIER:** Dr. Barone?

4 **DR. HOLLY DAVIES:** And that was it.

5 **DR. STANLEY BARONE:** Yes. This is
6 Stan Barone. So I'm doing a little bit of back-
7 and-forth internally about this to respond. So
8 part of the issue is there were no ongoing uses,
9 so we were able to SNUR the consumer products in
10 2016. There were ongoing uses in the occupational
11 commercial arena.

12 And again, there's a distinction
13 between the consumer products that we identified.
14 Then versus now, the ones we're looking at now in
15 the risk evaluation were ongoing uses in 2015. So
16 that's the distinction, to be more clear.

17 There may -- as Dr. Bennett pointed
18 out, there may have been transitions since 2015.
19 We'll be -- we have been looking at that. We're
20 trying to get more information. We're actually
21 hoping that by doing this risk evaluation on these
22 products and consumer uses that will alert folks

1 about the use of TCE in these products. I hope
2 that helps.

3 Oh, I did have one other point that
4 I wanted to make in something that's been brought
5 up earlier. And when we look at indoor air
6 studies, one of the concerns that we have about
7 consumer products is, is what you're measuring in
8 the indoor air the results of the products and the
9 product use, or is it the result of or part of
10 vapor intrusion through the indoor air space? So
11 that's another uncertainty and consideration that
12 we are wrestling with.

13 **DR. KENNETH PORTIER:** Dr. Davies, I
14 see your hand's still up. And it goes down. Dr.
15 Doucette?

16 **DR. WILLIAM DOUCETTE:** This is just
17 in response to Dr. Barone's recent comment about
18 distinguishing between indoor consumer product
19 contamination or vapor intrusion. And I'll try to
20 find a reference, but there was a fairly
21 significant study at and around Hill Airforce

1 Base, which is not far from our campus that I was
2 involved with. And then they continued.

3 And I think the conclusion was that
4 in almost all cases, it was the consumer products
5 that were driving the indoor air concentrations.
6 And I'll see if I can't find that reference for
7 you. That's all I have.

8 **DR. STANLEY BARONE:** That would be
9 most helpful if the committee --

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

11 **DR. STANLEY BARONE:** -- has any
12 information, additional data on that.

13 **DR. KENNETH PORTIER:** Dr. Morandi?
14 Dr. Morandi, your hand's up, and you're muted.

15 **DR. MARIA MORANDI:** I keep on doing
16 the same thing. I wanted to follow up on the
17 issue of the indoor residential concentrations.
18 One of the issues is that the measurements that
19 are done in terms of duration -- they tend to be
20 longer than computational measurements. There are
21 a number of reasons for this.

1 They typically are on the low side
2 of our -- some of the team studies up to 24 hours.
3 There are some studies that went as long as one
4 week. So in some cases, if indeed there is a
5 strong source of a compound, it may have a
6 significant impact on the concentration of product
7 and the concentration you measure. But typically,
8 this is difficult to actually tell because you
9 have multiple contributions to the indoor air
10 concentrations. But whatever those concentrations
11 are, from whatever sources, you could assume on
12 aggregate that they represent sort of a
13 background.

14 Some of it may be a small
15 contribution from a consumer product, given the
16 length of the measurement. But when you compare
17 that to the concentration measure or estimated for
18 a short-term use of the product, then that could
19 be measured quite different. I mean, just looking
20 at your estimate of exposures for a specific
21 product use versus the background concentrations
22 for the -- actually, I should say, the indoor

1 residential concentrations that have been
2 reported.

3 For the specific use of the product,
4 they are higher. So what I was -- in my earlier
5 proposal, in terms of perhaps trying to use this
6 data as context, obviously, you have to take into
7 consideration that some of the fraction of indoor
8 concentration may be related to a product use, and
9 you don't know unless you look into the
10 information regarding activity patterns for that
11 study if that information on a product was
12 reported or not. But at least it could give you
13 some general context for saying, well, even if we
14 consider the indoor residential exposures that
15 have been measured, it would change or not
16 significantly change the exposure estimates that
17 we have derived for product use. So that's all I
18 wanted to say.

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

20 Any additional comment? Dr. Anderson?

21 **DR. HENRY ANDERSON:** Yes. Just a
22 quick question as far as the commercial versus

1 consumer paint. I haven't been able to go back
2 into the document yet. But it would seem to me,
3 do we know the different types of paints? I would
4 wonder whether automobile paint and aircraft
5 paint, which there's not too many consumers are
6 going to use. Are those the types of paints that
7 would contain the TCE?

8 Most people think in terms of house
9 paint, and, of course, pretty much the same paints
10 are available to consumer as well as commercial.
11 So when they say commercial, what specific types
12 of use paints are we looking at?

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

14 Dr. Doucette, your hand's up?

15 **DR. WILLIAM DOUCETTE:** Sorry. I'll
16 take it down.

17 **DR. KENNETH PORTIER:** Okay. I think
18 we've kind of done everything. Dr. Morandi, I
19 think we've finished with 4.8; yes?

20 **DR. MARIA MORANDI:** Yes.

1 **DR. KENNETH PORTIER:** Okay. Why
2 don't we bring up Questions 4.9 and 4.10? Dr.
3 Bethel?

4
5 ***CHARGE QUESTION 4 (4.9 AND 4.10)***
6

7 **DR. HEIDI BETHEL:** Hello. Question
8 4.9: Dermal exposure was evaluated using the
9 permeability sub-model within CEM. Please comment
10 on the suitability and use of this modeling
11 approach for this evaluation. Please provide any
12 suggestions or recommendations for alternative
13 approaches, dermal methods, models, or other
14 information which may guide EPA in developing and
15 refining the dermal exposure estimates. See
16 Section 2.3.2.4.1.

17 Question 4.10: Please comment on
18 EPA's approach to characterizing the strengths,
19 limitations, and overall confidence for each
20 consumer exposure scenario presented in Section
21 2.3.2. Please comment on the appropriateness of
22 these confidence ratings for each scenario.

1 Please also comment on EPA's approach for
2 characterizing the uncertainties summarized in
3 Section 2.3.2.7.

4 **DR. KENNETH PORTIER:** Thank you.
5 Dr. Morandi, I guess we'll take Question 4.9
6 first.

7 **DR. MARIA MORANDI:** Okay. I
8 received a couple of comments on this. And both
9 were positive in terms of the suitability of this
10 particular sub-model for estimating dermal
11 exposure. I think I expressed before the concern
12 that the assumption for the justification for
13 assuming that only 10 percent of the hand area
14 would be exposed is not presented. At least, I
15 couldn't find it in the document.

16 And I think some of the comments
17 that Dr. Kissel made with respect to the dermal
18 exposure estimates for occupational would apply
19 here. But I would like him to address that issue
20 in this particular case. So those I have just
21 described are the comments I have for this
22 question.

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

2 I'll go down the list. Dr. Bennett, anything to
3 add?

4 **DR. STEVEN BENNETT:** I do not have
5 anything additional to add to this one.

6 **DR. KENNETH PORTIER:** Thank you.
7 Dr. Davies?

8 **DR. HOLLY DAVIES:** Nothing
9 additional to add.

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

11 **MR. ALAN KAUFMAN:** No, nothing
12 additional. I think some of the things we've
13 discussed earlier apply here. But we don't need
14 to reiterate them, so thank you.

15 **DR. KENNETH PORTIER:** Dr. Kissel?

16 **DR. JOHN KISSEL:** Okay. So I have
17 two issues. The first one is less important, and
18 that has to do with the derivation of the
19 permeability coefficient that's used in the model.
20 It's from a poet paper, which is a pharmacokinetic
21 paper. And that -- I had these same comments when

1 we were talking about dichloromethane, I believe,
2 because we were using a PBPK model there also.

3 PBPK models -- well, PBPK modelers
4 or almost never are almost never skin people. And
5 they're always happy to just treat skin as a CSTR,
6 as a continuously stirred tank reactor, which skin
7 people think of skin as a membrane rather than as
8 a well-stirred tank. And one of the consequences
9 of that, the numerical value of the permeability
10 coefficient that you get out depends upon how you
11 model the skin. And so both kinds of people, skin
12 people and PBPK people, are both using the term
13 KP, but what they are actually estimating is
14 slightly different.

15 And in addition to the kind of a
16 mathematical structural issue, PBPK models are
17 multi-variable models that involve fitting of a
18 lot of things. And you can have compensating
19 errors in there. So you can get one thing too
20 high and one thing too low, and the model looks
21 like a really nice fit. So I generally am not
22 keen on estimating permeability coefficients from

1 PBPK models, unless the people that are doing it
2 have a pretty good idea of what exactly they're
3 doing and what the limitations are. And I will
4 give you citations for a couple of papers that I
5 cited when we did dichloromethane on that
6 particular topic.

7 Now, having said that, there is some
8 risk that the permeability coefficient is too low.
9 It is, however, higher than the number you would
10 get using the modified Potchky relationship, which
11 EPA uses in the superfund world. On the other
12 hand, there are some experimental data out there
13 which suggest higher numbers. So the permeability
14 coefficient for trichloroethylene is not all that
15 well pinned down. And this number might be okay.
16 I would view it as not conservative but not
17 necessarily inappropriate.

18 That's the relatively simple
19 problem. The larger problem is that the
20 formulation of PDER2B, which is shown in line 1876
21 on page 140 of the DRE, is fundamentally in error.
22 So a permeability coefficient has to be multiplied

1 by a concentration. But mostly, we're dealing
2 here with not an aqueous solution of TCE but
3 rather 100 percent TCE.

4 So rather than concentration, what
5 is being used is the density times the dilution.
6 And the dilution is one, so it's the density. You
7 can't -- the problem is there's a mismatch there.
8 The permeability coefficient was determined for an
9 aqueous solution. And aqueous solutions can't
10 have concentrations greater than the solubility of
11 the compound.

12 So the equation on page 140 is
13 multiplying the permeability coefficient, which is
14 roughly .02 centimeters per hour, times 1,460
15 milligrams per cubic centimeter, when the maximum
16 number that you can legitimately multiply that
17 number by is 1,280 micrograms per cubic
18 centimeter. So the consequence of that is -- and
19 this illustrates why I've said multiple times that
20 it would be good if the implied fluxes were
21 reported along with these calculations -- is that
22 the implied flux here is 30 milligrams per square

1 centimeter per hour, which is not really plausible
2 for intact human skin.

3 It might be possible for damaged
4 rodent skin. But even there, it's higher than the
5 estimates that I can glean from the literature.
6 So I think basically, the model is structurally
7 incorrect. The implied maximum steady-state flux
8 from the calculated .02 centimeter per hour
9 permeability coefficient is about 20 micrograms
10 per square centimeter per hour for intact human
11 skin. And the implication in the equation on page
12 140 is a number which is 1,500 times larger, which
13 is very likely to be too big.

14 Now, the fact that skin may be damaged
15 here would cut into that 1,500-fold factor, but
16 still generally, the enhancement factors
17 associated with solvent degradation of skin aren't
18 anything like 1,500-fold. So you very seldom find
19 numbers bigger than 50. So I think there's
20 potential here for substantial overestimation, at
21 least with respect to the flux.

1 Now, that's different than the question
2 of how much skin is exposed, and how often things
3 happen, or all those other factors. But just with
4 respect to flux, I think the formulation here
5 leads to overestimation of uptake for consumers.
6 Oh, and I should also say that I did attempt to
7 find -- over the break, I did a little searching
8 trying to find some skin damage permeability data
9 specifically for TCE. And I couldn't find
10 anything for TCE.

11 **DR. KENNETH PORTIER:** Thank you,
12 John. Dr. Grant?

13 **DR. STEPHEN GRANT:** I have nothing
14 to add.

15 **DR. KENNETH PORTIER:** No? Okay.
16 Any additional comment on Question 4-9? I don't
17 see any. Dr. Morandi, why don't we go on to 4.10?
18 Oh, wait -- yeah. Dr. Morandi?

19 **DR. MARIA MORANDI:** I just clicked -
20 -

21 **DR. KENNETH PORTIER:** You're muted
22 again.

1 **DR. MARIA MORANDI:** I'm sorry? No,
2 I'm not muted. Can you hear me?

3 **DR. KENNETH PORTIER:** Yeah. Now
4 you're not muted. Yes, I can hear you.

5 **DR. MARIA MORANDI:** Okay. No, I --
6 okay. Maybe as you were saying, you are muted
7 again, I had just clicked. I wanted to follow up
8 with Dr. Kissel in terms of the KP value. And I
9 agree with him, in terms of what he said.

10 But EPA also provides a couple of
11 values based on the literature that had some
12 problems. But these values appear to be in the
13 range of those two other values that are based on
14 experimental data. So I wonder if he had any
15 comments about that.

16 **DR. JOHN KISSEL:** So the numbers in
17 the literature are fairly variable. And the KP
18 that EPA is using is not really the problem. I
19 would not view it as conservative because I have
20 reservations about the origin from a PBPK model.
21 But it is -- and I mentioned -- it's a bigger
22 number than you would get using the EPA's method

1 that's delineated in the superfund in RAGS Part E,
2 which has got a methodology.

3 So the permeability coefficient
4 isn't really the problem. It's in the plausible
5 range. It might be a little low. I view it as
6 not conservative but not completely inappropriate.
7 The problem is using the density of the compound
8 as the driving force instead of the saturation
9 concentration in water.

10 **DR. MARIA MORANDI:** Okay.

11 **DR. KENNETH PORTIER:** Okay. Dr. --
12 well, before we go on to 4.10, let's turn to EPA
13 and see if they have any clarifying questions.
14 Dr. Barone?

15 **DR. STANLEY BARONE:** Yes. I think
16 on the KP issue I'd like Dr. Sarraino to ask a
17 couple of clarifying questions.

18 **MS. STEPHANIE SARRAINO:** Hi. Yes.
19 Dr. Kissel, thank you for your comment. We were
20 aware that this might present an issue, so we're
21 grateful to hear more from you on this. Would

1 some of this issue -- this larger issue be
2 addressed if we use KP for neat TCE, or no?

3 **DR. JOHN KISSEL:** I'm sorry. I
4 didn't understand the last part of that question.

5 **MS. STEPHANIE SARRAINO:** I'm sorry.
6 If we were using a KP reflective of neat TCE
7 instead of what we had, of course, from
8 literature, which was the aqueous.

9 **DR. JOHN KISSEL:** Oh, yeah, that's
10 what you should do. So a KP --

11 **MS. STEPHANIE SARRAINO:** Okay.

12 **DR. JOHN KISSEL:** -- is vehicle-
13 specific. And if the vehicle is neat compound,
14 and you need a KP for neat compound. And there's
15 no predictive method for that, so you would need
16 experimental data specifically with neat compound.
17 And the only neat compound data that I know of is
18 not human skin, it's rat skin.

19 So one alternative would be to take
20 the rat data and then discount it a bit for --
21 human skin is generally less permeable -- but in a
22 pinch, that's what you could do. I don't know of

1 any neat compound to human skin data. That
2 doesn't mean it doesn't exist, but I didn't find
3 it in my quick search.

4 **MS. STEPHANIE SARRAINO:** Yeah. We
5 didn't either. Thank you though for that
6 clarification.

7 **DR. KENNETH PORTIER:** Dr. Johnson?
8 Dr. Johnson, I see your hand up, but you're muted.
9 I see now Dr. Johnson is not muted, but I don't
10 hear him.

11 **DR. MARK JOHNSON:** Can you hear me
12 now?

13 **DR. KENNETH PORTIER:** Now I can hear
14 you.

15 **DR. MARK JOHNSON:** Okay. Sorry
16 about that. I don't know if this is relevant to
17 the current discussion. But I think the last time
18 we had a volatile compound we had some data where
19 -- some published data -- where we did some body
20 only exposures to rats, to TCE. And we looked at
21 internal plasma concentrations.

1 So I just sent those -- it's not
2 much, but there is some dermal penetration,
3 obviously, from the vapor phase through the skin
4 and in a rodent model. So I shared that with John
5 and with you, Ken. If it's relevant, please feel
6 free to use it.

7 **DR. KENNETH PORTIER:** Thank you. I
8 won't know what to do with it, but Dr. Kissel
9 will. Dr. Morandi?

10 **DR. MARIA MORANDI:** Yeah. I wanted
11 to ask Dr. Johnson if you could include me also in
12 the list of people who would receive these data,
13 even if I don't use it myself. But I'm the lead
14 on the question, so I would like to also see.
15 Thank you.

16 **DR. KENNETH PORTIER:** And Mark, copy
17 that to Todd so that he can put it on the docket.

18 **DR. MARK JOHNSON:** Roger that.

19 **DR. KENNETH PORTIER:** Assuming it's
20 not private data.

21 **DR. MARK JOHNSON:** No. In fact, if
22 you would like to see the report, I may be able to

1 get that, too. I just don't have that at my
2 fingertips.

3 **DR. KENNETH PORTIER:** Yeah. If you
4 can find the report, please pass that along as
5 well. We'll put it in the docket. Okay. Dr.
6 Morandi, 4.10.

7 **DR. MARIA MORANDI:** Again, I
8 received a few comments on this. In terms of the
9 framework for presenting uncertainties and
10 confidence, I'd like the framework of using
11 variability and uncertainty. And I think one of
12 the reasons why this is used more in this
13 particular document is that it's kind of a
14 modelist type language. I like that because it
15 makes it clear.

16 One of the -- I like also Tables 271
17 and 272 because they are moving forward in sense
18 of showing clearly all the levels of confidence
19 across the board and the final confidence level.
20 But I didn't find the footnotes to those tables
21 particularly informative. I think that those --
22 and I have some suggestions for that, so they

1 could provide more information to understand
2 better how the confidence levels in each one of
3 those cells in those tables were derived.

4 In terms of other general comments,
5 I think some of the same comments as were done for
6 the issue of addressing uncertainties and
7 presenting them clearly also apply to the
8 estimates for exposures for consumers. And I
9 think that, as EPA thinks about how to make that
10 clear, it would obviously transfer to any of the
11 confidence estimates for the consumer products. I
12 have also a concern that I'll repeat in terms of
13 confidence -- is that it's a little bit -- the
14 summary section in terms of uncertainties,
15 assumptions, and overall confidence, I think it's
16 okay. But as you go through each particular
17 exposure estimates for the different product uses,
18 it becomes a little bit overwhelming.

19 And I think that EPA needs to think
20 about this a little bit. Perhaps using a
21 graphical way of presenting this information
22 because it becomes somewhat difficult to go

1 through them and then go back and forth when you
2 see some areas that may not make sense. And it's
3 hard to get the whole picture of what the
4 uncertainties and assumptions are. So you have a
5 sense of repetition over and over again for some
6 differences or some uses. So EPA needs to think
7 about how to make this a more believable type of
8 document.

9 Other comments that I had I'm going
10 to let -- I think I received also comments from
11 Dr. Grant. And to be frank, I didn't quite
12 understand one of his comments. So I'm going to
13 ask him if he can present his comments for me too.

14 **DR. KENNETH PORTIER:** Thank you, Dr.
15 Morandi. Let's go down the list. Dr. Bennett,
16 anything else to add?

17 **DR. STEVEN BENNETT:** I don't think
18 so at this point.

19 **DR. KENNETH PORTIER:** Thank you.
20 Dr. Davies?

21 **DR. HOLLY DAVIES:** I don't have
22 anything to add at this point.

1 DR. KENNETH PORTIER: Dr. Kaufman?

2 MR. ALAN KAUFMAN: Nothing to add.

3 Thanks.

4 DR. KENNETH PORTIER: Dr. Kissel?

5 DR. JOHN KISSEL: Nothing else.

6 DR. KENNETH PORTIER: Dr. Grant?

7 DR. STEPHEN GRANT: Let's see. I'm

8 checking things out here. There was a statement

9 in there that basically said we might be an

10 overestimation. And I thought that was a

11 directive sentence. So sometimes, when there is

12 uncertainty, maybe a statement of simple

13 uncertainty rather than directional uncertainty

14 would be more appropriate.

15 My other -- one question I had about

16 the consumer use as a gun scrubber, did we assume

17 a single gun? I think that guns come in flocks.

18 And one problem I had with this section is the use

19 of models. And the two models were labeled E1 and

20 E3. And unfortunately, that's not very good for

21 searching. You don't get to E1 very easily when

1 it's so simple a label. That's all I had.

2 Thanks.

3 **DR. KENNETH PORTIER:** Thank you, Dr.
4 Grant. Anyone else want to add to Question 4.10?
5 Dr. Johnson, I still see your hand up. I'm not
6 seeing any hands up on the question of
7 characterizing strengths, limitation, and overall
8 contents in consumer exposure.

9 Okay. At this point, I'll turn to
10 EPA. Any clarifying questions or comments on the
11 Panel's response?

12 **DR. STANLEY BARONE:** I don't think
13 so, Dr. Portier. This is Stan Barone.

14 **DR. KENNETH PORTIER:** Yeah. Okay.
15 well, I think we're at a good breaking point for
16 the day. We're a little ahead of schedule.
17 Tomorrow is going to be a busy day where we
18 actually address the human hazard aspects of the
19 Draft Risk Evaluation.

20 And I know that conversation is
21 going to be very interesting and involved. And I
22 think I'd rather have a fresh committee address

1 that than one that's already spent, what is it,
2 six-and-a-half hours, five-and-a-half hours. So I
3 think at this point, I'm going to turn the meeting
4 over to the DFO, Todd Peterson, who will have any
5 final comments for the day. Todd?

6 **DR. TODD PETERSON:** Yeah. This is
7 Todd Peterson, the DFO. So I want to thank you,
8 thank the SACC peer reviewers and the public for
9 listening online. This concludes the peer review
10 activities for the agenda for today. And we will
11 reconvene tomorrow morning for day 3 at 10:00 a.m.
12 Eastern Time. This day session is now adjourned.
13 Thank you. Have a great evening, folks.

14 **DR. KENNETH PORTIER:** Thank you,
15 everyone.

16 **(MEETING ADJOURNED FOR DAY)**
17

OPENING OF MEETING - DAY 3

OPERATOR: Good morning. Welcome to the third day of this meeting series on the U.S. EPA peer review of the draft risk evaluation for trichloroethylene or TCE. Battel is an EPA contractor providing meeting support for this series. This event is being recorded. The host may use chat to share announcements with all attendees, but attendees will not be able to respond to chat.

Panelists, please send direct messages to the host or panelist. I will now introduce Dr. Todd Peterson, the designated federal official.

DR. TODD PETERSON: Good morning. And, let me get my notes up here. Okay. So good morning. I am Dr. Todd Peterson. I am the designated federal officer. It is my pleasure to open the third day of the four-day meeting for the Science Advisory Committee on Chemicals -- for short we say TSCA SACC -- peer review of EPA's draft risk evaluation for trichloroethylene.

1 So Tuesday and yesterday's WebEx
2 hosted meetings went very well. However, if you
3 encounter any problems with audio or video
4 transmissions, we have the slide up with the link
5 at the bottom. So if you want to take a note of
6 that link and there is any problem, you can go
7 there for additional information.

8 As noted yesterday, the chair at his
9 discretion may call for an additional break during
10 the meeting today. Adding a 10-minute break here
11 or there may be helpful to the committee, and we
12 have extra time on the agenda to accommodate a
13 couple additional brief breaks. One note from the
14 DFO to the lead peer reviewers, the entire
15 committee was supplied a spreadsheet that I
16 created for the peer reviewers. That spreadsheet
17 not only provides a summary table for lead and
18 associate discussants, but one of the tabs on the
19 spreadsheet is a grid showing which of the
20 associates has indicated an interest in a specific
21 question.

22 So I refer the lead discussants to

1 take a look at that grid to see which one of the
2 associates is specifically showing an interest in
3 the charge question at hand. That might clarify
4 things a little bit. Also, you can refer to the
5 full agenda for specific assignments as well.

6 I also sent emails to a couple of
7 our participants. And just to review for everyone
8 on the line, first of all, use of a land line is
9 o- -- a land line is optimal. I know a couple
10 people don't have land lines and that's okay. But
11 if you're using a microphone, speak over the top
12 of the microphone and not directly into it. That
13 might help with clarity.

14 Also, if using a speaker phone to
15 listen in, picking up the handset during the times
16 when you're speaking to the committee is also very
17 helpful for clarity. Overall, the sessions are
18 going well and so I thank everyone for their
19 contributions. And at this point I turn the
20 meeting over to our chair, Dr. Portier.

21 **DR. KENNETH PORTIER:** Good morning
22 and welcome to everyone who's joining us for day

1 three of this TSCA SACC committee meeting. We'll
2 begin by going down the roster to assure the
3 public that all of the committee is attending
4 today's meeting as planned. Dr. Anderson.

5 Present, please. I didn't hear you Dr. Anderson.

6 Dr. Bennett.

7 **DR. STEVEN BENNETT:** I am present.

8 **DR. KENNETH PORTIER:** Dr. Barton.

9 Dr. Barton, I still see you muted.

10 **DR. CHARLES BARTON:** Okay. I'm
11 present.

12 **DR. KENNETH PORTIER:** Thank you.
13 Dr. Blystone.

14 **DR. SHERI BLYSTONE:** Good morning.
15 I'm here.

16 **DR. KENNETH PORTIER:** Dr. Bruckner.

17 **DR. JAMES BRUCKNER:** I'm here today.

18 **DR. KENNETH PORTIER:** Thank you.
19 Dr. Cory-Slechta.

20 **DR. DEBORAH CORY-SLECHTA:** I'm here.

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

22 **DR. HOLLY DAVIES:** I'm here.

1 DR. KENNETH PORTIER: Dr. Doucette.

2 DR. WILLIAM DOUCETTE: Virtually

3 present.

4 DR. KENNETH PORTIER: Dr. Jimenez-

5 Gonzalez.

6 DR. CONCEPCION JIMENEZ-GONZALEZ:

7 Present.

8 DR. KENNETH PORTIER: Dr. Gilbert.

9 DR. KATHLEEN GILBERT: I'm here.

10 DR. KENNETH PORTIER: Dr. Johnson.

11 DR. MARK JOHNSON: Good morning.

12 DR. KENNETH PORTIER: Dr. Kaufman.

13 MR. ALAN KAUFMAN: I am here.

14 DR. KENNETH PORTIER: Dr. Kissel.

15 DR. JOHN KISSEL: Here.

16 DR. KENNETH PORTIER: Dr. Rowlands.

17 DR. CRAIG ROWLANDS: I am present.

18 DR. KENNETH PORTIER: Dr. Schlenk.

19 DR. DANIEL SCHLENK: Here.

20 DR. KENNETH PORTIER: Back to Dr.

21 Anderson. We had him a minute ago. He may have

22 stepped away. He has a class meeting first thing

1 in the morning. Dr. Apte.

2 **DR. UDAYAN APTE:** Here.

3 **DR. KENNETH PORTIER:** Dr. Cobb.

4 George, we don't see your phone, so you need to
5 still call in. He's probably -- he's always had
6 some problems with -- technical issues. Dr.
7 Grant.

8 **DR. STEPHEN GRANT:** Present.

9 **DR. KENNETH PORTIER:** Dr. Hossain.

10 **DR. MUHAMMAD HOSSAIN:** I'm here.

11 **DR. KENNETH PORTIER:** Dr. Jenkins.

12 **MS. ALLISON JENKINS:** Here.

13 **DR. KENNETH PORTIER:** Dr. Lash.

14 **DR. LAWRENCE LASH:** I'm here.

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

16 Dr. Morandi.

17 **DR. MARIA MORANDI:** Here.

18 **DR. KENNETH PORTIER:** Dr. Morris.

19 **DR. JOHN MORRIS:** Here.

20 **DR. KENNETH PORTIER:** Dr. Pessah,

21 are you here this morning? I think Dr. Pessah was
22 uncertain whether he'd make it on Thursday. I

1 don't see him in the log in so he may be absent.

2 Dr. Rosol.

3 **DR. THOMAS ROSOL:** Present.

4 **DR. PORTIER:** Dr. Vorhees. Chip
5 Vorhees?

6 **DR. CHARLES VORHEES:** Here.

7 **DR. KENNETH PORTIER:** There he is.
8 Okay. So Dr. Cobb, he still hasn't signed in on
9 his phone yet. So we're missing Dr. Cobb and Dr.
10 Anderson, but we have a quorum and let's move
11 forward.

12 **DR. HENRY ANDERSON:** I'm here.

13 **DR. KENNETH PORTIER:** Oh, there's
14 Dr. Anderson. Good morning.

15 **DR. HENRY ANDERSON:** Sorry. Had
16 another call, something I had to deal with.

17
18 **FOLLOW-UP ON PREVIOUS DAY DISCUSSION**
19

20 **DR. KENNETH PORTIER:** Okey-doke.
21 Thank you. Okay. At this point, I'm going to
22 open it up if anyone had any follow up comments or

1 clarifying questions from yesterday's discussion
2 on chapter four -- I mean question four related to
3 occupational exposures. So is there any follow up
4 comments? I don't see any hands being raised. I
5 think what we're going to do then is about --
6 actually, I should ask the EPA staff -- Dr. Bethel
7 would you introduce who from EPA is present?

8 **DR. KATHLEEN GILBERT:** Excuse me. I
9 actually had my hand up.

10 **DR. KENNETH PORTIER:** Let's see,
11 who's got -- ah, there's Kath- -- Dr. Gilbert,
12 yes.

13 **DR. KATHLEEN GILBERT:** Thank you. I
14 don't actually have anything to say about
15 yesterday, but I do have a comment that I wanted
16 to make about the meeting. So I am one of the
17 people who thought this meeting should be
18 postponed for a variety of reasons. We were
19 concerned that public participation in the meeting
20 would suffer, that the stiltedness of the web-
21 based format would hurt the quality of the review.
22 We were also concerned about the unfair burden

1 this meeting placed on our physicians and public
2 health colleagues, and that the probability that
3 for all of us -- our extra personal and
4 professional responsibilities at this time made it
5 that much more difficult to give this review the
6 attention it deserves.

7 However, despite voicing our
8 concerns, we didn't hear anything from the EPA
9 until after the meeting had started when a brief
10 statement from Administrator Dunn was read. With
11 all due respect, that statement was not in any way
12 an explanation. It was just admin speak and was
13 insufficient to deal with our legitimate concerns,
14 especially for our colleagues whose virus
15 associated duties have prevented or limited their
16 participation in this meeting. I personally think
17 that we deserve a better explanation from the EPA
18 as to why this meeting had to be held this week.
19 That's all I wanted to say.

20 **DR. KENNETH PORTIER:** Thank you Dr.
21 Gilbert. Would you provide a copy of that to Dr.
22 -- to Todd so that he can include it in the

1 record?

2 **DR. KATHLEEN GILBERT:** Yes. I'll do
3 that.

4 **DR. KENNETH PORTIER:** I just wanted
5 to point out that yesterday during the bulk of the
6 discussion we had about 99 attendees listening in,
7 and as of this morning we have 49 attendees. So
8 there -- we recognize the fact that this chemical
9 is raising a lot of interest in the public. But I
10 leave it to EPA to answer the issues that you
11 arise.

12 Okay. Moving forward. Again, Dr.
13 Bethel, would you introduce the -- or introduce
14 yourself and the other EPA staff who are
15 participating in this morning's discussion?

16 **DR. HEIDI BETHEL:** Good morning.
17 This is Heidi Bethel. Grateful for all of you
18 participating under these circumstances today. We
19 have most of the team online this morning: Dr.
20 Keith Jacobs, who is our team lead and also very
21 adeptly handles our human health assessment. He
22 does a great job -- Dr. Stan Barone and Nhan

1 Nguyen who are management leads. We have our
2 other assessors who you heard from primarily
3 yesterday and will most likely not be speaking up
4 a whole lot during the conversation on human
5 health. We have Franklyn Hall, our engineer;
6 Kara Koehn, our eco-assessor; Sheila Kragie, one
7 of our consumer exposure assessors; Wen Lee, who
8 is our fate assessor; Sue Makris, a human health
9 assessor; Stephanie Sarraïno, who is a consumer
10 exposure assessor.

11 **DR. KENNETH PORTIER:** Thank you. So
12 this morning -- actually most of today's
13 discussion if not all of today's discussion is
14 going to be on the human health hazard issues that
15 are discussed in the TCE draft risk evaluation.
16 And we're going to begin this morning's discussion
17 with question 5.1, which is probably going to take
18 quite a while for the panel to work through. Dr.
19 Bethel, would you read question 5.1 into the
20 docket?

21 **CHARGE QUESTION 5 (5.1)**

1 **DR. BETHEL:** Question 5 is regarding
2 the human health hazard. EPA determined that the
3 weight of the scientific evidence supported liver
4 toxicity, kidney toxicity, neuro toxicity, immune
5 toxicity, reproductive toxicity, developmental
6 toxicity, and cancer as consistent adverse human
7 health effects associated with TCE exposure.

8 EPA identified the best
9 representative studies for dose-response analysis.
10 Benchmark dose and physiologically based
11 pharmacokinetic modeling were used where
12 practicable to generate the Point of Departure for
13 characterizing chronic and acute exposure
14 scenarios.

15 Question 5.1, on non-cancer human
16 health endpoints, EPA performed a weight of
17 evidence assessment for the endpoint of
18 developmental cardiac defects based on available
19 epidemiological, in vivo animal, and mechanistic
20 data. EPA concluded that the available literature
21 overall supported positive evidence that TCE may
22 produce cardiac effects in humans. However,

1 cardiac defects after developmental exposure were
2 not observed consistently across the available in
3 vivo animal studies.

4 The Charles River dissection
5 methodology differed from Johnson et al. (2003),
6 resulting in reduced sensitivity to the full range
7 of cardiac defects compared to Johnson et al.
8 (2003) and other studies. Therefore, EPA
9 concluded that the Charles River study did not
10 adequately recapitulate the methodology of Johnson
11 et al. Please comment on EPA's Weight of Evidence
12 analysis approach and conclusions for this
13 endpoint, including EPA's analysis of the Charles
14 River and Dawson/Johnson studies.

15 **DR. KENNETH PORTIER:** Thank you.
16 And someone was typing in the background. It
17 might have been Dr. Barone who I see is not muted.
18 I've asked Dr. Bruckner to take the lead on
19 question 5.1. Dr. Bruckner.

20 **DR. JAMES BRUCKNER:** Okay. Can you
21 hear me now?

22 **DR. KENNETH PORTIER:** Yes. You're

1 very clear.

2 **DR. JAMES BRUCKNER:** Okay. Okay.

3 Good. Okay. I've received comments from a number
4 of the panel members on this. Too many -- to --
5 in the too recent future to compile them, so I
6 think I'll just begin with my own comments. And
7 then some people sent me comments. If you have
8 additional comments, those same people should send
9 them to me. And if there are new comments,
10 obviously I'll try in the next week or two to
11 compile those. So I think I'll just start.

12 If you take a look -- I was looking
13 at page 224 of the document. That's where they
14 have the scoring system for cardiac defects and
15 their, I guess, three lines of evidence. One is
16 epidemiology studies, and one is in vivo animal
17 toxicology studies. And one is mechanistic
18 studies. So I have a number of problems. So let
19 me start with mechanistic studies.

20 I guess my problem is that the
21 mechanistic studies are really limited in scope.
22 We have some enzyme induction studies, some gene

1 expression studies but nothing in the way of
2 metabolomics or proteomics. So the score -- this
3 was given a higher score. If you look on page
4 224, it is given a +2 score as opposed to a +1 or
5 a 0 score. My problem is, with -- in view of this
6 limited information and the fact that these were
7 high dose studies -- they were in vitro systems
8 and (inaudible) systems -- I'm not sure how the
9 EPA came up with a +2 score. I guess the problem
10 I have is that, with limited data and with not
11 even a likely mechanism -- a number of possible
12 mechanisms, I'm not sure why that was given such a
13 high score.

14 Okay. Under in vivo studies, of
15 course, the majority of the evidence from in vivo
16 comes from the single -- actually -- actually,
17 three studies that were published by Dawson and
18 Johnson, and there are of course a number of
19 problems with those studies. One problem I have
20 is that data were combined from experiments done
21 several years apart to come up with the table that
22 was in the 2003 publication by Johnson, which is

1 the primary basis for the risk assessment.

2 Of course, these study results were
3 not replicated in any other in vivo studies. I
4 was -- actually, one of my graduate students
5 worked with Jeff Fisher to do a follow up study
6 which fairly high doses were given to rats by
7 bulbous administration. And in this study, they
8 actually brought Paula Johnson in so they could
9 replicate the precise cardiac surgical techniques
10 to get as closely as possible to what was done
11 before. And in this study, there were no adverse
12 effects seen at high doses of either
13 trichloroethylene, trichloroacetic acid or
14 dichloroacetic acid.

15 And of course, there's the study
16 that's been published -- actually, it's now
17 published by DeSesso, which is here known as the
18 Charles River Laboratory studies. That study was
19 also negative. There, of course, is a discussion
20 in the appendix about some of the deficiencies or
21 the way in which some of those study results may
22 have not picked up some of the effects of some of

1 the valvular defects. But nevertheless, it was --
2 that was a GLP study.

3 Beyond that, there have been, I
4 think, perhaps six inhalation studies in which
5 cardiac defects were looked at. Particularly, the
6 one that's best studied by Carney in 2006, again,
7 saw no evidence of any abnormalities in cardiac
8 defects. So I would just say that the weight of
9 evidence -- I question a dose -- a score of 0 for
10 in vivo in light of this. I question the score of
11 +2 for very limited mechanistic studies which
12 really don't come up with a definitive or even a
13 likely mechanism. And I leave it to the
14 epidemiologists on the committee to tell me what
15 they think of the weight of the epidemiology
16 evidence.

17 So those are my primary problems.
18 There was another -- which -- a study by Watson,
19 or actually a review study in which they looked at
20 all the evidence, whether there was no likely
21 evidence, at least in environmental exposure
22 levels for there being cardiac defects. So I

1 guess a problem I have is just using high dose
2 studies really, and particularly in in vitro
3 situations with non-mammalian species. I tend to
4 discount those.

5 So I have real problems. A number
6 of people who -- a number of committee members who
7 communicated with me also have some problems. So
8 I think we can go ahead and go to the next panel
9 members and see what their opinions are.

10 **DR. KENNETH PORTIER:** So Dr.
11 Bruckner, I have listed 13 associates on this
12 question, and I'm not quite sure which ones have
13 substantial comments. Do you have a suggestion
14 who should go next or should I just go
15 alphabetical like they're listed on my chart?

16 **DR. JAMES BRUCKNER:** I think it
17 might be good to have -- I've received real
18 substantial comments from five or six people. I
19 think, without pulling back into my emails, I
20 think they know who they are. If they could,
21 perhaps, just raise their hand, those people who
22 have substantial comments.

1 **DR. KENNETH PORTIER:** Okay. That's
2 a good suggestion. Why don't those of you who
3 have substantial comments go ahead and raise your
4 hand. And I'm going to start with Dr. Grant
5 because he was quick to get his hand up.

6 **DR. STEPHEN GRANT:** Hello, everyone.
7 Okay. So a couple of comments. First of all, on
8 methodologies, I did a study a while ago in which
9 we modeled carcinogenesis on data from the open
10 literature versus the NTP data. And the actual
11 data from the open literature, whereas the same
12 number of compounds were found actually did a
13 better job. So standardized methodologies don't
14 actually say to me that it's done right.

15 I usually find that standardized
16 methodologies have been standardized and made
17 obsolete. So I -- I am sympathetic to the fact
18 that someone who tried to use a more in-depth
19 procedure might come up with more detailed
20 endpoints. I can't prove that that happened in
21 this case, but you have -- I wouldn't say yes or
22 no that a non-standard protocol is necessarily

1 better or necessarily not better. But it is a
2 difference in the studies that we've seen.

3 There was -- it was commented that
4 there were a number of negative studies. It would
5 have been nice -- the way that I look at negative
6 studies is, did they have the power to have a
7 positive effect? And I would charge EPA's
8 checking to make sure that the negative studies
9 weren't under powered.

10 The accumulation of data, I'm very
11 sensitive to this because I do human
12 biomonitoring, and I'm involved in a couple of
13 consortiums where we standardize technology so
14 that we can accumulate our data, which is pool our
15 data. And especially in a lab, I mean, the
16 biggest -- the single disparity that's been
17 pointed out is tap water versus distilled water.
18 And unless you can show that that's probably the -
19 - causing cardiac defects, I probably would say
20 that is a change over time yes but not significant
21 enough to not allow the accumulation of data. I
22 haven't checked all of this, but the fact is, if

1 you publish things separately and then accumulate
2 them, you're probably doing a good job. I've been
3 doing secondary data analyses and I analyze one
4 data set, analyze another, and then I fuse them
5 together to get the best data set.

6 Okay. So here's the major issue
7 that I probably want to leave here is that the
8 question becomes should we use this cardiac effect
9 basically based on a single study, which I
10 acknowledge seems to be an outlier -- I will give
11 everyone that -- for the derivation of the POD?
12 And here I'm going to go both ways, which is, as
13 soon as you do your metanalysis -- and that's not
14 exactly what I would call a metanalysis but -- and
15 conclude that the cardiac defects are real, then I
16 would say, if that was the criteria you were
17 applying, you should use it.

18 On the other hand, in that
19 metanalysis, the in vivo data that you're now
20 proposing to use as the POD were a wash. They
21 were not used to support. They were not the
22 reason or contributing to the reason that the

1 metanalysis was positive. It seems to me that if
2 the data doesn't support the use of the data, you
3 shouldn't use the data. And I hope that wasn't
4 too convoluted. Let's see, I think -- I think
5 that's all I've got. Thank you.

6 **DR. KENNETH PORTIER:** Thank you Dr.
7 Grant. Dr. Gilbert, you're next.

8 **DR. KATHLEEN GILBERT:** So I wanted
9 to start off by saying I appreciate Dr. Grant's
10 comments about the problems with standardized
11 protocol. I think that was spot on. So I'm
12 looking at this from a different point of view.

13 I mean, I thought that the EPA's
14 Weight of Evidence approach was extremely
15 thorough. And they basically concluded that the
16 results from the Johnson and Dawson studies, which
17 identified cardiac defects following the
18 developmental exposure, were more compelling than
19 the results of the Charles River study. They
20 described in detail the strength and weaknesses of
21 the different reports and concluded that the
22 database provides positive overall evidence that

1 TCE may produce cardiac defects in humans based on
2 cumulative evidence from the epidemiology, mixed
3 evidence from the animal tox, and stronger
4 evidence for the mechanistic studies. This seems
5 to be an appropriate conclusion.

6 So I have worked on
7 trichloroethylene myself for over 20 years, and we
8 have done trichloroethylene developmental
9 exposures. And I know how difficult they are.
10 And as we know, it's not difficult to find
11 problems with any published study. Especially
12 when you're conducting animal work in academia,
13 there are financial and practical constraints that
14 we all have to deal with.

15 There are few papers in the history
16 of toxicology that have been scrutinized more than
17 the Johnson paper. Some reviewers believe that
18 the problems associated with it negate its
19 conclusions. Most notably it's the issue of
20 pooling the control results and the issue of the
21 distilled versus tap water. Others, including
22 myself, believe that the results of the Johnson

1 study have merit.

2 Now, our developmental studies on
3 TCE in mice focused on immune parameters other
4 than cardiac defects. However, since we, similar
5 to the Johnson et al., found results at parts per
6 billion levels, I'm ready to believe that the
7 results of the Johnson paper are important and
8 should be part of the risk assessment. And that's
9 all I want to say at this point.

10 **DR. KENNETH PORTIER:** Thank you, Dr.
11 Gilbert. Dr. Cory-Slechta.

12 **DR. DEBORAH CORY-SLECHTA:** Sorry for
13 the delay. I am going to agree with Dr. Gilbert,
14 and I want to highlight a couple of things here.
15 Number one, the fact that you find these effects
16 several years apart to me is more evidence.

17 It's like a replication and a
18 reproducibility that we don't always necessarily
19 see in science these days. It's been a big issue.
20 So the fact, to me, that you're collecting these
21 data across several years was not a deterrent. In
22 fact, it seems like a strength to me. I don't

1 really see any biologically plausible mechanism by
2 which the difference between distilled and tap
3 water is going to make this big of a difference.

4 I also had significant problems with
5 the Charles River study that were actually brought
6 up by one of the public commenters, and that was
7 how they carried out the statistics. And I think
8 if you go and look at that paper, it's very
9 unclear, in a way, how the statistics were carried
10 out. There's no presentation of any of the
11 outcomes nor the actual p-values themselves. And
12 I also did not see that study as really being a
13 replication. It was a very limited assessment in
14 terms of cardiac defects.

15 I just want to close by saying that
16 we keep focusing on the fact that this is a very
17 low dose, and of course toxicology has gotten
18 itself into the bind of everything has to be
19 linear dose-effect functions. I think if you go
20 back to your basic lessons in physiology, you'll
21 see quite clearly that most dose-effect curves for
22 enzymes, steroids, whatever are not in fact

1 linear. They're U-shaped or inverse U-shaped
2 where you have to be in the middle. Just like
3 when you take your vitamins, too little is not
4 good; too much is not good. So I don't understand
5 why we continue to put so much evidence on that.

6 So low doses also don't bother me
7 because as somebody who worked on lead exposure
8 for years and years, I know that I can have pounds
9 of lead in the bone and teeny-tiny little bits in
10 the brain and yet the brain is the target organ.
11 So those are my comments.

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

14 **DR. CRAIG ROWLANDS:** Thank you. So
15 I have, kind of, three issues and they're all on
16 the same topics that have already been discussed.
17 As far as the Weighted Evidence Analysis
18 conclusions go, I think there are three areas that
19 need to be reassessed by the Agency. The one is
20 the quality reliability assessment of the
21 Dawson/Johnson study and the Charles River study.
22 If you're doing one, you should do both. And

1 there are some additional studies considering the
2 weighted evidence that were not included. And I
3 also have some comments about the mechanistic data
4 integration mapping that really needs to take
5 place in order to understand where that
6 mechanistic data fits into a causal pathway.

7 So EPA placed a significant weight
8 on the Dawson/Johnson study in its Weight of
9 Evidence, even though we all know that's had
10 several problems. They've been raised over the
11 years. Dr. Gilbert pointed out, you know, that
12 that was a problem in terms of the pooling the
13 data together, especially the controls where you
14 have two different control groups. One is tap
15 water and one was distilled water. But based on
16 the EPA TSCA methodology or systematic review,
17 this actually should have been scored as
18 unacceptable for risk assessment for that
19 criteria. But instead, the study was given a
20 medium quality rating in the end.

21 And that actually does relate to
22 this pooling of the data for controls and

1 treatment groups across the separate studies that
2 was conducted over six years. And I'm not aware
3 that these two studies were actually independently
4 assessed and demonstrated effects. It wasn't
5 until they pooled them they then actually started
6 to measure the effects are reported.

7 So there's also inadequate reporting
8 on the methods that were used so it's difficult to
9 follow what they actually did. And the Agency
10 spent quite a bit of time working with the
11 investigator trying to get some of these questions
12 answered. There's also -- I believe there's a
13 record the study more so can no longer be
14 independently verified.

15 So the use of non-concurrent pool
16 controls per the TSCA scoring definition for this
17 metric meets the definition of unacceptable for
18 risk assessment. You have to use concurrent
19 negative controls for comparative treatments
20 group. And by combining them, you now have --
21 half the studies are not using the same controls.
22 You combined the two. And TSCA rules also

1 indicate that even one study quality of metric
2 rating's unacceptable for risk assessment. Okay?
3 So that means the whole study would be determined
4 unacceptable if that one criteria was
5 unacceptable.

6 So if we look at the Charles River
7 study though -- and this study, as is already
8 noted, didn't have any observed cardiac effects in
9 the rats that were exposed to the same dose ranges
10 as the Dawson/Johnson study. The Charles River
11 study was the guideline study, GLP, Good
12 Laboratory Practices. It followed EPA guidelines
13 for dissection methodology, and the Agency did
14 score that as a high-quality study.

15 But even so, at the end EPA -- the
16 Charles River study was downgraded to a medium
17 quality study based on the EPA opinion that that
18 dissection methodology was insufficiently
19 sensitive to identify all the possible cardiac
20 effects. So that means that the pooled
21 Dawson/Johnson study conducted over six years and
22 meeting TSCA criteria as unacceptable for its

1 assessment was scored as a medium quality study,
2 which is equivalent to the modified medium quality
3 score for the Charles River study, the guidelines
4 study. So I see that as problematic.

5 I mean, very least EPA should
6 objectively, transparently reassess that
7 Dawson/Johnson study and the Charles River study
8 for quality according to the TSCA systematic
9 review guidelines and EPA guidance for the
10 dissection methodology. And yet they decide to
11 waive a systematic review criteria. They need to
12 provide a rationale with citations to
13 authoritative sources substantiating that EPA
14 rationale. And that should be true any time this
15 waiver of a significant opinion is waived about
16 the quality of something now. It really should
17 have the underlying authoritative source of
18 information substantiating invalidating that EPA
19 opinion.

20 In addition, the EPA Weight of
21 Evidence didn't include a lot of studies, actually
22 four, that were oral repeats of TCE studies. And

1 they need to include all of these or provide again
2 another rationale that substantiates for why they
3 shouldn't be included in the Weight of Evidence.
4 And they were all negative. I won't provide --
5 the references will be provided in the written
6 comments. But those are four more studies that
7 were negative that really are important to
8 consider in the Weight of Evidence, unless they
9 find they don't meet some criteria.

10 Okay. And then just regarding the
11 mechanistic studies, EPA did summarize some
12 mechanistic studies, but it didn't integrate these
13 in any organized manner to a coherent causal
14 pathway from an initial exposure to an average
15 outcome, here the cardiac effects. They did
16 provide a mode of action narrative in the risk
17 evaluation. They proposed several hypotheses for
18 potential modes of action but concluded that the
19 evidence to date does not identify specific mode
20 of action. So it's very difficult to understand
21 what the relevance is of the mechanistic
22 information. If we don't know where it's supposed

1 to fit into a causal pathway, it's just sort of
2 hanging out there.

3 So it would be valuable for EPA to
4 go ahead and create a conceptual model, such as an
5 adverse outcome pathway, or another mode of action
6 if they prefer, and compare the integrated
7 mechanistic data against each key event in that
8 causal pathway to determine the level of
9 supporting evidence from that molecular mutating
10 event to the adverse outcome, the cardiac effects.
11 And then we'll have the ability to really assess
12 how much weight is really behind the key event
13 along a causal pathway. Does it support the
14 outcome or not? Until that's done, I don't know
15 what you do with this mechanistic data. So that's
16 what I have. Thanks.

17 **DR. KENNETH PORTIER:** Thank you Dr.
18 Rowlands. I'm glad you brought up the AOP Pathway
19 discussion because I kind of noticed its absence
20 in this draft risk assessment. Dr. Vorhees.

21 **DR. CHARLES VORHEES:** Yes. Well,
22 Dr. Rowlands has done such a thorough job I don't

1 have a tremendous amount more to add. But my
2 concern about the Johnson studies are the same as
3 his. And, you know, in the Makris systematic
4 review where they went through the data of Johnson
5 in great detail, they show a figure, Figure 5 in
6 Makris' paper, that shows the actual timeline of
7 the experiments that Dr. Johnson did.

8 And one of the things that Dr.
9 Rowlands just brought up was the absence of
10 concurrent controls. And if you look at the
11 timeline of when the controls were actually
12 conducted, what you see is that most of the
13 controls were actually done without experimental
14 groups present at all. They were just -- they
15 were done after the first study was done in, like,
16 1990. Then they did controls year after year.
17 And then, starting in 199- -- about midway through
18 1994 then did another set of animals at different
19 levels of TCE. That is the strangest experimental
20 design I have ever seen.

21 And if anyone -- if any collaborator
22 or graduate student brought me data like that I'd

1 look at it and I'd say, well that's an improper
2 design. Yeah. I don't care whether you collect
3 the data over all those years or not. These
4 controls that are done without experimental
5 animals done concurrently make no sense and should
6 be completely excluded. My guess is, however,
7 that, if those controls that were done during the
8 intervening years were excluded, they probably
9 wouldn't have found a statistically significant
10 effect in the experiment done at the beginning and
11 the experiment done at the end with TCE.

12 The other thing that I would mention
13 is there is another study on which Dr. Johnson
14 participated and it was done by Fisher. I don't
15 remember the year, but it was a gavage study
16 instead of a drinking water study. So there, you
17 know, Dr. Johnson participated in the analysis of
18 the data for heart, and again, no effect was found
19 on cardiac defects.

20 What's interesting is that in
21 teratology, most typically when compounds are
22 given by gavage where you get large peaks in the

1 drug concentration and then valleys, those tend to
2 produce more malformations than steady levels. So
3 for giving TCE in drinking water where you would
4 get steadier levels -- higher at night presumably
5 than during the day -- you're distributing the
6 dose out in such a way that, for teratogenesis,
7 you're less likely -- and there are a number of
8 studies in the literature which demonstrate this
9 effect where drugs that are teratogenic are given
10 either in bolus doses or they're put into osmotic
11 mini pumps. And the most striking teratologic
12 effects appear when you give bolus doses not
13 distributed doses. So that to me represents a
14 significant piece of evidence in the Fisher study,
15 again in which Dr. Johnson did the pathology, that
16 argues against the Johnson 2003 data which seemed
17 to suggest a very striking cardiovascular effect.

18 About the Charles River study, I
19 would just bring up that they did find cardia- --
20 a low level of cardiac defects, mostly ventricular
21 defects rather than valvular or atrial defects.
22 EPA has criticized their methodology I realize.

1 But the fact is that although Charles River says
2 they didn't find an effect that was largely
3 because their control group had an unusually high
4 number of cardiac defects. If you use a more
5 typical average cardiac defect rate in control
6 litters, they actually do find a small increase in
7 cardiac defects, but they're ventricular. They're
8 not atrial and they're not valvular. And I think
9 the Charles River study do argue against the
10 Johnson data.

11 I think the Johnson data are outlier
12 data. The fact that they can't seem to be
13 replicated, I think the EPA should -- I think it's
14 for -- using those data for hazard identification
15 may be okay, but for dose-response and POD
16 determination, I don't think they should be used.
17 Thank you.

18 **DR. KENNETH PORTIER:** Thank you, Dr.
19 Vorhees. Dr. Hossain.

20 **DR. MUHAMMAD HOSSAIN:** Yes. I agree
21 with Dr. Gilbert and Dr. Grant and others --

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

1 DR. MUHAMMAD HOSSAIN: Yes.

2 DR. KENNETH PORTIER: Dr. Hossain,
3 you sound -- you sound like you're coming out of a
4 tunnel. You need to get closer, or if you're on
5 conferencing, you need to actually get on the
6 phone. We have a hard time hearing you.

7 DR. MUHAMMAD HOSSAIN: I am right on
8 the phone.

9 DR. KENNETH PORTIER: That's much
10 better. Thank you.

11 DR. MUHAMMAD HOSSAIN: Okay. I am
12 in agreement with Dr. Gilbert and Dr. Grant and
13 others. They all made very nice comments on this
14 but I -- my comment is, I think all the data had
15 problem with experimental design in Johnson's
16 study. Still, I think this data would be useful
17 for hazard determination.

18 I -- only I have a problem with they
19 didn't use equal number of dams per group. If you
20 see that in the use 55 dams in control group but
21 only 9 or 10 in treatment group. And in the high
22 dose, they use only 9 dams. But the -- still they

1 effects are so significant and robust, so I think
2 that this data could be useful.

3 And another thing, I think I want to
4 look at the graph in Charles River study for water
5 consumptions. I saw that there's a big difference
6 between the water consumption in people in control
7 and treatment groups. I think the animals treated
8 with the trichloroethylene, this group did not get
9 that much concentration because the consumption
10 was too significantly differen- -- low, when you
11 contrast to the control. That could be the
12 problem why they did -- unable to reproduce the
13 results of Johnson study. That's all.

14 **DR. KENNETH PORTIER:** Thank you, Dr.
15 Hossain. Before I get to Dr. Grant, I wanted to
16 add in my comments on this. This is Ken Portier.
17 I looked at both of these studies but concentrated
18 more attention on the Charles River study.

19 I think the weight of evidence
20 approach is well described and seems to be
21 consistently performed. Several uncertainties
22 that I've identified impact the adequacy of the

1 conclusions from the Charles River and the Johnson
2 et al. studies. These uncertainties should lower
3 the reliability, especially of the Charles River
4 study, to a single plus and have relevance to the
5 -- to this question 5.1.

6 So one of the things I've noticed in
7 the two studies is it's not clear how they handled
8 the low limits of quantification data. And this
9 can be very important in the subsequent analysis
10 and comparison of the study groups as well as it
11 will impact the BNB, BNBL dose-response modeling.
12 For the Charles River, on text Table 11, "summary
13 of serum TCA concentration data," there's a lot of
14 BLQ less than 150 statements. And I assume that
15 indicates that the quantification level was 150
16 nanograms per milliliter, but that's not stated
17 anywhere.

18 And when they report statistical
19 mean estimates I -- there's three ways I can look
20 at those data. I don't know if all the
21 observations are above limits of detection and so
22 it's just the simple mean of actual measured

1 values. Or the LOD values of recorded at half the
2 LOD, and it's a simple mean of observed
3 measurements and half LOD estimates. Or the LOD
4 values are not included and the mean is only of
5 the values that are measured. And the LOD values
6 were disregarded, which would really produce an
7 overestimate of the values.

8 And they may have done something
9 more appropriate like using right censored
10 estimation, which a statistician would have
11 recommended. The Johnson et al. studies, I could
12 find no discussion on serum TCA concentrations and
13 no discussion of limits of quantification. The
14 Charles River study mentions using HPLC with UV
15 absorptions, but it really doesn't talk about the
16 BLQ of that method. And it refers to an
17 unavailable internal technical report that I was
18 unable to find.

19 There's a big difference between
20 nominal test substance consumption and measured
21 test substance consumptions between the two
22 studies. And the Charles River study, text Table

1 13, we find big differences between what they say
2 they administered and what they measured -- the
3 measured consumption was. And to give you an
4 idea, the nominal 0.25 ppm treatment actually had
5 measured consumption of 0.04 ppm. The nominal 1.5
6 ppm had a measured consumption of 0.21 ppm. So
7 the -- you know, if you do the analysis on the
8 nominal levels, especially a dose response on the
9 nominal level, you're really overestimating the
10 actual dose that was administered to the animal.
11 So in fact, the Charles River study is much more
12 of a lower dose study than it seems to indicate
13 when you look at the nominal readings.

14 The Johnson study on the other hand,
15 their nominal readings and their average 24-hour
16 concentration values, which is reported on page
17 290 of that study, you see that they're actually
18 quite close. The nominal 0.0025 ppm has an
19 average 24-hour concentration of 0.0021, and their
20 0.25 ppm has average concentration of 0.20 ppm or
21 0.21 ppm. So it's very close. So I -- you know,
22 doing dose-response on the Johnson data, given all

1 the other comments we had before, at least their
2 nominal levels are very close to what was actually
3 administered to the animal.

4 The third thing I looked at was the
5 fact -- the randomization. So in the Charles
6 River study page 608, they talk about doing a
7 stratified random allocation of dams to treatment
8 groups and, you know, with the goal of creating
9 treatment groups with similar mean body weights.
10 And because we -- you can actually download and
11 look at the Charles River technical report, I was
12 able to confirm that this randomization, even
13 though they don't describe it -- you know, to a
14 statistician this has a certain meaning of how
15 they did the randomization.

16 And I was able to confirm that, in
17 fact, their initial maternal body weights on day 0
18 of the study were very close to each other, but
19 that the group with the most variability in
20 maternal body weight on gestation day 0 and on
21 gestation day 21 is the negative control group.
22 So the control group, while starting out at the

1 same level, had a lot more variability from animal
2 to animal, dam to dam both at the beginning at the
3 end of the study. And of course, having more
4 consistent group means, I think, at the beginning
5 and consistent variances improves the power of the
6 study, which means the Charles River study should
7 have actually had more power to observe a dose
8 effect, if in fact one was there.

9 I was surprised that there's no
10 discussion in either study of incorporating
11 maternal body weights or fetal body weights in
12 estimating the likelihood of observing a heart
13 abnormality. Charles River reported that maternal
14 and average fetal weights -- average fetal weights
15 were unaffected by treatment. And differences
16 from vehicle control groups were slight and not
17 statistically significant. But I wasn't able to -
18 - I didn't have time to replicate that analysis to
19 confirm that finding.

20 But this is not the same as asking
21 whether the likelihood of observed heart defect is
22 impacted by small changes in maternal or fetal

1 body weights. Johnson used a probit analysis to
2 establish a dose-response curve. And this
3 analysis could be modified to account for other
4 potential explainers of outcome, such as maternal
5 or fetal body weights, assuming they were
6 recorded. But I couldn't determine whether those
7 were available or not.

8 The draft risk assessment does
9 mention that different methods and different
10 statistical analysis were used to describe the
11 effects, and someone had already mentioned that.
12 The source and strain of rat is mentioned on page
13 609. And I think this is a bigger effect than is
14 discussed in the draft risk assessment.

15 So Dawson and Johnson studies used
16 Harlan Sprague Dawley rats whereas the Charles
17 River study used, as you would expect, the CRL CD
18 SD Sprague Dawley rats. And this may have more of
19 an effect than indicated in the draft risk
20 evaluation. A quick search of the literature
21 shows that Sprague Dawley rats from the two
22 sources are genetically quite different, and I

1 have a reference by Galaida (phonetic) 2018. They
2 differ in their incidents of neoplasms in their
3 historical controls.

4 There's an article by Webber. And
5 they display very different growth characteristics
6 as a 2015 paper by Brower et al. that discussed
7 that. And the draft risk assessment doesn't
8 really mention that, and I think that -- should be
9 more discussion on that.

10 And then, finally, as Dr. Vorhees
11 had mentioned, when you look at the Charles River
12 historical controls for visceral malformations on
13 Appendix 8, page 713, it shows 0.01 with a
14 standard deviation of 0.045 as percent for liver
15 for the interventricular septal defect.

16 The average for the study
17 contemporaneous controls was 2.4, so the
18 historical control's 0.01, 0.045 standard
19 deviation. The historical controls -- I mean, the
20 study controls 2.4 with a standard deviation 6.47.
21 So this study controls is far in the upper tail of
22 the historical controls distribution suggesting

1 there may be issues with whether the sample -- the
2 study sample was a normal sample from the Charles
3 River Ashman population. And I don't know quite
4 what to make of that. But I think that's another
5 big deal.

6 And then finally, something I hadn't
7 written down but came to me as I listened to this
8 conversation is that, in the Johnson study, there
9 is not -- no discussion of historical controls
10 over time in the Harlan Sprague-Dawley rats and
11 that should be available, and that could help to
12 explain or at least help support the discussion of
13 whether the controls -- the use of two controls is
14 reasonable or not. And I suspect, Dr. Vorhees,
15 that those controls that you see in the middle
16 there may be historical control studies that were
17 done by Harlan to establish these background
18 levels and that the Johnson studies just utilized
19 those studies as their controls. And that's a
20 guess on my part. And that's all of my comments.

21 I wanted to see if Dr. Vorhees had
22 raised his hand and whether he wanted to go in.

1 And Dr. Jacobs, I see your hand's up but let me
2 let Dr. Grant come in. Dr. Grant.

3 **DR. STEPHEN GRANT:** Hello again.

4 Just some comments and unfortunately, they do not
5 come to a conclusion. They're not all based --
6 all going in the same direction. I just wanted to
7 make sure the -- that there was a distinction
8 between replication and independent replication.
9 I tell my students that they can always go out and
10 if they see something really exciting and practice
11 changing that they should replicate it and that
12 the most important thing we can do is have people
13 decide that replicating our work is the most
14 important thing they can do.

15 This is not -- whereas they've seen
16 the same result several times, they're not -- it's
17 not an independent replication. And I can point
18 to a number of things in the literature which are
19 very interesting except that no one else has ever
20 been -- other than the main lab, has been able to
21 replace it. Another question is study design. I
22 have some experience from my modeling with trying

1 to rationalize using data from industry that don't
2 necessarily reach academic standards. And the
3 question is, do you want to use the data? Do you
4 believe they did the experiment and did it
5 properly? But are you going to stand on ceremony
6 and say they didn't do it as we would have wanted
7 it done and therefore we just reject it? It does
8 raise a -- in that case, most of the time we
9 decide to use the data but because it is a part of
10 a larger whole.

11 We have the problem here that
12 Johnson/Dawson isn't contributing to it; they are
13 establishing it. So it does change the criteria.
14 And what I specifically bring up here is the fact
15 that I have rejected papers that have done the
16 wrong controls. And I have said there is no
17 publishable data here because, if you go and do
18 the controls now, they're not concurrent.

19 On the other hand, it sounds --
20 Dawson/Johnson seems to bracket their studies with
21 -- their studies with controls. And one might
22 look at that like the industrial data as, that's

1 the constraints I'm under, I can't do the size of
2 animal studies that -- concurrently so I'm going
3 to do them in a slightly different way that I --
4 that is okay for me. The final thing is that --
5 kind of comes back to accumulating data or is that
6 a metanalysis? Can you pool data? And the
7 guidelines for evaluation of quality.

8 I teach ethics and one of the things
9 that we say to begin with is that the ethical
10 guidelines cannot apply to all situations. And so
11 they have to form a framework for the special
12 cases. And I think, in this case, we're justified
13 in treating these papers as special cases, and we
14 need to go beyond the standard guidelines. And I
15 think EPA did a good job of that. That's it.
16 Thanks.

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

18 Dr. Keith Jacobs, with EPA you have a comment or
19 question.

20 **DR. KEITH JACOBS:** Hello. Can
21 everyone hear me? I changed how I was calling in.

22 **DR. KENNETH PORTIER:** Yes.

1 DR. KEITH JACOBS: Okay.

2 DR. KENNETH PORTIER: You're very
3 clear, Keith. Thank you.

4 DR. KEITH JACOBS: I just wanted to
5 first thank the committee. There's clearly, as
6 expected, a diversity of opinions. Wanted to
7 point out, because there's -- this is so dense in
8 the risk evaluation that the body of the Weight of
9 Evidence section has an overview. The majority of
10 the discussion of the Charles River was in
11 Appendix G.1. An overview of the scoring for
12 weight of evidence was G.2.

13 But I think one of the earlier
14 comments was about it was unclear justifying why
15 the mechanistic scoring got what it did. The
16 individual -- we have an individual metric-by-
17 metric breakdown in one of the supplemental files
18 that's an Excel document. So if anyone on the
19 committee want -- didn't get an opportunity to
20 look at that, that goes into detail on each
21 individual study and how for each metric it got
22 the score it did.

1 I wanted to touch just on a few
2 issues or maybe perhaps clear some things up. In
3 terms of the mode of action and discussion of
4 nonmonotonicity, we agree that there's not a clear
5 single AOP or mechanism that can be derived. On
6 page 224, we do touch on some of the potential
7 mechanisms. And I agree we can try to perhaps
8 turn that into a better model.

9 And on the next page, 225, we
10 discuss some of the data showing -- there's
11 actually a lot of evidence that this effect has a
12 nonmonotonic dose-response. There's several
13 mechanistic studies where you see either only an
14 effect at low dose or sometimes you actually see
15 the complete opposite effect at the low dose. 8
16 ppb has a completely different effect than 800
17 ppb.

18 And sometimes that's on the SIP
19 enzymes. Sometimes it's just in oxidative stress
20 genes. Sometimes it's in calcium pump reporters
21 -- promoters. But part of the support for
22 mechanistic data and why it was considered a value

1 was that it does support this nonmonotonicity.

2 And then, final point is on the
3 Fisher study. We did include a short discussion
4 of that, and it was actually downgraded, I
5 believe, either for relevance or strength. I'd
6 have to look it up. While it was true that there
7 was no statistically significant effect found, if
8 you look at the actual incidences reported in that
9 study for TCE, the negative control was with
10 soybean oil and had an extremely high background.
11 I think there was up to 36 percent of the pups had
12 cardiac defects and it went up to 55 percent with
13 TCE.

14 So you actually had a 20 percent
15 increase. But because the negative control was so
16 high that's why there was not necessarily
17 statistical significance. But there was clearly,
18 in terms of just looking at the data there was a
19 difference. So I -- we consider that much more
20 ambiguous as opposed to negative.

21 They also didn't do the stats on all
22 the different possible analyses. They kind of

1 separated cardiovascular from cardiac defects, and
2 they only ran the stats on either -- it was either
3 on the combined or on one of them, but they didn't
4 do all the possible combinations. So I think on
5 the statistical analysis of that study there's
6 reasons why we didn't actually necessarily
7 consider it negative.

8 And then final point on the
9 concurrent controls, it is true that the -- when
10 you look at the dates, the controls were not done
11 necessarily the same time as the equivalent study
12 shown in Dawson. However, they were concurrent
13 with many of the other studies do- -- which -- of
14 evidence including the metabolite studies on DCA,
15 TCA. So they weren't just done on their own.
16 They were done as part of other experiments, and
17 that's why the pooled number is so high because
18 they used the same control data for all of their
19 experiments. But it was done concurrent with some
20 experimental variable. Thank you.

21 **DR. KENNETH PORTIER:** Thank for that
22 clarification, Dr. Jacobs. Dr. Vorhees?

1 **DR. CHARLES VORHEES:** Oh, hi.

2 There. I had to turn off the mute. So that
3 actually is what I thought is that probably those
4 controls that Johnson did were done with different
5 experimental groups. But, you know, that's part
6 of experimental design is that, you know, you
7 prepare concurrent controls with the experimentals
8 that you're studying at that time and those go
9 together. And you don't go around back through
10 your experimental history and say, well, you know,
11 I'm going to take controls from a bunch of
12 different experiments. And I'm going to put them
13 all together, and then I'm going to compare those
14 to just the selected experimental groups that I
15 want to do an analysis on now.

16 I mean, that's just not kosher.

17 That's not the way you -- any -- I bet no one on
18 this committee goes around doing experiments like
19 that. I certainly don't. And it seems to me it's
20 just part of sound experimental design that you
21 use the contemporary controls with the
22 contemporaneous experimental groups. And I --

1 what I don't understand is why Johnson didn't do a
2 separate analysis in which they simply compared
3 the TCE groups with their concurrent controls and
4 -- to determine whether or not there was an effect
5 on the particular kinds of cardiac defects that
6 they saw.

7 The other thing that is striking to
8 me in this whole controversy about cardiac defects
9 is that some of the cardiac defects are seen as
10 septal. Some are valvular. Some are ventricular.
11 And so what we're debating here is sort of the
12 edge of -- the leading edge of controversies in
13 teratology. I remember when the teratology field
14 struggled for decades over the meaning of skeletal
15 defects. And, you know, it took 20-some years to
16 get that issue finally resolved.

17 Here we're arguing over something
18 that is an ongoing controversy in teratology about
19 these different kinds of defects. Sept- -- what
20 is the meaning of these defects? Are they
21 pathological? We know that some of these defects
22 close if you allow the animals to progress into

1 the post-natal period. And then there's a debate
2 about, well, which ones close -- can be considered
3 just delays in development and they'll close and
4 they'll cause no harm to the animal and which ones
5 are actually pathologic and require a surgical
6 repair, at least in a human.

7 So I don't think that the DRE should
8 get in and delve into the ins and outs of issues
9 which are so in the midst of controversy. I think
10 rather they -- the Johnson data are outlier data.
11 They haven't been replicated, and I think they
12 shouldn't be carried into the dose-response and
13 POD part of the DRE. They're fine for risk -- for
14 hazard identification. I don't have a problem
15 there. I just think carrying them forward into
16 the latter parts of the DRE is really, sort of,
17 pushing the boundaries of the -- based on the
18 problematic aspects of those data. Thank you.

19 **DR. KENNETH PORTIER:** Dr. Davies?

20 **DR. HOLLY DAVIES:** Hi. First, I
21 really want to appreciate that EPA showed the
22 Agency's work in the supplemental files that we

1 might disagree with some of the ratings, but it's
2 really helpful to be able to see how they rated
3 everything in the Weight of Evidence. I came down
4 on the side of not including Johnson et al. into
5 the POD because of all the issues. I think we all
6 agree we've brought up the different issues, and I
7 tend to give more benefit of the doubt to the
8 academic lab with why they did things with
9 different constraints.

10 But it comes down to what Dr.
11 Vorhees just said. It's an outlier and it hasn't
12 been replicated. And that just would make me
13 uneasy about using it for the POD. I think
14 everything -- all the evidence shows that there
15 are cardiac defects both from Johnson et al. and
16 from the other, the mechanistic, the chick data,
17 the epidemiology data, the in vitro data. That
18 all supports the developmental cardiac effects.
19 But again, I just think Johnson's too much of an
20 outlier that hasn't been replicated. So I think
21 that's what I wanted to say for now.

22 **DR. KENNETH PORTIER:** Thank you, Dr.

1 Davies. Dr. Gilbert.

2 **DR. KATHLEEN GILBERT:** Yes. It's
3 been very interesting listening to everybody. And
4 Dr. Portier, I must say that your comments made me
5 believe that if you took any two papers that came
6 out with opposite results and subjected them to
7 the scrutiny that these two have been subjected to
8 that we would -- we might conclude that neither
9 one of them are acceptable. But I have to admit,
10 you know, that there's a lot of issues with the
11 Johnson paper, and I thought Dr. Vorhees' comments
12 were particularly compelling, even though I'm
13 still not clear as to why you could use this paper
14 for hazard identification but not POD.

15 But the bottom line is I happen to
16 believe the results of the Johnson paper are
17 important and should be included. On the other
18 hand, I realize that there's a lot of controversy
19 surrounding this whole approach, and it may not be
20 possible to reach a consensus at this point, even
21 though I believe that developmental toxicity to
22 TCE is probably one of its most sensitive

1 outcomes. And at some point in time that will be
2 verified. But at this point in time, because of
3 all the controversy, I think it may be more
4 practical to instead use the immunotox results to
5 devise the acute and chronic non-cancer PODs.
6 That's all I want to say.

7 **DR. KENNETH PORTIER:** Dr. Gilbert,
8 having been through the wars with bisphenol A and
9 glyphosate, I tend to agree with you. When these
10 studies get looked at, they get put under the
11 microscope you see all the warts. The bigger
12 issue here is, you know, what does EPA base its
13 hazard assessment moving forward? And I think I
14 agree with you that we're not going to come to a
15 consensus on this, but I think this conversation
16 is very useful to EPA. It may be one they've
17 heard before, but they need to hear it again. Dr.
18 Hop- -- Dr. Davies, I see your hand's still up.

19 **DR. HOLLY DAVIES:** Yes. I realize I
20 had forgotten to make one of the points I had
21 written down which is -- which goes to your not
22 reaching a consensus because we had the two

1 different reviews that were done by Wikoff et al.
2 and Makris et al. that both came to different
3 conclusions. So I don't think there is a
4 systematic review that, you know, we would all
5 agree on. Just kind of talking about the
6 difficulty of coming to consensus.

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

8 And I will make a comment for the public that EPA
9 does -- while EPA requests that the Science
10 Advisory Committee on Chemicals make every attempt
11 to come up with a consensus statement, it's not a
12 requirement that we provide EPA with consensus
13 comments. And that in situations such as this
14 it's quite common for us to actually agree to
15 disagree. Who? Dr. Barone, maybe I'll give you a
16 chance to step in here, and then I see Dr. Grant
17 and then Dr. Johnson following up. Dr. Barone
18 with EPA.

19 **DR. STANLEY BARONE:** Yeah. I just
20 wanted to provide some clarification. Dr. Vorhees
21 had commented on the figure that was in the Makris
22 paper. I think it's Figure 5 that shows the

1 timeline of the different experiments. We did a
2 lot of subsequent analysis -- we, EPA, did a lot
3 of subsequent analysis based upon information that
4 was communicated to us about the studies and which
5 groups were done when and the timelines. That's
6 in information that's actually provided in the
7 docket and referred to in the assessment.

8 The experimental groups did have
9 concurrent controls, contemporary controls. This
10 analysis, which included the additional control
11 groups for the metabolite studies, was provided by
12 the authors in their later paper to show that they
13 had additional power -- to provide additional
14 power. We did separate analyses of the control
15 groups to see if there were differences in the
16 control groups, which I think you eluded to in
17 your discussion of the statistics. That's also
18 provided in the background documentation. So
19 again, we did consider these issues very carefully
20 and did not dismiss them.

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

22 Dr. Johnson.

1 **DR. MARK JOHNSON:** Yes. Thank you.

2 I was going to save this comment for the next
3 question, but it seems to be at least relevant to
4 this discussion. We -- what EPA did is they
5 treated oral and inhalation data as equivalent.
6 And I don't know if that's justified. I mean, we
7 used the PBPK model, and I think that's a great
8 idea. We should. But it's a model. We make
9 assumptions when we do route-to-route
10 extrapolation.

11 These tox studies have not
12 identified a mode of action. They have not
13 identified a mechanism. We don't know exactly
14 which metabolite's responsible for these effects.
15 We don't know -- and I know the model did a good
16 job at looking at secondary metabolites. I don't
17 know about tertiary, quaternary metabolites. We
18 don't know the metabolite, as I've mentioned,
19 that's responsible for these potential effects.

20 And so I think it's kind of a
21 mistake to treat the oral data as equivalent to
22 inhalation. If we're developing an inhalation

1 benchmark, we should treat the inhalation data
2 with a higher degree of confidence. And so I
3 think that's a comment I would like to make, and I
4 would appreciate if the EPA would just consider
5 that when they do their Weight of Evidence
6 evaluation. That's all I had. Thank you.

7 **DR. KENNETH PORTIER:** I think, Dr.
8 Johnson, you meant with a higher weight in the
9 discussion -- that the inhalation data should
10 weigh more than the, you know, water consumption
11 data.

12 **DR. MARK JOHNSON:** Yeah. I'm sorry.
13 Did I get that backwards? Yes. That's what I
14 meant.

15 **DR. KENNETH PORTIER:** Yeah.

16 **DR. MARK JOHNSON:** Because I have
17 seen it where we do route-to-route extrapolation
18 when we don't have the proper exposure pathway
19 data. So if we don't have inhalation data, it's
20 perfectly acceptable to use the oral data. I've
21 seen it done and that's fine.

22 But here we have inhalation data.

1 We have inhalation developmental data. We have a
2 lot -- we have a robust data set for this
3 particular compound. I think that's the same
4 thing that probably the NIOSH individuals do when
5 they develop the REL, that ACGIH do when they
6 develop the TLV, which by the way is about three
7 orders of magnitude higher than this value that
8 the EPA is providing.

9 **DR. KENNETH PORTIER:** Dr. Grant.

10 **DR. STEPHEN GRANT:** Hello again.

11 Sorry. Again, it comes back to the idea that I
12 kind of work in different fields. And what I see
13 in the Johnson/Dawson data is something that I see
14 far more in epidemiology than I do in bench
15 science. And it kind of comes from the background
16 of doing pilot studies.

17 You can do pilot studies two ways:
18 an independent pilot study that then sets up the
19 larger study. But there's another thing that we
20 do called a nested pilot study. And that is if
21 you do 50 samples and then things work out and you
22 get the money to do more, you do another 150, but

1 you include the 50 pilot samples in the total
2 overall amount. And it kind of opens up the idea
3 that you can continue to add n and therefore
4 increase your power.

5 And I would just give you -- I'm not
6 saying, yes, no, maybe. But it seems to me that
7 Dawson/Johnson consider this one ongoing
8 experiment and that, when we see time periods or
9 papers, we're breaking it in ways that they don't
10 really see it. And that's why I talked about an
11 accumulation of data. It seems to be an ongoing
12 pursuit in that laboratory. And the question is,
13 how should we evaluate that, quote/unquote, study
14 design.

15 **DR. KENNETH PORTIER:** Thank you. I
16 see Dr. Morris, Dr. Apte, and Dr. Bruckner. I'm
17 going to leave Dr. Bruckner for last. Dr. Morris.

18 **DR. JOHN MORRIS:** Yeah. I just have
19 a quick comment just to agree with everything Dr.
20 Johnson said about PBPK and the uncertainties
21 associated with extrapolating across routes of
22 administrations and also, you know, the level of

1 confidence in picking that total oxidative
2 metabolite as a dosimetric. I'm not sure we
3 really know. I agree with everything he said
4 relative to that. And that's it.

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

6 Dr. Apte.

7 **DR. UDAYAN APTE:** Yeah. Hi. I want
8 to just get on the record here that I
9 wholeheartedly agree with Dr. Vorhees' comments
10 about the Johnson paper and the sort of
11 unsuitability of it. I think I'm fine with using
12 it for hazard identification but nothing more than
13 that. And I agree with the discussion that went
14 along with it. Thank you.

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

16 Dr. Bruckner, and I think after Dr. Bruckner we're
17 going to take a 15-minute break. So, Jim.

18 **DR. JAMES BRUCKNER:** I just wanted
19 to mention along the lines of route of exposure.
20 I think probably more emphasis or more attention
21 should be paid to the Carney study, which was an
22 inhalation study in which there were no adverse

1 effects seen. I think, actually -- well, I have a
2 problem with, particularly at low doses, with oral
3 exposure studies. And the liver, of course, with
4 first pass is going to eliminate a considerable
5 portion of that dose.

6 We did some studies with
7 trichloroethylene where we looked down to parts
8 per million levels. We found that the -- with
9 rats, we found that the liver removed virtually 98
10 percent of the trichloroethylene in parts per
11 million levels from ever reaching systemic
12 circulation. So I would like to see more
13 attention EPA paid on the inhalation studies. And
14 I would again point out the Carney study, which
15 was inhalation exposure, and focus on cardiac
16 defects. That's all.

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

18 Actually, Dr. Jenkins popped her hand up. We'll
19 hear from her and then take a break. Dr. Jenkins.

20 **MS. ALLISON JENKINS:** Well, I was
21 going to talk about the human studies, so do you
22 want to wait until after the break or go now?

1 **DR. KENNETH PORTIER:** Actually,
2 maybe that's a good thing. When we come back from
3 the break, we'll talk about the epi studies. So,
4 hold that hand up. I have 11:20. Let's reconvene
5 at 11:35, take a 15-minute break. Thank you.

6

7 (Break)

8

9 **DR. KENNETH PORTIER:** Okay. I have
10 11:35. It's nice to take a break, walk around,
11 get some blood flowing. But let's get back to the
12 discussion. Dr. Jenkins, you're up next. I also
13 notice that Dr. Apte, you're hand's still up. Dr.
14 Jacobs, your hand's up. And Dr. Brucker, your
15 hand's up. Please check. Leave them up if you
16 have a comment then I'll call on you. Dr.
17 Jenkins.

18 **MS. ALLISON JENKINS:** Hello? Hi. I
19 wanted to talk a little bit about the epi studies,
20 but first I wanted to weigh in that I also support
21 not carrying the Johnson studies through to -- or
22 just keeping them in the hazard identification

1 stage. In regard to the epidemiological studies
2 presented in Appendix G, there are three epi
3 studies that show positive associations varying in
4 strength, and EPA uses them to make statement --
5 the statement that there is evidence that TCE may
6 produce cardiac effects in humans.

7 They state that, together, those
8 three studies and some others shows suggestive
9 evidence for an association between TCE exposure
10 and cardiac events in offspring, and they give
11 those scores a summary score -- the epi studies a
12 score of plus. These studies look at the
13 residential location of the women at time of
14 birth, and so the location of the women during
15 that critical time period for cardiac effects,
16 about the third to eighth week of pregnancy, is
17 not known. Forehand et al. 2012 states that other
18 studies have shown between 22 and 32 percent of
19 women move between conception and delivery. And
20 in addition, the TCE concentrations are not
21 available in the Brander and Forehand (phonetic)
22 study. And Wright is a study that looked at

1 disinfection biproducts in drinking water and
2 which two of those are TCE metabolites.

3 I suggest that the conclusion of the
4 epi study section also state that these are not
5 sufficient to establish a causal association
6 between TCE exposure and cardiac effects as is
7 stated in Makris et al. 2016 and some other Weight
8 of Evidence analyses. There's also at least one
9 study -- that Camp Lejeune epi study Ruckart et
10 al. 2013 that was discounted. But that study
11 looked at children born to mothers who did have
12 exposure to TCE via the base's drinking water that
13 had high levels of TCE and some other VOCs.

14 For example, the maximum
15 concentration of TCE in the drinking water was 215
16 parts per billion and -- for comparison, the MCL
17 is 5 parts per billion. There were -- there are
18 limitations in that study also because there were
19 less than three cases of heart defects. However,
20 the exposure was to TCE on the individual level.
21 That's all I have. Thank you.

22 **DR. KENNETH PORTIER:** Thank you, Dr.

1 Jenkins, and thank you for waiting until after the
2 break. Let's see, actually, Dr. Jacobs with EPA,
3 do you have a clarifying question?

4 **DR. KEITH JACOBS:** Yes. Pretty
5 short, just, I guess, more asking the committee to
6 put in context during the recommendations when
7 they're written up to -- as Dr. Portier pointed
8 out, there's differences in the rat strains. And
9 actually a lot of the epi studies showed either
10 much stronger effects or only showed effects in
11 older women. So we do think that this might be an
12 effect and an explanation for the inconsistency
13 where it's applicable to certain test populations,
14 either genetically or based on age, where, you
15 know, the whole population might not have effect.
16 But if we are supposed to protect against PESS, it
17 might be applicable to them.

18 And then along the same lines, if
19 the committee can write up, if there is a
20 recommendation that it sounds like the Weight of
21 Evidence perhaps supports the overall effects, but
22 there's a question about the dose response from

1 Johnson, if they could go into then a specific
2 recommendation for what we should do in order to
3 protect for the effect, if they're agreeing that
4 the Weight of Evidence is supporting it overall
5 qualitatively.

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

7 And the next question obviously gets into the
8 dose-response stuff, so we're -- especially for
9 the non-cancer risk, so the conversation will
10 continue. Dr. Bruckner.

11 **DR. JAMES BRUCKNER:** Okay. Here I
12 am. What can I do for you?

13 **DR. KENNETH PORTIER:** Your hand was
14 up.

15 **DR. JAMES BRUCKNER:** Oh, that was
16 long ago. Let's let that go.

17 **DR. KENNETH PORTIER:** Okay. Put
18 your hand down. Anybody else want to comment on
19 the non-cancer weight of evidence assessment? I
20 think we've heard a lot. I have that we've heard
21 from 17 different sets of comments of this. So
22 Dr. Bruckner has his work cut out for him in terms

1 of integrating this all together.

2 And we'll keep in mind what Dr.
3 Jacobs mentioned about the epidemiology study. I
4 think I'm going to leave that as an open question
5 and we can go in and do some research during our
6 breaks and maybe come back to that issue at some
7 point. That was not something that I looked at
8 specifically when I read through those -- when I
9 read through the DRE and the appendices.

10 Any additional comments? So at this
11 point I'll turn back to EPA. Dr. Bruckner, your
12 hand's still up.

13 **DR. JAMES BRUCKNER:** It's up again.
14 I just want to ask everyone to do their best job
15 in presenting their logic and to send that to me
16 again -- your most recent updated comments so I
17 can -- since I have nothing else to do this next
18 week, I can integrate all of those responses and
19 try to fit them together and make it coherent.

20 **DR. KENNETH PORTIER:** The joys of a
21 retired academic, right, who's not really retired.
22 Let's -- I want to turn to EPA. Do you have any

1 clarifying comments? Oh, Dr. Johnson, you're
2 hand's up.

3 **DR. MARK JOHNSON:** Yeah. Dr.
4 Portier, did you say any other comments on the
5 non-cancer section? Am I correct in that
6 assumption? I do have a comment to make on some
7 of the immunotoxicological endpoints. Is that now
8 or is that later?

9 **DR. KENNETH PORTIER:** So this is the
10 Weight of Evidence assessment and -- for
11 development cardiac defects. And I think what
12 we're going to do is come in question 5.3 or 5.- -
13 - yeah, 5.3 is the immuno-effects, so maybe you
14 can hold those until we get there.

15 **DR. MARK JOHNSON:** Yeah. Sure. No
16 problem.

17 **DR. KENNETH PORTIER:** Okay. Just
18 checking to see if anybody else has their hand up.
19 I can turn to Dr. Barone. Any additional
20 questions or comments?

21 **DR. STANLEY BARONE:** Yes. In
22 several cases, I think the panel members have

1 referred to papers or citations that we should
2 consider. If those citations could be sent on to
3 us as soon as possible through the DFO that would
4 be extremely valuable.

5 **DR. KENNETH PORTIER:** Okay. My
6 charge to the panel is please send them on. I
7 know I have three of them in my comments, and I'll
8 send that on to Todd who will pass that on to the
9 team at EPA. So at this point, let's go ahead and
10 move onto question 5.2. And I'll ask Dr. Bethel
11 to read it into the docket.

12
13 **CHARGE QUESTION 5 (5.2)**
14

15 **DR. HEIDI BETHEL:** Hello. Question
16 5.2, please comment on the assumptions, strengths,
17 and weaknesses of the non-cancer and cancer dose-
18 response approaches used to estimate risk to
19 workers, occupational non-users, and consumers.
20 Please also comment on whether EPA sufficiently
21 justified its selections of benchmark responses
22 for benchmark dose modeling results and

1 uncertainty factors -- factor values in deriving
2 the points of departure and benchmark margins of
3 exposure. As part of this discussion, please
4 comment on EPA's justification for selecting a 1
5 percent BMR for the cardiac malformation endpoint
6 based on the severity of the endpoint potential
7 mortality.

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

9 And Dr. Grant has the lead but Dr. Johnson, your
10 hand's up. I don't know if that's a legacy hand
11 up or whether you wanted to make a new comment.
12 It's gone. Okay, Dr. Grant.

13 **DR. STEPHEN GRANT:** Okay. So the
14 vast majority of comments that were submitted for
15 question 5.2 are really more appropriate for 5.1,
16 and most of them have already been brought up.

17 And I have forwarded that to Dr. Bruckner. Also,
18 we -- I got a fair smattering of material that's
19 really more appropriate for 5.3, so I'm really
20 going to say we dealt with the fetal cardiac
21 issues in 5.1. We're going to deal with the
22 immunotox in 5.3, so 5.2 is everything else. And

1 that's pretty easy because we're talking about
2 liver tox, kidney tox, neuro tox, reproductive
3 tox, and developmental tox. And for the most
4 part, the comments are fairly positive that
5 everything was done well.

6 We had one issue that Dr. Lash felt
7 that the exclusion of the Woolhiser study for
8 liver tox was not justified well enough, and he
9 made some comments on the fact that in other
10 places there was supporting data and that the
11 information had been well synthesized. A comment
12 on reproductive effects that only two studies are
13 cited. Perhaps there's more supporting data.

14 I could stop there but I'll go on
15 because, strangely, the last part of the question
16 goes back to the cardiac malformation endpoint.
17 And despite the fact that we've had a robust
18 discussion of that, in my notes, everyone who
19 weighed in on that was positive. So I don't know
20 whether -- I'd have to and cross-check to see
21 whether it was the people who did not have a
22 problem with the Johnson/Dawson data that did not

1 comment on that. But I have four comments that
2 say that the 1 percent BMR was justified in most
3 cases, not specifically tying to cardiac defects,
4 however, just saying it was well justified.

5 And from that I've asked people to
6 think about the other endpoints, but I haven't
7 gotten any specific input. It's a big group. I
8 think, again, we need to ask for anyone who wants
9 to weigh in. And if Dr. Portier agrees, we can --
10 it would be -- we're finished with cardiac
11 malformations and we haven't gotten onto the
12 immunotox, so it would be everything else.

13 **DR. KENNETH PORTIER:** Thank you.
14 Yes. And please put your hand up if you've got --
15 you want to comment on it. I see Dr. Apte.

16 **DR. UDAYAN APTE:** Yeah. Hi. Thank
17 you. This is Udayan Apte. I have a comment about
18 the liver endpoints. In general, I agree with the
19 assessments done here, and the only thing I wanted
20 to bring out is that the change in demographic in
21 the U.S. in terms of liver disease is something
22 that should be considered going forward, I think.

1 More than 30 percent of our
2 population is now either obese or overweight. A
3 large percentage of people are going to have early
4 stages of non-alcoholic fatty liver disease. Some
5 of them may even have non-alcoholic
6 Steatohepatitis that's NAFLD and NASH. These
7 people will have increased amount of fat in their
8 bodies including in their liver, which will
9 definitely change the bioavailability and, in
10 general, toxicokinetics of TCE and may affect the
11 endpoints, specifically the liver endpoints.

12 The exposures -- the doses might
13 change, and, you know, we don't know exactly how
14 that works because not many studies have been
15 done. But that is something that I wanted to
16 bring up at this juncture. I don't know if this
17 is part of the PESS issue, but I thought that
18 since we are talking about everything else other
19 than cardiac and immune, I just wanted to point
20 that out and leave it there for any discussions or
21 comments. Thank you.

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

1 And I think potentially susceptible sub-
2 populations certainly can be discussed here.
3 There may be another -- it'll come up in question
4 6 again, I think.

5 **DR. UDAYAN APTE:** Yes. I realize
6 that.

7 **DR. KENNETH PORTIER:** Anyone else
8 want to comment? Dr. Gilbert.

9 **DR. KATHLEEN GILBERT:** Yes. I --

10 **DR. PORTIER:** And then Dr. Bruckner.

11 **DR. KATHLEEN GILBERT:** I wasn't sure
12 whether my comments about the dose-response of the
13 immunotox go here or in the next, 5.3. Is this --
14 I have specific comments about dose response, and
15 I wasn't clear that that should go here or the
16 next question. Dr. Portier, help me.

17 **DR. KENNETH PORTIER:** Yeah. I'm --
18 I'm -- I'm looking just really quickly. Well --
19 and let's save it for question 5.3 because part C
20 of that gets into the Keil study and -- oh, that's
21 the autoimmunity. But I think we do talk about
22 the appropriate dose method -- metric and the

1 modeling, so why don't we save that -- I -- it's
2 up to you Dr. Gilbert. I -- we can entertain it
3 here. When we write up the report, we'll put it
4 in the more appropriate place, but why don't you
5 go ahead and say it because you're here. And
6 let's go for it now.

7 **DR. KATHLEEN GILBERT:** Okay. So in
8 terms of the dose-response analysis for the
9 immunotoxicity risk, the EPA identified only four
10 animal studies as suitable: the Keil, Kaneka,
11 Sanders and Woolhiser. All these studies scored
12 medium or high in EPA's data quality evaluation.
13 These papers are listed in Table 3-11. These
14 papers all included at least three concentrations
15 of TCE.

16 However, there were severe
17 limitations for some of these studies that were
18 not apparently factored into their scores.
19 Although the Keil study that was ultimately
20 selected for deriving a POD for chronic TCE
21 exposure and the associated outcomes selected,
22 namely autoantibody production were appropriate,

1 the inclusion of the other studies in the
2 selection process generated, for me, grave
3 concerns in the systemic review of the literature.
4 And I have specific comments concerning the
5 limitations of these papers which I will submit in
6 writing to the committee later. That's all.

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

8 Dr. Bruckner.

9 **DR. JAMES BRUCKNER:** Would this be a
10 -- the appropriate place to talk about the point
11 of departure for liver toxicity?

12 **DR. KENNETH PORTIER:** Yes.

13 **DR. JAMES BRUCKNER:** I heard Larry
14 mention -- Larry mentioned something. I'm just
15 looking at the study that was the basis for that
16 was -- I can't pronounce it, Kjellstrand, and our
17 -- had to pay \$42.00 to purchase here online to
18 purchase a copy of that article. And in looking
19 at it, I couldn't tell where the LOAEL or the
20 NOAEL were.

21 And another concern I had was that
22 apparently the -- either a 75 or 150 parts per

1 million caused an increase in liver weight, which
2 the EPA equated with an adaptive response not a
3 toxic response. And in looking at those two lower
4 levels, I couldn't tell -- of their article really
5 doesn't have much information in it whether there
6 was some adverse -- or some effect looking at
7 liver cells other than an increase in liver
8 weight. It appeared there may have minor
9 bacterialization in those cells. I'm not sure if
10 that was water or glycogen or lipid.

11 It was entirely reversible, so I
12 guess my question is was that really a toxic
13 response or merely an adaptive response? So I'd
14 like the EPA to go back and take a look at that
15 and see what their point of departure for liver
16 toxicity really might be. Be more specific and
17 take another look at that.

18 **DR. KENNETH PORTIER:** Thank you. I
19 think Dr. Lash wants to join in on this. Dr.
20 Lash.

21 **DR. LAWRENCE LASH:** Yes. Hi. Well,
22 I just wanted to elaborate a little bit because I

1 guess my comments were kind of summarized by the -
2 - you know, by the lead and by Dr. Bruckner. But
3 just to say that, I guess, the -- what I -- I
4 found it, the rationale for, you know, choosing
5 between the Woolhiser and the Yelstrand --
6 Kjellstrand study, to me, didn't seem very clear.
7 And, you know, they ended up both having almost
8 identical BMDL 10 values, so -- but just the way
9 it was presented was my point about, you know, it
10 was concluded that the increased liver weight was
11 an adaptive response rather than an indicator of
12 toxicity. So I thought that was -- needed better
13 explanation and support.

14 And the other concern was that that
15 study only observed increased liver weight but no
16 other signs of toxicity. So I think there needs
17 to be a better examination of that so there had to
18 -- the liver. So that was all I wanted to say
19 about that.

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

21 Dr. Anderson.

22 **DR. HENRY ANDERSON:** Yeah. I

1 actually want to go back to just briefly to get
2 some information on the cardiac malformations.
3 And that has to do with the differing dissection
4 processes. I mean, it's pointed out and you look
5 at the table with the Johnson study. It appears
6 to have done quite a different dissection
7 approach.

8 And I haven't heard anyone say, you
9 know, how to -- clearly on the Charles River study
10 is it unlikely that the way the Charles River
11 study did it would miss those abnormalities that
12 were found in the dissection process in the other?
13 And that, in my mind, we're talking about
14 replicating studies.

15 I can't see in the Charles River
16 write up they clearly had the results of the
17 Johnson study, and their intent was to try to
18 replicate that. But it's not clear there that
19 they thought their dissection process would have
20 been able to identify the abnormalities that were
21 seen in the Johnson approach. So not being a
22 pathologist for animals, I didn't hear anybody say

1 would both approaches have been able to detect
2 that or not.

3 **DR. KENNETH PORTIER:** Dr. Anderson,
4 I think in the DRE EPA points out that there's a
5 big difference. The Charles Rivers did a -- kind
6 of a standard pathology but they only really
7 looked at that one defect. And that Johnson et
8 al., you know, did a very different -- not
9 necessarily non-standard, but a different kind of
10 pathology that did a deeper dive that looked at a
11 large number of heart defects.

12 And that one of the big differences
13 between the two studies is that, in a sense, the
14 Charles River study didn't duplicate Johnson
15 because it only looked at one defect and not at
16 the others. And I think the DRE points that out.
17 You know, it's a we don't know kind of thing
18 because they didn't look that hard. Does that
19 answer your question?

20 **DR. HENRY ANDERSON:** Yeah, no.
21 That's the way I understood it, but there was a
22 lot of discussion here about, you know, the

1 Johnson study hasn't been duplicated. And I took
2 that to be that that was the intent of the Charles
3 River study was to duplicate the Johnson. But in
4 reality, one of the key factors is they did not do
5 that on the ability to identify the abnormalities.

6 And I don't -- I guess the question
7 really is it isn't answered there is for the
8 pathologist. I think what you're telling me is
9 that the way Charles River did it would not have
10 identified the same -- to the same degree that the
11 Johnson study did. And that -- to me that then
12 raises the question of calling the Charles River
13 negative. And that somehow that negates what
14 Johnson found is somewhat problematic, if in fact
15 they were not using the same degree of pathologic
16 determination. But thank you. That's kind of
17 what I understood.

18 **DR. KENNETH PORTIER:** So I think
19 Dr. Bruckner, Dr. Gilbert, Dr. Lash, and Dr. Apte
20 all still have their hands up, and I don't know if
21 this is new or not new. But I'll start with Dr.
22 Apte. Do you have an additional comment?

1 **DR. UDAYAN APTE:** Yeah. This is Dr.
2 Apte. I have some additional comments.

3 **DR. KENNETH PORTIER:** Go ahead.

4 **DR. UDAYAN APTE:** Okay. So my
5 comment is about the TCE induced liver cancer mode
6 of action. I feel that the analysis done for this
7 was not as deep as it should have been. The
8 current conclusion is that they cannot agree --
9 EPA cannot agree on one particular mode of action,
10 which may be true. But there is significant data
11 on how TCE may be causing, you know, cytotoxicity,
12 and, you know, and there is very little discussion
13 about non-PPAR alpha mediated mechanisms,
14 especially cytotoxicity and its consequences.

15 The well-known effects of TCE in the
16 liver are DNA synthesis, hypertrophy, proliferation
17 leading to hepatomegaly which are in general in
18 response to cytotoxicity cell death in the liver.
19 And that might be due to either chloralhydrate or
20 TCE or DCA. I think there is enough evidence in
21 literature to figure that out, and I think a
22 deeper look at this would have actually helped to

1 narrow down the mode of action. Thank you.

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

3 Dr. Bruckner.

4 **DR. JAMES BRUCKNER:** I just wanted
5 to reiterate that Paula Johnson participated in
6 the Jeff Fisher study and to make sure that the
7 end- -- or the surgical technique was precisely
8 the same. And she actually participated in
9 evaluation of the pathology samples. I know that
10 because one of my graduate students worked with
11 Jeff Fisher to conduct that study. They tried to
12 conduct that one as carefully and as precisely the
13 way that Johnson did their study. So anyhow,
14 Carver Johnson was a part of that study.

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

16 Dr. Vorhees.

17 **DR. CHARLES VORHEES:** Yeah. I
18 wanted to just -- I don't know that I can address
19 Dr. Anderson's point, but one of the things,
20 depending on exactly how you do the heart
21 dissection, most people when they do heart
22 analyses in fetuses, they'll slice through the

1 heart. And, of course, the heart in the fetus of
2 a rat is really small. And so if you -- depending
3 on where you choose to slice, you can obscure some
4 defects like valve defects.

5 At least -- I mean, I haven't done a
6 teratology study for more than 20 years, but where
7 you slice can damage things that you might want to
8 look at. So where you slice, if you're doing the
9 slice technique rather than the dissection
10 technique -- but if you do the slice technique
11 sometimes you slice through the structure that you
12 -- and then it's somewhat ambiguous whether you
13 can see the defect or not. And so, these
14 different techniques each have their strength and
15 their weaknesses in terms of finding these fetal
16 cardiac defects in a rodent.

17 So I do think it's possible that
18 those -- the Charles River study versus the
19 Johnson technique, they may have actually caused
20 some obscuring in one technique versus the other
21 for picking up a particular defect. So that's all
22 I can say about that, but I just wanted to throw

1 that in that there are some technique issues that
2 can cause some problems. Thank you.

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

4 Dr. Barone, you wish to clarify or ask a question?

5 **DR. STANLEY BARONE:** No. This is a
6 clarification to get to the point that Dr. Vorhees
7 was eluding to in response to Dr. Anderson. That
8 is the dissection techniques do differ quite
9 dramatically. We did try to provide some
10 comparisons in our narrative for the potential
11 differences in sensitivity. We also looked at the
12 positive controls and the degree of sensitivity
13 with the positive control data as well and
14 compared Johnson to Fisher to the HSIA study. And
15 there are some stark differences between the
16 results for the different techniques.

17 **DR. KENNETH PORTIER:** Thank you, Dr.
18 Barone.

19 **DR. HENRY ANDERSON:** Thank you.
20 That's very helpful for me.

21 **DR. KENNETH PORTIER:** This is Ken
22 Portier. I wanted to comment on the BNB modeling

1 for -- especially for the cardiac malformation.
2 And I made a comment on question 5.1 about the
3 differences between nominal and measured test
4 consumption. And when I look at Appendix N I
5 can't tell whether the modeling is done with the
6 measured consumption or nominal consumption. And
7 especially for the Charles River data, that would
8 produce two very different model fits. And so I
9 think EPA should definitely look at that and
10 consider it. So that's kind of issue number one.

11 Issue number two, with the Johnson
12 data as I was listening to the conversation, I
13 realized that, if I were analyzing these data, I
14 would take out some degrees of freedom from the
15 controls because they're done in different groups.
16 So I would -- you know, for each group of controls
17 I would kind of remove what I'd call a blocking
18 effect. Now that wouldn't -- that's not a
19 standard analysis. It wouldn't easily fit into
20 the BNBL programming. It's a type of nested
21 modeling, but it's one that would, to a certain
22 extent, kind of penalize the overall degrees of

1 freedom for concurrent controls by taking out some
2 of the degrees of freedom because the controls
3 were done in different groups.

4 And because I don't have the actual
5 data, I can't re-do the analysis. But I will try
6 to write that up ,and I ask Dr. Grant to remind me
7 to write that up and send it to him. But I think
8 that would -- in my mind, it would alleviate a
9 little bit the concern that these controls are in
10 multiple groups. And I realize that in the
11 analysis, EPA did it with the controls separate,
12 with the controls combined, dropping the highest
13 dose, not dropping the highest dose.

14 I know they did a lot of
15 combinations, but this is kind of a more non-
16 standard analysis that, again, I think a
17 statistician looking at this might say, "I might
18 do this just to penalize." Because combining all
19 these controls, and as somebody mentioned, Johnson
20 is able to increase the power in the analysis for
21 seeing an effect. And that increased power also
22 translates into a tighter confidence limit on the

1 fitted dose response model, which would translate
2 into the BNBL.

3 So I, you know, I'd want to be able
4 to kind of see that. By taking out the degrees of
5 freedom for control groups, you actually increase
6 the uncertainty. And that would affect the BNBL
7 at the 1 percent BMR, at least the estimate.

8 One of the other things I haven't
9 heard from the committee is a discussion on the
10 uncertainty factor values and whether EPA has kind
11 of appropriately assigned uncertainty values,
12 especially with regard to the Johnson et al.
13 study. You know, I'm hearing uncertainty. And
14 when we make statements like, "Well, I accept the
15 findings for hazard but I'm not going to put it
16 into a dose-response modeling," to me that
17 translates to something -- says something about
18 uncertainty. Does anybody want to jump in on
19 that? I'm not seeing any hands go up.

20 Are there any other issues that
21 anyone on the panel would like to bring up on
22 question 5.2? Am I still connected? Is anyone

1 there?

2 **DR. KATHLEEN GILBERT:** We hear you.

3 **DR. KENNETH PORTIER:** Okay. I'm
4 hearing a lot of silence, so I'm assuming at this
5 point there is no additional comments. I'm giving
6 people a chance to think.

7 **MR. ALAN KAUFMAN:** Yeah. This is --

8 **DR. KENNETH PORTIER:** Dr. Gilbert.

9 **MR. ALAN KAUFMAN:** -- Al Kaufman.

10 **DR. KENNETH PORTIER:** Oh, Al. Okay.

11 **MR. ALAN KAUFMAN:** Hi. Yeah. I
12 think after listening to everybody I -- you know,
13 I think there are enough issues, I guess would be
14 the way to put it, with the Charles River study
15 that, you know, I think the best we can say is
16 that it is suggestive of a problem. I don't know
17 that there's enough there, you know, given the
18 differences in how the study was conducted.

19 And I think you mentioned, Dr.
20 Portier, that the fairly high rate among the
21 controls -- the negative controls. You know, I
22 have a hard time taking it to the bank. On the

1 other hand, I also have a hard time ignoring it
2 entirely. I think there may be some suggestions
3 of a potential issue there, but I think at this
4 point further study would be needed to try and
5 nail those down. Thanks.

6 **DR. KENNETH PORTIER:** Yeah. Thank
7 you. I -- you know I -- as I keep thinking about
8 the fact that if you use measured concentrations
9 and if the control group had been closer to the
10 historical controls, the Charles River study might
11 have actually shown a dose response. I don't
12 think it would predict near to the lowest level
13 we've seen at the Johnson et al. study, but, you
14 know, it's one of those things that happens. And
15 we keep talking about when the controls -- the
16 concurrent controls don't quite follow the
17 historical controls, what are we to conclude at
18 that point? Dr. Gilbert.

19 **DR. KATHLEEN GILBERT:** Oh, I just
20 wanted to say that I didn't want to seem rude by
21 not responding that I think there's places later
22 on where we talk about uncertainty factors. At

1 least, I remember that, so maybe that's why people
2 aren't speaking up at this point.

3 **DR. KENNETH PORTIER:** Kathleen you
4 broke up as part of the conversation. Could you
5 resay that again?

6 **DR. KATHLEEN GILBERT:** Okay. It
7 wasn't really that useful, but I was just saying I
8 think we talk -- there -- I remember sections
9 later on where we talk about uncertainty factors.
10 And maybe that's why people are not bringing that
11 up at this point.

12 **DR. KENNETH PORTIER:** Okay. I just
13 know that uncertainty is mentioned in this -- the
14 modeling results and the uncertainty factors for
15 deriving the POD. Dr. Vorhees.

16 **DR. CHARLES VORHEES:** Yeah. I just
17 wanted to return to the point. There is, you
18 know, our primary concern is about the inhalation
19 route. And several people have brought this up
20 that there is an inhalation teratology study by
21 Carney. And that's the most relevant. We don't
22 have to do extrapolations from routes, and they

1 saw no major cardiac defects. So I just want to
2 keep that in the forefront of our thinking. Thank
3 you.

4 **DR. KENNETH PORTIER:** Dr. Morandi.

5 **DR. MARIA MORANDI:** Yes. Yes. Just
6 a couple of points. One is on this issue that Dr.
7 Portier underlined several times, which to me is a
8 major issue related to the nominal dose estimate
9 and the actual dose concentration measurement.
10 And that to me is a big issue for the Charles
11 River's study.

12 But in addition, I just wanted to
13 say that I hope when the committee reports comes
14 out that the lack of, for lack of a better term,
15 of robust toxicology data to derive a POD does not
16 translate into saying that heart defects are
17 likely to occur. Because if you look at the epi
18 data, particularly some of the epidemiology
19 studies, they seems to be fairly consistent in
20 terms of finding cardiac birth defects for women
21 occupationally exposed to solvents, including
22 chlorinated solvents and including

1 trichloroethylene as part of those chlorinated
2 solvents. So I'm a little bit concerned that,
3 because these studies all have major problems in
4 terms of demonstrating with an animal model the --
5 biologically that effects do occur and they are so
6 weak, that the whole issue that relationship to
7 exposure to TCE and the potential for fetal heart
8 defects, that that's not kind of dismissed all
9 together when we write this report. That's all.

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

11 Dr. Johnson.

12 **DR. MARK JOHNSON:** Yeah. Thank you.

13 I kind of sorry we keep going back to this, but
14 I'm not convinced that the method that the Charles
15 River study used to excise the heart is less
16 sensitive than the method that Johnson did. I'm
17 not a veterinary pathologist. I have one that
18 works for me but -- and I wish we had one on the
19 panel who could elucidate this more.

20 But as I understand, the method they
21 used was Staples method. And I think it does --
22 it reduces the likelihood, as I understand it,

1 that what Dr. Vorhees said is accurate that it --
2 you don't do damage by slicing it in that manner.
3 I'm not convinced that the method that Johnson did
4 could result in abnormalities just by the act of
5 just doing it. I don't know, but I'm -- right now
6 I'm just not convinced that the method that
7 Charles River did is any less sensitive than the
8 method that Johnson did.

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

10 Dr. Cory-Slechta. Dr. Cory-Slechta we're not
11 hearing you.

12 **DR. DEBORAH CORY-SLECHTA:** Sorry. I

13 just unmuted. I just want to agree with Dr.
14 Morandi, and I think her point is a very valid
15 point. We need to be looking at the weight of the
16 collective evidence, not focusing necessarily just
17 on, you know, one study or another.

18 I'm also very troubled by the
19 difference between the stated values and the
20 consumed values in the Charles River study because
21 I think that gives a very different interpretation
22 to the outcome. And I go back to another comment

1 made about the small number of litters used in
2 those studies, as well as the deficits in the
3 statistical approaches. But all in all, again, I
4 concur with Dr. Morandi that it's really about a
5 collective weight of evidence across these.

6 **DR. KENNETH PORTIER:** Yeah. Dr.
7 Cory-Slechta, but for doing dose-response
8 modeling, which is question 5.2, we have to come
9 down to the data and say which of these data sets
10 is of enough quality that EPA can do an acceptable
11 dose-response model and then be able to use the
12 results effectively to set a point of departure.
13 Dr. Rosol.

14 **DR. THOMAS ROSOL:** Yes. Thank you.
15 So I'm responding as a veterinary pathologist.
16 And so we do have one on the panel. But in terms
17 of the comparison of the Johnson study to the
18 Charles River study, I think we're sort of
19 comparing apples and oranges. You know, the
20 Charles River study is a standardized GLP
21 developmental toxicology study. And if you look
22 at all the variables that they have to examine and

1 what they do in this study, it's extremely robust
2 and broad.

3 And you compare that to the Johnson
4 study, and that's a very focused investigation on
5 the heart. And that wasn't the purpose of the CRL
6 study, so I don't think we're doing justice in
7 comparing them one on one. I think what's
8 important is to take away the valuable data from
9 each study. And, you know, one thing I find very,
10 very important is to look at the primary data
11 before I evaluate the statistical tests and things
12 like that.

13 And when I look at the Johnson Table
14 2 on page 290 of the manuscript, the atrial septal
15 defect shows a very nice dose response, which I
16 put a lot of strength in. Now, I know there's a
17 lot of concern whether the controls are
18 appropriate, and I'm assuming the -- if you make
19 the assumption there that the data reported in the
20 table is appropriate, then it's an impressive
21 effect and I think we should take that into
22 consideration. My guess is the Charles River

1 study did not thoroughly look at the atria because
2 that's not part of the standard protocol when they
3 prepared the heart to evaluate for ventricular
4 septal defects. And that was the goal of the
5 study and their data stands as is. So I don't
6 really like the idea of saying of -- that their
7 replication except for the total number of
8 ventricular septal defects.

9 And in terms of the ventricular
10 septal defects in the Johnson study, there is some
11 evidence of a dose response between 1.5 and 1,100
12 so I -- so to me, the Johnson study raises the
13 flag of potential septal defects in the atrium and
14 the ventricle. The Charles River study does find
15 ventricular septal defects. I think the
16 historical controls would be -- should be taken
17 into account for the Charles River data since we
18 have that information. Thank you.

19 **DR. KENNETH PORTIER:** Thank you, Dr.
20 Rosol. Do we have any additional comments on
21 this? I'm going to first turn to Dr. Grant and
22 say, did you get all of this?

1 **DR. STEPHEN GRANT:** No. I hope Dr.
2 Bruckner did.

3 **DR. KENNETH PORTIER:** Oh. Is
4 Bruckner the -- I thought you were 5.2.

5 **DR. STEPHEN GRANT:** We're talking in
6 5.2, but it's all about 5.1. We can't seem to get
7 off it.

8 **DR. KENNETH PORTIER:** Well, there
9 were a few comments on 5.2. You're right. You're
10 right. Okay. At this point I'm going to turn to
11 EPA and say, do you have any comments or
12 clarifying questions on the panel response?

13 **DR. STANLEY BARONE:** No further
14 comments. This is Stan Barone. I think the panel
15 has gone backwards but appreciate the comments and
16 capturing the robust dialogue.

17 **DR. KENNETH PORTIER:** We keep trying
18 to go forward, but sometimes the conversation has
19 to cycle a little bit. Dr. Rosol your hand is
20 still up, but I'm assuming that's just legacy
21 unless you want to make a comment. Okay. At this
22 point, let's move on to question 5.3. We can at

1 least get a start on this before we break for
2 lunch a little after 1:00. Dr. Bethel, please
3 read in question 5.3 into the docket?

4 **DR. HEIDI BETHEL:** Okay. I'm here.
5 Question 5 -- hello? Can you hear me?

6 **DR. KENNETH PORTIER:** Yes.

7
8 **CHARGE QUESTION 5 (5.3a, 5.3b AND 5.3c)**
9

10 **DR. HEIDI BETHEL:** Hello? Yes.
11 Okay. Good. Question 5.3, EPA determined that
12 the immune effects from Selgrade and Gilmour
13 (2010) represent the best dataset for use -- to
14 use for evaluating acute effects and the
15 autoimmunity effects from Kiel et al. (2009)
16 represent the best dataset to use for evaluating
17 chronic non-cancer effects.

18 Question 5.3a, please comment on
19 EPA's selection of these studies as the best
20 representative endpoints, including consideration
21 of the point of departure derivation and the
22 benchmark margins of exposure.

1 EPA -- question 5.3b, EPA did not
2 input the data on response to pulmonary infection
3 from Selgrade and Gilmour into the TCE PBPK model
4 due to uncertainty over the proper dose metric to
5 be used. Therefore, EPA relied on standard
6 methods for cross-species scaling, in other words,
7 blood to air partition coefficient for human
8 equivalent concentration, allometric scaling for
9 human equivalent dose, and accordingly reduced the
10 default 10x animal to human uncertainty factor to
11 3. Please comment on whether this approach is
12 appropriate and whether the uncertainty factor is
13 sufficient.

14 5.3c, EPA acknowledges that in using
15 the Keil et al. study, EPA is relying on an early
16 clinical marker to account for susceptibilities
17 and the endpoint is a precursor to adverse effects
18 for autoimmunity. This lowest observed adverse
19 effect level was considered in this context and
20 the LOAEL to No Observed Adverse Effect Level, or
21 NOAEL, uncertainty factor was reduced from 10 to
22 3x. In light of this, please comment on EPA's use

1 of a 3x uncertainty factor for human variability
2 and LOAEL to NOAEL extrapolation.

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

4 Dr. Grant.

5 **DR. STEPHEN GRANT:** Okay. Well,
6 starting with A, and we'll probably -- I'm
7 probably going to stop and let everyone else weigh
8 in on A before I go on to B. What we have in
9 Selgrade and Gilmour was what I consider to be an
10 excellent study with a functional endpoint, which
11 is mortality. They demonstrated immune
12 suppression by mortality upon exposure to a
13 pathogen. You can't really ask for more than
14 that, but I, and at least one other panel member,
15 suggest that using mortality as the point of
16 departure is probably an underrepresentation on
17 sublethal effects. So that one could anticipate
18 that there would be toxic effects on the immune
19 system below the level of allow- -- of causing of
20 death when against a challenge.

21 A couple of other things about
22 Selgrade and Gilmour. One, Dr. Morris wanted to

1 highlight that this was a single study and in a
2 single species. Let's see. Okay. And Dr.
3 Johnson had issues with the model fit to Selgrade
4 and Gilmour, that the data was questionable --
5 model fit was questionable, and I'll let him go
6 farther if they feel they need to.

7 So that's immunotox from the point
8 of view from acute, and it doesn't seem to have a
9 lot of background. And one of the things that
10 several panel members indicated that there seemed
11 to be and ide- -- the idea that immunotox was
12 monolithic and that the Keil et al. autoimmunity
13 was in some way supporting of the results of
14 Selgrade and Gilmour. And again, several panel
15 members said induction of autoimmunity is to some
16 degree the opposite of an immunosuppressive
17 effect. So we're in fact invoking immunotox but
18 in one way for an acute dose and in another way
19 for a chronic effect.

20 With the chronic effect, it was
21 noted by Dr. Hossain, I think, that the --
22 although we had markers there was no progression

1 of autoimmune disease in an autoimmune prone
2 mouse. So there wasn't that demonstration of a
3 clinical effect going forward from that. And Dr.
4 Gilbert suggested that there needed to be a --
5 further study on disease progression in autoimmune
6 mice.

7 And let's see. There were more
8 issues with Keil. Dr. Johnson had issues with the
9 data dose level were misreported from Keil et al.
10 and that the dose levels from Keil et al. were
11 outside the range of other values and are of
12 questionable significance. Okay. I think that's
13 enough for now, and we'll come back to B. Again,
14 there's many, many people on this subsection, so
15 probably the people that I mentioned, if you felt
16 that I encapsulated your story, fine. Otherwise,
17 please feel free to elaborate.

18 **DR. KENNETH PORTIER:** This is Ken
19 Portier. I'd like to hear a little bit of the
20 elaboration. Maybe I can start with Dr. Johnson,
21 and you can kind of elaborate more, Mark, on your
22 comments.

1 **DR. MARK JOHNSON:** Yeah. Sure. I
2 do have a slide I'd like to show. I don't know if
3 you can get that up in a reasonable time. But
4 until then I can go on with further elaboration on
5 some other ones.

6 There we go. Let's just go along
7 with that. This is a slide we put together a
8 while back, adjusted doses for immune response.
9 And what you have is a combination of inhalation
10 and oral data. And I think this sort of
11 representation really helps me to see patterns.
12 And I think, you know, there's a reason why people
13 do this in tox profiles. It's the reason why
14 ACIGH in theirs and other entities do it as well.
15 It helps you to see where the patterns are.

16 And to me, you know, it seems that
17 maybe the inhalation effects occur at different
18 levels than what the oral effects occur on. Now,
19 there could be really good reasons for this. It
20 may not have anything to do with route of
21 exposure. It may have to do with what you're
22 measuring and the methods and how administered and

1 that sort of thing. But this sort of depiction of
2 endpoint data in the studies is useful, and I
3 would encourage the EPA to do this whenever
4 possible, this sort of depiction.

5 To be more precise regarding some of
6 my comments, when I reviewed the Debra Keil's
7 study, I noticed that the doses reported in the
8 DRE is not what is reported in the paper. What
9 she reports is 0.001, 0.4 and 14 parts per
10 million, or if you like, 0, 1, 400, and 14,000
11 parts per billion of TCE in water. Purity,
12 stability, and homogeneity is not reported, but
13 they said they do analytically analyze their
14 concentrations. I just could not find those data.

15 The exposures were static three-day
16 renewal, which is probably as good as it gets.
17 But I still question why this study got a high-
18 quality rating. As Dr. Grant said, I wonder about
19 the combining of the endpoints, and I would like
20 to hear Dr. Gilbert's assessment of measuring the
21 thymus farther along in that stage of development.
22 Typically, the thymus is very small, and you can

1 get a lot of variability just in trimming.

2 And regarding the model fit, when I
3 looked at the benchmark dose, it looks like
4 there's a clear threshold, but the other -- it
5 wasn't a dose -- quite a dose response and lots of
6 variations. So I mean, a straight line would have
7 represented those data as well as any kind of
8 logistic or other fit to me, just looking at the
9 data spread. So I question the lack of model fit
10 for the benchmark dose. And that's all I have.
11 Thank you.

12 **DR. KENNETH PORTIER:** Dr. Barone, I
13 saw your hand up. Did you want to make a comment
14 or ask a question?

15 **DR. STANLEY BARONE:** Yes. This is a
16 clarifying question. I think Dr. Johnson may be
17 making a recommendation for exposure response
18 arrays for each effect domain. We included
19 exposure response arrays in our summary for
20 critical effects for the domains, but we did not
21 include a presentation for each -- within each
22 domain. And if that's a recommendation I'd like

1 some clarity.

2 **DR. MARK JOHNSON:** Yeah. Well, what
3 I meant is figure diagrams. Scatter diagrams such
4 as this one helps us to see where the data are in
5 relationship to the effects. And so I think as
6 biologists we're all incumbent in discriminating
7 patterns. One could argue the entire discipline
8 of epidemiology is based on the search of
9 patterns. And so this just aids us to be able to
10 see, you know, what are the effects, what are the
11 outliers, what are the things that are coming
12 together, and helps us discern more about where
13 these effects occur and at what dosages.

14 Now, optimally you like to be --
15 have them harmonize to human equivalent
16 concentrations, which I believe is what we did
17 here in terms of parts per million. So I'm sorry,
18 Dr. Barone. If you did do this, I didn't see it
19 in the DRE. Is it in the appendix?

20 **DR. STANLEY BARONE:** Actually, in
21 our slide presentation, it's slides 63 and 64.

22 **DR. MARK JOHNSON:** Okay. Roger. So

1 I guess the recommendation would be to put that in
2 the DRE.

3 **DR. STANLEY BARONE:** Thank you.

4 **DR. KENNETH PORTIER:** Dr. Gilbert.

5 Dr. Gilbert, you unmuted and then muted back
6 again.

7 **DR. KATHLEEN GILBERT:** Sorry.

8 **DR. KENNETH PORTIER:** You're
9 unmuted.

10 **DR. KATHLEEN GILBERT:** Okay.

11 **DR. KENNETH PORTIER:** Now we can
12 hear you.

13 **DR. KATHLEEN GILBERT:** Okay. I just
14 wanted to say that I agree that the Selgrade and
15 Gilmour paper was excellent. They got a dose
16 dependent increase in mortality when the mice were
17 exposed to TCE through inhalation. And this
18 increase induced mortality basically corresponded
19 with a decrease in lung clearance of the bacteria.
20 So not only did you see dose dependent effects on
21 your outcome, you also saw a mechanism associated
22 with that. So I thought it was a really well-done

1 paper and represents an appropriate choice for
2 evaluating acute effects.

3 Now, we've heard that there might be
4 conflicting results when you say that we're
5 talking about acute immunosuppression when we're
6 talking about chronic autoimmunity which tends to
7 be -- you would think they would be the opposite.
8 But I don't have a problem at all with thinking
9 that a three-hour exposure -- inhalation exposure
10 to TCE could have a suppressive effect on the --
11 look -- on the lung macrophages resulting in the
12 immunosuppression we saw on the Selgrade paper.
13 When we're talking about the Keil paper and other
14 kinds of autoimmunity, we're talking about
15 systemic autoimmunity, which is a whole different
16 ballgame, and it is mediated, of course, by lots
17 of other different kinds of cells. So I don't
18 have any trouble with reconciling the two studies.

19 Now, the Keil paper, as Dr. Johnson
20 said, they looked at thymus, and I'm not a big fan
21 of looking at thymus size because, as he said,
22 it's very hard to trim accurately to know that for

1 sure that you've -- from one mouse to the next
2 you're doing this exact same thing. But
3 ultimately the EPA decided not to go with the
4 thymus size and went with the autoantibody
5 production, the selection of the anti-single-
6 stranded and anti-double-stranded DNA read outs.
7 And that seemed to me appropriate with the
8 relative consistency of the results in their non-
9 autoimmune prone mice, which were the B6, C3, F1.

10 However, they did not see an effect
11 in the NZB WF1 mice, which supposedly were
12 autoimmune prone. And there's possible issues
13 associated with that, and there are plenty of
14 other papers that do show that TCE exposure in
15 autoimmune prone mice do lead to actual pathology.
16 So I would have liked to have seen that included
17 in the EPA's assessment. But overall, I thought
18 that the Keil paper would be the development of
19 the autoimmune antibodies in the non-autoimmune
20 prone mice represented an appropriate choice for
21 looking at the chronic effects. And that's all I
22 have.

1 **DR. KENNETH PORTIER:** Thank you Dr.
2 Gilbert. Did I hear Dr. Hossain also added some
3 comments? Dr. Hossain, do you want to clarify any
4 of your comments?

5 **DR. MUHAMMAD HOSSAIN:** I don't have
6 additional comments.

7 **DR. KENNETH PORTIER:** Okay. Thank
8 you. Does anyone else want to comment of 5.3a,
9 selection of studies for best representative
10 endpoints? Dr. Jacobs with EPA, you have a
11 comment?

12 **DR. KEITH JACOBS:** Just some
13 clarifications based on some comments I'd heard.
14 There was discussion about trying to relate the
15 immunosuppression in Selgrade acutely to the
16 chronic autoimmunity in Keil. We actually relate
17 the immunosuppression in Selgrade to other chronic
18 immunosuppression studies. I think one of them
19 was Sanders et al., and I think there was an
20 additional one as well. So there are chronic
21 immunosuppression studies, not just the Keil which
22 is -- I -- we agree is a distinct endpoint.

1 And then there was talk about model
2 fit for Keil and that's correct. It was -- I
3 believe it was actually not BNB modeled, and it
4 was just the LOAEL value that was run through the
5 PBPK because there was not the model fit. So that
6 was accounted for there, but that was adjusted and
7 that's why it has a LOAEL, which is part -- which
8 is one of the questions here, I think C. It has
9 the LOAEL to NOAEL adjustment of three because it
10 was the lowest model.

11 And then we did try modeling
12 sublethal effects in Selgrade. I think one of
13 them is provided in the appendix. However, there
14 was not enough statistical power. The study
15 authors even did a power analysis and essentially
16 said they used many mice for the mortality and
17 then kind of did the other assays as a proof of
18 principle but at much lower *n*. So there wasn't
19 sufficient power to get, unfortunately, a
20 sublethal POD. And that's all.

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

22 Dr. Gilbert and then Dr. Johnson.

1 **DR. KATHLEEN GILBERT:** I just wanted
2 to say that in terms of the chronic
3 immunosuppression studies, I know there's some out
4 there where they look at responses for example to
5 sheep red blood cells. But overall, I think the
6 evidence is much more overwhelming that, as far as
7 a chronic exposure, you tend to get
8 hypersensitivity of some sort, including
9 autoimmune diseases, rather than
10 immunosuppression. And I think that the
11 immunosuppression is much more compelling in a
12 study such as the Selgrade where they look at
13 acute exposure in a very specific model where
14 you're looking at effects on the macrophages.

15 **DR. KENNETH PORTIER:** Dr. Johnson.

16 **DR. MARK JOHNSON:** Yeah. Just to
17 clarify a comment. The immunosuppression versus
18 immunoenhancement or autoimmunity I was taking
19 from the Keil paper where you saw a decrease in
20 thymus size or mass, weight. Also, it says in the
21 DRE there was a difference in thymus cellularity,
22 a lower trend dose-response, which that's not

1 accurate. It wasn't statistically significant.

2 And so that's the confusion that I
3 had in my mind when I saw that. Because typically
4 when the thymus gets smaller and you a reduction
5 in cellularity, you have an immunosuppressive
6 event. But yet the single strand, double-stranded
7 DNA in the non-sensitive mice goes in the opposite
8 direction. So that was the point of confusion I
9 was having. Over.

10 **DR. KENNETH PORTIER:** Dr. Gilbert,
11 your hand's up.

12 **DR. KATHLEEN GILBERT:** Yes, in
13 regard to that point, I mean, I understand the
14 confusion. And so the Keil paper looked at the --
15 supposedly got a decrease in thymus size, but they
16 really didn't get a decrease in thymus
17 cellularity. And a decrease in thymus size is not
18 something that's normally associated with adult
19 exposure to TCE.

20 So I kind of discounted that and
21 went with the results that they got for the
22 autoantibody responses, which were more -- much

1 more consistent. And they looked at those over
2 multiple time points and saw those effects. So I
3 don't have a problem with using the autoantibody
4 production as opposed to trying to talk about the
5 thymus size, which I didn't really find
6 convincing.

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

8 **DR. STEPHEN GRANT:** Okay. Just to
9 finish off that last point, we -- I think Keil et
10 al. -- and there's been other discussion -- are
11 not the point. I think we've got some other
12 chronic long-term studies. The issue would be
13 Selgrade and Gilmour were specifically pulled out
14 as being a single paper with a significant
15 endpoint. And I think other people felt that
16 going onto Keil et al., despite the fact one is
17 acute one is chronic, was to imply that Keil et
18 al. and the data on the chronic exposures were
19 supportive of Selgrade.

20 Selgrade and Gilmour everyone agrees
21 is a good paper. The question that we should ask
22 is has it been replicated? Is it representative

1 of other studies that show acute immune
2 suppression? And again, I'll -- I think I'll open
3 it up again before we go on to see if anyone can
4 offer anything there.

5 **DR. KENNETH PORTIER:** Anyone? Dr.
6 Gilbert.

7 **DR. KATHLEEN GILBERT:** So I'm trying
8 to understand what your concern is. Are you
9 saying that you don't think the TCE does cause
10 immunosuppression under any circumstances? I
11 mean, I agree that I don't see that the Keil et
12 al. paper supports the Selgrade and Gilmour paper,
13 except that they both demonstrate some type of
14 immunotoxicity. But I'm not aware that there's
15 been any other studies that tried to duplicate the
16 Selgrade and Gilmour and didn't -- and found
17 opposite results. So I don't actually have any
18 trouble with accepting their conclusion.

19 **DR. STEPHEN GRANT:** Okay. I just
20 wanted to put it out because it is a comment from
21 one of the panelists that Selgrade and Gilmour,
22 for all of its positive aspects, basically stands

1 alone. So we do have a problem. We've just gone
2 over an awful lot of work on the cardiac heart
3 defect issue about whether or not the results can
4 -- are replicated. And I just want to be sure
5 that we are applying the same criteria to two
6 different endpoints. I'm ready to go on with B if
7 everyone else is.

8 **DR. KENNETH PORTIER:** Well, I think
9 Dr. Morris and then Dr. Jacobs wants to come back
10 with a clarification. Oh, Dr. Jacobs just dropped
11 his hand. Dr. Morris.

12 **DR. JOHN MORRIS:** Yeah. I mean, I
13 was one that raised the idea that this was a
14 single study in isolation. And I only raised in
15 in the context that perhaps that should be
16 mentioned in the uncertainty discussion about
17 this, not that we should discount the results.
18 But it certainly hasn't been replicated, not that
19 it wouldn't be if someone had done it. So I think
20 it's a matter of uncertainty.

21 **DR. KENNETH PORTIER:** That's a good
22 point. Thank you.

1 **DR. MARK JOHNSON:** Yeah. I just
2 want to say I don't disagree with anything that
3 Dr. Gilbert said, but this endpoint still is -- at
4 least I don't -- I don't quite understand the
5 validity of the single-stranded, double-stranded
6 anti-DNA antibody response. I don't know how well
7 it's been calibrated. I don't know how much of a
8 change you would see to see a difference.

9 And I guess the same question that
10 we just asked of Selgrade and Gilmour, do we see
11 the same sort of thing in any other data that --
12 that suggests, you know, a hyper immuno-response
13 would help support that? I just don't know. It's
14 an outlier. Again, it's from an oral exposure.
15 Those two things give me concern.

16 **DR. KENNETH PORTIER:** Dr. Gilbert.

17 **DR. KATHLEEN GILBERT:** So the oral
18 exposure issue, I'm not exactly sure why that
19 gives you concern. I mean, maybe not for
20 occupational exposure but certainly for the
21 general population, oral exposure is of concern,
22 and there are many people who use that model when

1 they're looking at TCE toxicity. In terms of the
2 auto antibodies, they're also a number of papers
3 showing that TCE increases different kinds of auto
4 antibodies.

5 And I agree that the single-stranded
6 and -- and double-stranded DNA are harder than
7 certain kinds of antibodies to quantitate.
8 They're harder to do ELISAs for, but they have
9 been used for decades, as I'm sure you know, to
10 look at the initial stages of autoimmunity. And
11 they're certainly used in humans to look at
12 autoimmunity. So I -- and as I said, there are a
13 number of papers in other mouse models where they
14 have found similar things, and I'd be happy to
15 forward those to the committee.

16 **DR. STEPHEN GRANT:** Please do.

17 **DR. KENNETH PORTIER:** Dr. Grant, I
18 think this is a good time to move on the B, 5.3b.

19 **DR. STEPHEN GRANT:** All right. I
20 didn't get very many responses to this one. In
21 fact, I was considering just letting Dr. -- okay,
22 there's -- let's see. So from Dr. Morris, I think

1 a PBPK estimate to total absorbed dose would be
2 better than the default RFC based dosimetric
3 studies. It -- okay.

4 And from Dr. Lash, the use of
5 standard methods for cross-species scaling, this
6 is only addressed in a pair of footnotes, and he
7 provides the footnotes. This is an important
8 point and should be more prominent in the text
9 rather than simply relegated to footnotes of a
10 table. And that's basically all the comments I
11 got on B. Several people said not their area of
12 expertise.

13 **DR. KENNETH PORTIER:** So maybe, Dr.
14 Morris, you can elaborate on your comments.

15 **DR. JOHN MORRIS:** Yeah. This has
16 sort of come up in a lot of my comments as we have
17 a validated PBPK model, so why don't we use it?
18 Seems to me that, you know, total absorbed dose is
19 a perfectly appropriate dosimetric when you have
20 no idea about the mode of action. So I think a
21 model-based estimate is better than the default
22 assumption. I agree that actually this only shows

1 up in footnotes, and it ought to be explicitly
2 indicated along that they are assuming it's a
3 category 3 gas and using the RFC because it
4 doesn't really say that.

5 And I'll get to this later. I have
6 a problem with the concentration times time Haber
7 rule linear time course extrapolation. Again, you
8 got a PBPK model, so you could use that model to
9 do the, you know, the time duration of exposure
10 extrapolations. But basically, you got a model,
11 so let's use it.

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

13 Dr. Lash, do you want to elaborate on your
14 comments? Dr. Jacobs, you want to -- you have a
15 question?

16 **DR. KEITH JACOBS:** Yes, I just
17 didn't catch that. Can I hear the first comment?
18 What would be a potential dose metric that was
19 recommended? I just missed that in this comment.

20 **DR. JOHN MORRIS:** Sure. Sure. How
21 about total absorbed dose? Your model gives it,
22 inhaled exhaled, right? Just do total absorbed

1 dose.

2 **DR. KEITH JACOBS:** Okay. I'm not
3 sure if the model does allow for time adjustment,
4 but we can look into that.

5 **DR. JOHN MORRIS:** We'll get to that
6 later.

7 **DR. KEITH JACOBS:** Yeah. In the
8 Haber's rule. Yeah.

9 **DR. JOHN MORRIS:** We'll get to that
10 later.

11 **DR. KEITH JACOBS:** That's a separate
12 question. Yeah.

13 **DR. JOHN MORRIS:** Yeah. Yep.

14 **DR. KENNETH PORTIER:** Does anyone
15 else want to comment on 5.3b? It's a pretty
16 technical area. Dr. Grant, did we get any
17 comments on the uncertainty factor issues? I
18 mean, it looked pretty standard to me, I guess.
19 I'm just wondering.

20 **DR. STEPHEN GRANT:** I didn't -- I
21 stopped short of saying that. Let me see.

22 **DR. KENNETH PORTIER:** Dr. Morris.

1 DR. JOHN MORRIS: I mean, I just --

2 DR. STEPHEN GRANT: No. It's just
3 that where I got comments they were positive.

4 DR. KENNETH PORTIER: Oh, okay. Dr.
5 Morris.

6 DR. JOHN MORRIS: Yeah. That's what
7 I was going to say. It's appropriate to use three
8 if you're doing dose-symmetry in modeling.

9 DR. KENNETH PORTIER: And for the
10 allometric scaling, where they didn't use the
11 model. Right?

12 DR. STEPHEN GRANT: It's actually,
13 they do -- using the RFC methodology, that is a
14 dosimetric approach, so a three is useful --

15 DR. KENNETH PORTIER: Oh.

16 DR. STEPHEN GRANT: -- and
17 appropriate for that as well.

18 DR. KENNETH PORTIER: Okay. Just
19 wanted to assure myself that someone on the panel
20 had looked at that and was comfortable with it.
21 Dr. Grant, is there anything else on 5.3b?

22 DR. STEPHEN GRANT: Nothing that I

1 have. So I --

2 **DR. KENNETH PORTIER:** Does anyone
3 else on the panel want to comment on 5.3b? EPA,
4 do you have any additional comments on the panel's
5 response to 5.3b?

6 **DR. STANLEY BARONE:** Sorry. I was
7 on -- we were on mute. This is Stan Barone. I
8 think we've covered it.

9 **DR. KENNETH PORTIER:** Okay. Let's
10 go on to 5.3c. Dr. Grant. Dr. Grant, we're not
11 hearing you if you're speaking.

12 **DR. STEPHEN GRANT:** Oh. Sorry. My
13 personal comment on this section was that the --
14 sorry, I've got many things open here. The
15 uncertainty factor was stated as being reduced to
16 three, and it wasn't clear the rationale. Another
17 panel member said, again, the rationale for this
18 is not presented in the document. Presumably this
19 is done because this is a precursor effect.
20 However, given that an autoimmune response was
21 actually seen isn't it clear that this is, in and
22 of itself, an effect and should use a UF of 10?

1 Okay.

2 Another -- however, Dr. Morris says
3 he's fine with three. Again, the only explanation
4 provided was that, yeah, it's just a statement
5 because it's considered an early subclinical
6 response. I guess the answer is that the question
7 -- we don't see exactly why, because this is a
8 subclinical response, the adjustment in the
9 uncertainty factor is justified.

10 **DR. KENNETH PORTIER:** So it sounds
11 like a recommendation would be to further --

12 **DR. STEPHEN GRANT:** Better --

13 **DR. KENNETH PORTIER:** -- justify or
14 better justify this. There's not a lot of concern
15 around the three versus 10, but we feel the EPA
16 needs to better justify that choice.

17 **DR. STEPHEN GRANT:** I think so. If
18 anyone else does-- -- if anyone feels differently,
19 now is the time to weigh in.

20 **DR. KENNETH PORTIER:** Who was it you
21 said was okay with the three? Dr. Lash or was
22 that Dr. Morris? Dr. Lash.

1 **DR. STEPHEN GRANT:** Dr. Morris. I
2 don't have a problem with using UF 3.

3 **DR. KENNETH PORTIER:** Oh. Okay.
4 John?

5 **DR. JOHN MORRIS:** This is Dr.
6 Morris. Yeah. Actually, I agree with the other
7 comments that it needs to be better substantiated.

8 **DR. KENNETH PORTIER:** Okay. Anyone
9 else want to chime in here? Dr. Lash your hand is
10 up. I'm still not hearing you. You went off mute
11 but I'm still not hearing you.

12 **DR. LAWRENCE LASH:** I'm sorry. Can
13 you hear me?

14 **DR. KENNETH PORTIER:** Yes, we can
15 hear you now.

16 **DR. LAWRENCE LASH:** Okay. Sorry.
17 Too many buttons to press to mute and unmute.
18 Yeah. No. Basically, my point I think was stated
19 that, if this is -- the fact that it's an early
20 clinical or subclinical marker -- if this is some
21 standard -- because I don't recall that -- this
22 isn't really my expertise per se. But if this is

1 a standard practice to reduce the uncertainty
2 factor because of that, then it should be, you
3 know -- something should be cited and, you know,
4 reference made. That was all.

5 **DR. KENNETH PORTIER:** Yeah. That's
6 a good point. I -- yeah, I think EPA should point
7 to that. I don't remember seeing that standard.

8 **DR. LAWRENCE LASH:** Right.

9 **DR. KENNETH PORTIER:** But the other
10 question is do we agree that this is early
11 clinical marker? And, you know, I wasn't sure.
12 In listening to this conversation, I'm not quite
13 sure that we have agreement on that. Dr. Grant?

14 **DR. STEPHEN GRANT:** I think the
15 reason that we consider it an early clinical
16 marker is because we don't see progression of
17 disease. And so it's still hypothetically
18 clinically important rather than demonstrably
19 clinically important.

20 **DR. KENNETH PORTIER:** Dr. Barone,
21 clarification.

22 **DR. STANLEY BARONE:** Sorry. Also

1 struggling to get to the unmute button. That last
2 point -- that last part of the question is the
3 critical part. If the committee -- if the experts
4 -- we want input on whether the experts agree that
5 this is an adverse effect in and of itself or just
6 the antecedent to an adverse effect. And there
7 was some debate or question about whether this is
8 a pre-clinical marker or not. So we wanted to get
9 some dialogue around that, and that would inform
10 whether we stick with a 10 or 3x for this.

11 **DR. KENNETH PORTIER:** Yeah. I was
12 trying to get there. Dr. Grant.

13 **DR. STEPHEN GRANT:** It's just Dr.
14 Gilbert actually said that, you know, in the -- we
15 would have expected there to be effects if you
16 have autoimmunity to a bodily component like DNA.
17 But since it hasn't been demonstrated, she was
18 actually asking for further study on that. And
19 the question is without it I don't think we can
20 simply assume that there's a clinical effect.
21 It's not demonstrated.

22 **DR. KENNETH PORTIER:** Dr. Gilbert.

1 **DR. KATHLEEN GILBERT:** Well, I'm not
2 exactly sure what you mean by that. I mean, I
3 agree that the presence of autoantibodies is not
4 necessarily an indicator of autoimmune disease,
5 but it's certainly an indicator of some alteration
6 in the immune system. So what has to occur for us
7 to call something a toxicity? We look at
8 increases of liver enzymes, even though we don't
9 necessarily see hepatitis, and we indicate -- we
10 seem to indicate that that is a sign of toxicity.

11 And to me, when you're altering the
12 immune system into the effect that you're starting
13 to make antibodies against a self-component, even
14 though you may not actually have kidney pathology
15 or any other kind of pathology at that point, then
16 is that toxicity or not? I tend to think it is.

17 **DR. STEPHEN GRANT:** Well, is that
18 something we should put back on the EPA that there
19 should be a literature on -- and I would invite
20 you to put other things than DNA -- autoantibodies
21 and the association between them should be between
22 that and clinical effects should be a part of this

1 discussion? They're kind of throwing it on us,
2 but I -- it doesn't sound like anyone here's an
3 expert on this.

4 But the assumption seems to be that
5 this is a good, well-associated marker for immune
6 disease -- autoimmune disease, not just induction
7 of autoimmunity. And that, if it is strongly
8 linked to clinical effects that -- then it should
9 be considered to be a biomarker of clinical
10 effects, not potential clinical effects. Is that
11 -- anyone have anything -- more clarification than
12 that?

13 **DR. KATHLEEN GILBERT:** Well, this is
14 Kate Gilbert again. It's not necessarily an
15 indicator of actual tissue pathology, but, like I
16 said, it's not clear to me what the EPA regards as
17 toxicity. Does that have to mean actual tissue
18 pathology, or can that mean alterations that you
19 would not otherwise expect in any kind of tissue?
20 So that's where I'm -- I have my confusion. I
21 don't think they are --

22 **DR. KENNETH PORTIER:** Well, let's

1 ask --

2 **DR. KATHLEEN GILBERT:** Hmm?

3 **DR. KENNETH PORTIER:** Let's ask Dr.
4 Barone to step in and maybe address that. Stan?

5 **DR. STANLEY BARONE:** Yeah. This
6 actually gets into some of the earlier
7 conversations that you raised, Dr. Gilbert. We
8 don't have to have tissue pathology to have an
9 adverse effect. We do, in our immunotox
10 guidelines, look for convergence of evidence and
11 want to be able to see that we have functional
12 effects. And we can't have functional effects in
13 the absence of tissue pathology or full blown,
14 quote/unquote, disease pathology. So again,
15 that's why we're interested in your expert input
16 from the panel and we have -- we've discussed this
17 internally. So we wanted to get -- we wanted to
18 solicit input.

19 **DR. STEPHEN GRANT:** So this Steve
20 Grant again. And I think that, you know, I'm --
21 really it sounds like we need as many people on
22 the panel to weigh in as whether they feel that

1 the induction of antibodies against a primary
2 bodily component, DNA, is sufficiently adverse
3 effect to be a primary endpoint or simply a
4 biomarker of a clinical endpoint. And we can talk
5 about it all we want, but really what we need is -
6 - I envisage writing this up by saying the
7 majority of the panel or all of the panel. So
8 please weigh in on that.

9 **DR. KENNETH PORTIER:** Well, all of
10 the panel probably doesn't know enough to be able
11 to do that. Dr. Gilbert.

12 **DR. KATHLEEN GILBERT:** Well, I hate
13 to keep talking in circles, but there's no
14 question that people develop antibodies against
15 DNA and who never have any kind of clinical
16 outcomes associated with it. Certainly, lots of
17 people, as you get older, develop autoantibodies.
18 So I'm not sure that we can necessarily say it's
19 going to lead to a clinical outcome but is it of
20 itself an indicator of immune -- it's certainly an
21 indicator of immune alteration.

22 Whether that rises to the level of

1 toxicity is what I'm trying to get at. I agree
2 with Dr. Barone that we don't necessarily have to
3 have tissue pathology to talk about toxicity but
4 is any kind of alteration considered -- it's
5 certainly a sign of immune alteration. We're
6 certainly impacting the immune system. Does that
7 mean it's toxic? That's what I don't know.

8 **DR. KENNETH PORTIER:** Dr. Anderson,
9 you want to weigh in here. Dr. Anderson, you're
10 still muted.

11 **DR. HENRY ANDERSON:** Sorry about
12 that. Yeah. I think autoimmunity is kind of a
13 continuum sort of issue, and they're -- is it a
14 kind of effect I would say probably you need in
15 order to go on to get an autoimmune disease, but
16 they don't all progress to that standpoint. So
17 I think it is a -- I would be worried if this was,
18 you know, being seen in populations. And some
19 would go on and some would not because it may not
20 advance or the body may not continue to build
21 their autoimmunity impact. So I would tend to
22 view it as an adverse effect even though it has --

1 it isn't 100 percent goes on to -- does -- these
2 findings would not necessarily always progress to
3 autoimmune disease, tissue pathology.

4 **DR. STEPHEN GRANT:** Well, another
5 way to look at it is --

6 **DR. HENRY ANDERSON:** I would lean
7 toward the 10 uncertainty factor.

8 **DR. STEPHEN GRANT:** Well, the 10
9 uncertainty factor is based on this being an
10 endpoint in and of itself. And in fact, I think I
11 agree with you in that you don't have to show 100
12 percent development of clinical disease. We're
13 supposed to protect susceptible populations.

14 If there's a feeling that this
15 indication is ever going to be associated with a
16 greater effect, because unfortunately having
17 antibodies against your DNA doesn't -- people walk
18 around with that all the time. But if that is a
19 marker for some element of the population showing
20 clinical effects, then I think we need to use the
21 UF of 10.

22 **DR. KENNETH PORTIER:** Dr. Morandi.

1 You're still on mute, Dr. Morandi.

2 **DR. MARIA MORANDI:** Sorry about
3 that. I was going to comment on this very issue.
4 It seems to me what we are saying is that there is
5 variability in the progression or not of that
6 early marker and actual disease. So this to me
7 means uncertainty. So it seems to me I could be
8 more inclined to us a factor of 10 uncertainty for
9 human variability.

10 **DR. KENNETH PORTIER:** Thank you.
11 Dr. Blystone.

12 **DR. SHERI BLYSTONE:** Yeah. And I am
13 definitely not an expert. I'm just sort of here
14 representing the regulatory community. And it's -
15 - the discussion is, as I understand it, whether
16 this is considered an adverse effect or not, put
17 in very simplistic terms. I'm hearing a lot of
18 discussion that that is not clear. And if it
19 isn't clear, then I think it's -- this is not the
20 place to make that determination. I think we need
21 to stick with standards as much as we can.

22 **DR. KENNETH PORTIER:** So that means

1 the 10x.

2 DR. SHERI BLYSTONE: No. I don't
3 know that that's what that means.

4 DR. KENNETH PORTIER: Okay.

5 DR. STEPHEN GRANT: So I think that
6 means 3x because it's --

7 DR. SHERI BLYSTONE: I think it
8 means 3x.

9 DR. STEPHEN GRANT: -- it's an
10 indicator.

11 DR. SHERI BLYSTONE: Yes.

12 DR. KENNETH PORTIER: Okay. Dr.
13 Johnson.

14 DR. MARK JOHNSON: Yeah. I would
15 tend to agree because I think, ultimately, if
16 we're so uncertain of the clinical significance of
17 the endpoint, maybe we shouldn't use it. I mean,
18 because in the end, EPA's going to make a decision
19 whether this is unreasonable risk or not, and this
20 is clearly the lowest indicator that we have of
21 toxicity. So I think we need to think about that.

22 DR. HENRY ANDERSON: Again, I would

1 --

2 **DR. KENNETH PORTIER:** Dr. -- oh.

3 **DR. HENRY ANDERSON:** -- say this is
4 not -- clinically, this is not the kind of a thing
5 you would ignore. And yes, there's people walking
6 around with this, but, typically, this would
7 result in some kind of an evaluation to be sure,
8 at least monitoring over time to try to catch are
9 there any other more significant changes in
10 progression.

11 **DR. STEPHEN GRANT:** So this is Dr.
12 Grant, and I do work on biomarkers. And I
13 certainly don't want to discount biomarkers, which
14 is, if we have a biomarker which is indicative of
15 an at-risk population and there's every reason to
16 believe that that at-risk population is going to
17 go forward, then we are charged with defending --
18 with protecting them. So it's clear that this is
19 part of an autoimmune reaction.

20 It's an early indicator, which is
21 good. And I would say that we should use it and
22 use the UF of 10. But again, I don't think we are

1 going to come to a consensus here so anyone who
2 wants to weigh in, please send me your opinion.
3 Yes or no.

4 **DR. KENNETH PORTIER:** So I've got
5 Dr. Rowlands and then Dr. Cory-Slechta. Dr.
6 Rowland.

7 **DR. CRAIG ROWLANDS:** Yeah, thanks.
8 Yeah. I'm going to pick up on the biomarker
9 concept because, if it's a biomarker, we really
10 need to understand a biomarker of what pathology,
11 what disease? And I want to go back to an early
12 comment that maybe what we need here is some
13 better liver shown. What is this biomarker
14 associated with in terms of a pathology or adverse
15 outcome of some disease? We don't know that, and
16 we also hear that a lot of people walking around -
17 - it's certainly it's not uncommon to find people
18 already with a reaction to their DNA.

19 Now, I think of -- that's a pretty
20 common thing in our bodies, DNA, right? So if you
21 have a reaction to it and it's real, we ought to
22 be able to pick up some pathology, ought to have

1 some sort of an association with a disease of some
2 sort. You know, I also work in biomarkers. And
3 when I was at FDA, we used to scratch our heads
4 all the time trying to figure out, what does this
5 biomarker really mean?

6 You've got biomarker changes, but we
7 can't associate it with any -- and it's very
8 difficult to do. So I'm very -- you know, I'm a
9 little bit concerned that if we pick this out as
10 some biomarker that we think this is important for
11 developing later disease, what are we going to
12 base that decision on? I don't see what it's
13 based on other than we see this potential
14 biomarker of something.

15 **DR. KENNETH PORTIER:** Dr. Cory-
16 Slechta.

17 **DR. DEBORAH CORY-SLECHTA:** Yeah. I
18 appreciate all of the discussion on this. I would
19 also, I think, encourage folk -- we talk a lot
20 about what's an adverse effect or is this going to
21 have a clinical outcome? Just ask yourself when
22 you go to the doctor, if he tells you you're

1 developing antibodies to yourself, is that
2 something that you want to walk around with when
3 you start talking about what really is an adverse
4 effect.

5 **DR. KENNETH PORTIER:** Dr. Gilbert.

6 **DR. STEPHEN GRANT:** If I can --
7 again, remember that, in this case, we're simply
8 using DNA as a normal component and showing that
9 we're getting expansion of the immune system
10 against inappropriate targets. We all know what
11 autoimmune disease looks like. It destroys joints
12 and bones and things like that. And the question
13 is are we creating the early stages of this?

14 People walk around with this all the
15 time as they get older and their immune system
16 stops being regulated properly. A simple
17 indication if you've got an autoimmune antibody is
18 that you're killing cells, and there's slightly
19 greater apoptosis in your body. We can pick that
20 up with circulating DNA.

21 Is it always going to -- is it going
22 to kill you? Is it -- or is it something -- is it

1 a chronic disease? And what are the symptoms of
2 that chronic disease? It's an indicator that
3 these antibodies probably aren't going to kill you
4 but other -- it's an indicator of other antibodies
5 like that are being developed. And they may
6 target something that will result in disease.

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

8 **DR. KATHLEEN GILBERT:** Yeah. I just
9 wanted to clarify what I said earlier. I mean, I
10 definitely think that the development of
11 antibodies against double-stranded or single-
12 stranded DNA represent an adverse effect. And
13 everybody knows that autoimmune diseases are
14 notoriously difficult to diagnose, and so they
15 usually set up multiple criteria that you have to
16 fulfill in order to be diagnosed as an autoimmune
17 disease.

18 And one of those for several
19 autoimmune diseases is the development of
20 antibodies against single-stranded and double-
21 stranded DNA. That's true for scleroderma. It's
22 true for Lupus. And it's -- they even look at

1 them for rheumatoid arthritis. So it's not a
2 guarantee that you're going to get disease, but
3 it's certainly considered as a biomarker of at
4 least, you know, you meeting one of the criteria
5 for developing autoimmune disease.

6 **DR. KENNETH PORTIER:** Dr. Morandi,
7 your hand's still up. Now it's down. So Dr.
8 Gilbert, before I let you go, I wanted to ask a
9 question about age inappropriate. If this is
10 occurring in young mice versus, say, in older
11 mice, is it more or less of a biomarker?

12 **DR. KATHLEEN GILBERT:** Well, that's
13 a good point. And probably the answer would be it
14 would be more of a biomarker because, well, the
15 controls are not developing high levels of this.
16 So obviously, if we're giving the effect in the
17 TCE treated mice, then that's considered an
18 adverse effect. It's not occurring naturally as
19 the mice get older. So I would say it would be
20 more important in the younger mice versus in the
21 older mice where you might get higher levels of
22 background autoantibodies.

1 **DR. STEPHEN GRANT:** Dr. Grant again.
2 And the definition of that to me is called
3 premature aging, at least in that -- in the immune
4 system. And that would be a significant adverse
5 effect.

6 **DR. KENNETH PORTIER:** So in the Keil
7 study, the dose of the Keil study was done with
8 mice that were susceptible. Is that right?
9 Genetically modified mice?

10 **DR. KATHLEEN GILBERT:** No.
11 Actually, they used non-autoimmune -- they used
12 two types, but the effects that are being used by
13 the EPA were detected in non-autoimmune prone
14 mice.

15 **DR. KENNETH PORTIER:** And the
16 detection occurred at what point in the life stage
17 of these mice?

18 **DR. KATHLEEN GILBERT:** I don't
19 remember exactly when they started treating them,
20 but they were not old mice.

21 **DR. KENNETH PORTIER:** Yeah. I'm
22 trying to remember, too. I think they were kind

1 of like early middle age. So, you know, I'm just
2 trying to get at whether this biomarker -- I think
3 we've established the biomarker is there, but that
4 link that Dr. Barone was seeing, is this a
5 precursor for an adverse effect? And I don't
6 think we've settled on that. We think -- I think
7 there's still some discussion on that.

8 I think what I'd like to do at this
9 point -- I'm seeing it's 1:18 eastern time. And
10 for many of us it's probably -- our blood sugars
11 are starting to crash, and we need to go and get
12 some sustenance for the remainder. I'd like to
13 leave this question open right now.

14 We'll come back after our lunch or
15 break and continue the discussion at least for a
16 few minutes. We're behind by about an hour at
17 this point, which doesn't distress me very much.
18 We will get there. But at this point I'd like us
19 to break and return at 2:05 Eastern if we would.
20 So I have 1:18. We'll return at 2:05 eastern.
21 We'll be in our lunch break at this point. Thank
22 you.

1 (Break)

2 DR. KENNETH PORTIER: Good

3 afternoon. This is Ken Portier with the TSCA
4 SACC. We're reconvening at this point. I'm
5 assuming everyone can hear me. A number of our
6 panelists seem to have -- their phones have
7 disconnected from the WebEx. You'll need to have
8 WebEx call you back in to continue participating.
9 First, I'll check to make sure the DFO is here.
10 Todd?

11 DR. TODD PETERSON: Sorry. I tried
12 to unmute. Anyways, I'm here. And --

13 DR. KENNETH PORTIER: Okay.

14 DR. TODD PETERSON: -- I see one of
15 my admin team doesn't have a phone, but only one
16 of the peer reviewers, I think, needs to dial back
17 in. But that's good notice. And so start away
18 and we can go down the checklist.

19 DR. KENNETH PORTIER: Well, Craig
20 Rowlands and George Cobb need to dial back in at
21 this point. Okay. We need to quickly run through
22 the roll. And all of you, if you thought you

1 were disconnected -- I mean, were muted -- or not
2 muted, you are muted now so you will have to
3 unmute. Dr. Kaufman.

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

5 **DR. KENNETH PORTIER:** Dr. Jenkins.

6 **MS. ALLISON JENKINS:** Here.

7 **DR. KENNETH PORTIER:** Let's see, Dr.
8 Anderson.

9 **DR. HENRY ANDERSON:** Here.

10 **DR. KENNETH PORTIER:** Dr. Bennett.

11 **DR. STEVEN BENNETT:** I am here.

12 **DR. KENNETH PORTIER:** Dr. Barton.
13 Dr. Barton? I see him as still muted. Dr.
14 Blystone.

15 **DR. SHERI BLYSTONE:** I am here.

16 **DR. KENNETH PORTIER:** Thank you.
17 Dr. Bruckner. I'll come back. Dr. Cory-Slechta.

18 **DR. DEBORAH CORY-SLECHTA:** I'm here.

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

20 **DR. HOLLY DAVIES:** I'm here.

21 **DR. KENNETH PORTIER:** Dr. Doucette.

22 **DR. WILLIAM DOUCETTE:** Here.

1 DR. KENNETH PORTIER: Dr. Jimenez-
2 Gonzalez.

3 DR. CONCEPCION JIMENEZ-GONZALEZ:
4 Here.

5 DR. KENNETH PORTIER: Dr. Gilbert.

6 DR. KATHLEEN GILBERT: Here.

7 DR. KENNETH PORTIER: Dr. Johnson.

8 DR. MARK JOHNSON: Here.

9 DR. KENNETH PORTIER: Dr. Kissel.

10 DR. JOHN KISSEL: Here.

11 DR. KENNETH PORTIER: Dr. Rowlands.
12 Yeah. Dr. Rowlands is one of those that needs to
13 call back in. Dr. Schlenk.

14 DR. DANIEL SCHLENK: Here.

15 DR. KENNETH PORTIER: Dr. Apte.

16 DR. UDAYAN APTE: I'm here.

17 DR. KENNETH PORTIER: Dr. Cobb. Dr.
18 Cobb's the other one that needs to call back in.
19 Dr. Grant.

20 DR. STEPHEN GRANT: Here.

21 DR. KENNETH PORTIER: Dr. Hossain.

22 DR. MUHAMMAD HOSSAIN: Yes. I'm

1 here.

2 DR. KENNETH PORTIER: Dr. Lash.

3 DR. LAWRENCE LASH: I'm here.

4 DR. KENNETH PORTIER: Thank you.

5 Dr. Morandi.

6 DR. MARIA MORANDI: I'm here.

7 DR. KENNETH PORTIER: Dr. Morris.

8 DR. JOHN MORRIS: I'm here.

9 DR. KENNETH PORTIER: Dr. Rosol.

10 DR. THOMAS ROSOL: Present.

11 DR. KENNETH PORTIER: Dr. Vorhees.

12 DR. CHARLES VORHEES: Here.

13 DR. KENNETH PORTIER: Let's see. I

14 think that's everyone with the exception of Dr.

15 Cobb and --

16 DR. GEORGE COBB: I just joined.

17 DR. KENNETH PORTIER: Okay. Thank

18 you. And Dr. Rowlands --

19 DR. CRAIG ROWLANDS: Yep. I'm here.

20 DR. KENNETH PORTIER: -- did he

21 join? Oh. Okay. So the only one we're missing

22 is Chuck Barton, Dr. Barton. It shows him dialed

1 in and muted but he's on a cell phone. So I don't
2 know exactly what that means.

3 Okay. Well, when we broke for
4 lunch, we were still discussing question 5.3, sub
5 question C, on the Keil study and whether the --

6 **DR. CHARLES BARTON:** I'm here.

7 **DR. KENNETH PORTIER:** Ah, good.

8 Thank you, Dr. Barton -- whether the endpoint is a
9 precursor for adverse effects on autoimmunity.

10 I'll first turn to Dr. Grant and say do you have
11 anything else to add? And at the same time,
12 anybody else on the committee want to comment? I
13 think we've been kind of going around in circles,
14 and I'm not sure additional discussion is going to
15 help us here. But I'm willing to continue the
16 discussion at this point. Dr. Grant.

17 **DR. STEPHEN GRANT:** Well, I did
18 spend my -- this is Dr. Grant. I did spend my
19 lunch hour googling and the -- what I found was
20 that the anti-DNA antibodies were considered
21 fairly definitive for some diagnoses earlier in
22 the decade but that the -- and I say that because

1 they may have been considered a definitive
2 endpoint and therefore chosen to -- for study. In
3 subsequent times, they have been found to be no
4 better than others. So the -- they are still what
5 we would call a biomarker. They're an indication
6 of bad things but not necessarily of clinical
7 disease.

8 **DR. KENNETH PORTIER:** Dr. Gilbert.

9 **DR. KATHLEEN GILBERT:** Yeah. I just
10 wanted to say that, in terms of my qualifications
11 for spouting off on this stuff, I have published
12 extensively on different mouse models of
13 autoimmunity, and I have taught autoimmunity and
14 autoimmune diseases to medical students and
15 graduate students for over 20 years. So I think
16 what Dr. Grant said was correct. I mean, I don't
17 think there's any question that autoantibodies are
18 biomarkers of disease in certain situations.

19 And for most autoimmune diseases,
20 that's the first thing they look for are different
21 autoantibodies. Now, some of those are more
22 specific and sensitive than others. And it's true

1 that anti-single stranded DNA and anti-double
2 stranded DNA are not among those which are
3 considered the most sensitive or specific. But
4 for certain autoimmune diseases, those are the
5 only ones that they really have to look for.

6 And they are certainly among the
7 first that people look for, for looking at
8 autoimmune diseases. So I have to say I consider
9 them a pretty good marker -- biomarker of
10 autoimmunity or at least autoimmunity if not
11 necessarily autoimmune disease.

12 **DR. KENNETH PORTIER:** Dr. Rowlands.

13 **DR. CRAIG ROWLANDS:** Yes. I also
14 spent a little time over lunch just taking a look
15 at the data, and I pulled in the Keil paper. And
16 I'm looking at the figures, and what I'm seeing is
17 -- you all were talking about the age and
18 dependency on the single-strand and double-strand
19 expression. And it's definitely an age dependent
20 increase over time with both the double-strand and
21 single-strand DNA.

22 In fact, when -- in the two doses of

1 TCE they use in this study, 1,400 ppb and 14,000
2 ppb, they did not get a very good dose-response
3 between the two treatments. But in some cases,
4 the control levels are higher than the actual
5 treatment groups. I don't know how you get a
6 really good dose-response off of this. It looks
7 like it's barely over the control on most, you
8 know, a very -- only slightly over the control
9 with most treatments across those age groups.

10 So I would have to say it would be
11 very difficult to have a sensitive enough study to
12 see a real difference without a different dose-
13 response than the study has here. And I think
14 that's something we ought to consider as well. So
15 it's normally going up with TCE treatment as well
16 over time, and so it's obviously a natural thing.
17 The only difference is the single-strand DNA for
18 the B6 C3 F1 mice, but the -- I'm sorry the
19 double-strand. But the single-stranded actually
20 looks fine. It tracks the same way with age as
21 the background goes up with age, just like the
22 treatment groups.

1 So, you know, I look at that data
2 thinking it's not the best data I'd want to use
3 for any dose-response modeling, and -- but maybe
4 that's just me. So maybe it's worth the committee
5 taking a look at this data before we make and real
6 decisions on it.

7 **DR. KENNETH PORTIER:** This is Ken
8 Portier. I think the whole point is they aren't
9 doing dose-response; they're just using LOAEL.
10 And the issue is whether to attach a 3x or a 10x
11 to that LOAEL.

12 **DR. CRAIG ROWLANDS:** Right.

13 **DR. KENNETH PORTIER:** So you -- kind
14 of, you want to think in terms of that. You know,
15 if they're using the LOAEL, would you attach a 3x
16 uncertainty factor or a 10x uncertainty factor?

17 **DR. CRAIG ROWLANDS:** Well, that's a
18 real tough question because you're looking at a
19 1,400 ppb and a 14,000 ppb. And in many cases
20 there -- actually, the 1,400 is higher than the
21 14,000. It's a really strange dose-response. So
22 -- different response. It is two doses, so I

1 guess it is a dose response.

2 So yeah. You're right. I mean, it
3 would also be a LOAEL. That's all you have in the
4 study is a LOAEL, I think, for most of these.
5 But, you know, they're very small differences
6 between the treatments and the controls. And so
7 in these models, it's naturally going up with
8 time. It's not definitely just a chemical
9 dependent effect.

10 **DR. KENNETH PORTIER:** Anyone else?
11 Turn back to Dr. Grant. Any final comments before
12 we move on?

13 **DR. STEPHEN GRANT:** Well, I will try
14 to encapsulate everybody's discussion. I -- and I
15 sent a message to Dr. Barone essentially saying I
16 don't think at the beginning we appreciated the --
17 what he was looking for here. And in fact, it is
18 an issue, and I hope that he's gotten enough
19 discussion. I'm certainly not going to come up
20 with a definitive conclusion when I put all of
21 this together.

22 **DR. KENNETH PORTIER:** Yeah. I think

1 EPA's recommendation in the draft risk evaluation
2 was a 3x. And they were -- I think they were
3 looking for some stronger justification to go to a
4 10x, and I didn't hear that. I mean, I can still
5 understand the 3x. So oh, well. I'll turn to EPA
6 at this point and ask are there are any closing
7 comments or clarifying questions of EPA on this
8 issue?

9 **DR. STANLEY BARONE:** Thank you, Dr.
10 Portier. This is Stan Barone. Yes, we're -- I
11 think the conversation's been helpful. I don't
12 think it has been definitive, but I do think it's
13 been helpful. And we'll take this conversation
14 and your written recommendations dialogue into
15 account in our justification for the reduction
16 from the default 10x to 3x.

17 **DR. KENNETH PORTIER:** Dr. Gilbert,
18 you want some last words?

19 **DR. KATHLEEN GILBERT:** Yeah. Sorry.
20 Yes. So I was just hurriedly looking back at the
21 manuscript again. I hate to drive this into the
22 ground, but the figure for the double-stranded DNA

1 -- the trouble with looking at these kinds of
2 autoantibodies is that there is very often not a
3 standard curve to compare them to, so you have to
4 just compare within your particular ELIZA on a
5 particular date. So hopefully they ran all the
6 different age groups at the same time in one
7 ELIZA.

8 But the -- I agree that there's not
9 an ideal dose-response curve in this, but I do
10 think, in terms of the double-stranded DNA for
11 example, yes, we do see it increase in the NZB
12 WF1, which is the autoimmune prone mouse. And
13 you're going to see an increase in those
14 antibodies in those mice, just naturally, not
15 necessarily anything to do with the TCE. But if
16 you look at the B6 mice, which are the non-
17 autoimmune prone, you do see a fairly good
18 increase in the autoantibodies in the non-
19 autoimmune prone mice. So I think it's a
20 legitimate way of looking at things.

21 **DR. CRAIG ROWLANDS:** I got my hand
22 still up there, so is it okay if I just say

1 something?

2 DR. KENNETH PORTIER: Yeah, I --

3 DR. CRAIG ROWLANDS: So --

4 DR. KENNETH PORTIER: -- I'm sorry.

5 I was muted.

6 DR. CRAIG ROWLANDS: That's ok- --

7 yeah. So this Craig again, Craig Rowlands. So
8 yeah. You know, all of them are going up over
9 time except for the Figure 2 -- I don't know if
10 we're looking at the same figure. I'm looking at
11 Figure 2b. That is the B6 mice and that's looking
12 at the single-strand DNA. So the single-strand,
13 the B6, the control is almost flat, and the TCE
14 includes at the two doses cross.

15 But that's the only one. If you go
16 back over to the B6 on the -- looks like it's
17 called glomerular -- or I guess -- I can't say it,
18 glomerular antigen, it's also age dependent.
19 There's no difference really. I mean, you can see
20 some treatment effects here where the control's
21 higher than the two treatments in some age groups.
22 So it's -- that does seem to be a little bit

1 different than the autoimmune sensitive mice, the
2 -- I guess it's the New Zealand BWF ones.

3 So, you know, one out of the three
4 panels there actually is definitely chemical
5 induced effect, but the rest are really -- it's
6 hard to say there's a real chemical induced
7 difference relative to the control.

8 **DR. KATHLEEN GILBERT:** Well, I have
9 to say that I disagree, of course. They obviously
10 decided not to use the antibodies against the
11 glomerular antigens. They used the double-
12 stranded and single-stranded. And I think that in
13 both Figure 1 and Figure 2 in the non-autoimmune
14 prone mice, they got legitimate levels of toxicant
15 induced increase in antibodies.

16 **DR. CRAIG ROWLANDS:** That's true.
17 1b -- 1b definitely is chemically induced. You're
18 right.

19 **DR. KATHLEEN GILBERT:** And so is 2b.

20 **DR. CRAIG ROWLANDS:** And 2b, 1b and
21 2b. Right. Which is the B6 mice.

22 **DR. KATHLEEN GILBERT:** Right. But

1 that's the one they actually selected for use in
2 the risk evaluation, the LOAEL.

3 **DR. CRAIG ROWLANDS:** And so if you
4 also look at the dose, the two doses though you
5 see that they're not necessarily dose dependent,
6 right?

7 **DR. KATHLEEN GILBERT:** Well --

8 **DR. CRAIG ROWLANDS:** So if we just
9 looked --

10 **DR. KATHLEEN GILBERT:** -- yeah --

11 **DR. CRAIG ROWLANDS:** -- at the B6 at
12 age 34 weeks, it's the mid-dose. The low dose
13 actually is much higher than the high dose. So
14 it's not necessarily a very good chemically dose-
15 response.

16 **DR. KATHLEEN GILBERT:** Well, once
17 again, it depends on how fixed you are on dose
18 dependency. And so that's a tough one to say for
19 sure. I mean, they got responses. Yeah. It's
20 not always exactly dose dependent, but they don't
21 have the whole-time curve, too. So you might have
22 seen something different if they'd actually looked

1 at every single week.

2 DR. CRAIG ROWLANDS: Yeah.

3 DR. KENNETH PORTIER: So I just --

4 DR. CRAIG ROWLANDS: So I guess --

5 DR. KENNETH PORTIER: -- want to
6 encourage --

7 DR. CRAIG ROWLANDS: -- strain
8 dependent, right? It's a mouse strain dependent
9 as well is what we're looking at.

10 DR. KATHLEEN GILBERT: Yes. It's --

11 DR. CRAIG ROWLANDS: Okay.

12 DR. KATHLEEN GILBERT: That's a
13 whole other story, but yes. In terms of this,
14 yes.

15 DR. KENNETH PORTIER: Okay. I'm
16 going to end the conversation at this point and
17 just encourage both of you to write up your point
18 of view and provide it to Dr. Grant so he can
19 incorporate it into our response to this question.
20 At this point I think we need to move on to
21 question 5.4. So Dr. Bethel.

CHARGE QUESTION 5 (5.4)

DR. HEIDI BETHEL: Hello. Welcome back. Question 5.4 relates to the cancer hazard. EPA performed a meta-analysis on the published database for liver cancer, kidney cancer, and non-Hodgkin's lymphoma, concluding that there was statistically significant association between TCE exposure and all three cancers when accounting for various sensitivity analyses. Please comment on EPA's methodology and conclusions, Section 3.2.4.2.1 and Appendix H.

DR. KENNETH PORTIER: Dr. Grant.

DR. STEPHEN GRANT: Yes. Hello. In general --

DR. KENNETH PORTIER: I can hear you.

DR. STEPHEN GRANT: Okay. In general, everyone -- oh, I'm sorry. Okay. Should be -- in general, everyone -- most people agree that the meta-analysis or agreed with the meta-analysis and the methods. It was noted that the

1 difference between this and a previous analysis
2 was largely driven by the exclusion of Vlaanderen
3 et al. 2013 and that this exclusion was well
4 discussed and justified.

5 The exception to that was one person
6 who felt that the evidence for liver tumors was
7 particularly -- wasn't particularly strong. And
8 we all basically agree that kidney shows the
9 biggest effect. There was something that was said
10 earlier that the metabolism to the active
11 metabolites -- and we'll get to that in a second -
12 - is specific to liver and kidney. And at some
13 point, someone will have to tell me how liver
14 specific metabolism isn't systemic metabolism.

15 Let's see if there's anything else.
16 No. The other issues will be more for 5.5 where
17 we talk about mechanisms. So basically, most
18 people thought that everything was fine. There's
19 one issue with liver, and since it's not the main
20 cancer, I'm not sure we should spend that much
21 time on it.

22 **DR. KENNETH PORTIER:** Let me open it

1 up to any comments, especially the associates who
2 may want to clarify or spend a little time on
3 their response. Just raise your hand so I'll know
4 you want to speak. I'm not getting -- I'm not
5 seeing any hands. Oh, there's Dr. Johnson.

6 **DR. MARK JOHNSON:** Yes. I agree
7 with what the EPA did for the weight of evidence
8 for non-Hodgkin's lymphoma and for kidney cancer,
9 and certainly the human evidence is incredibly
10 strong. I was referencing this National Academy
11 of Sciences report that was published in 2006
12 assessing the human health risks of TCE where they
13 didn't think that the mode of action for mice was
14 relevant for humans basically due to PPAR-alpha
15 and the evidence of liver tumors. And so if the
16 EPA disagrees, I think they need at least to make
17 that reference and make a stronger case.

18 **DR. KENNETH PORTIER:** Well, that's a
19 good recommendation. Anyone else wish to join in
20 with discussion of 5.4? I'm not seeing any. Dr.
21 Grant, do you want to have any closing remarks on
22 this before I turn to EPA?

1 **DR. STEPHEN GRANT:** No. The only
2 reason that I didn't bring that up with Dr.
3 Johnson's is based on mode of action, and
4 basically, I'm going to bring that up again in
5 5.5.

6 **DR. KENNETH PORTIER:** Okay. Well,
7 let me turn to EPA and ask whether they have any
8 clarifying questions on the panel's response.

9 **DR. STANLEY BARONE:** Not at this
10 time. If the panel has additional comments --
11 written comments about the mode of action analysis
12 that would be helpful.

13 **DR. KENNETH PORTIER:** I think that's
14 the next question and why don't we just move along
15 ahead to question 5.5. Dr. Bethel.

16
17 **CHARGE QUESTION 5 (5.5)**

18
19 **DR. HEIDI BETHEL:** Question 5.5, for
20 the cancer dose-response assessment, EPA derived
21 an inhalation unit risk and oral cancer slope
22 factor based on epidemiological kidney cancer from

1 Charbotel et al. 2006, adjusted upward to also
2 account for the relative contribution of non-
3 Hodgkin's lymphoma and liver cancer. Per EPA
4 guidelines for carcinogen risk assessment,
5 overall, the totality of the available data and
6 information and the Weight of Evidence analysis
7 for the cancer endpoint was sufficient to support
8 a linear non-threshold model.

9 Please comment whether the cancer
10 hazard assessment has adequately described the
11 methodology and justification for the cancer dose
12 response approach, including the use of a linear
13 model and the adjustments made for the other tumor
14 sites.

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

16 Dr. Grant.

17 **DR. STEPHEN GRANT:** This is Dr.

18 Grant. First of all, I'd like to remind you that
19 Dr. Apte has already weighed in on this, and we
20 will bring that back up if -- as necessary. In
21 general, there was a feeling that the basis on --
22 basing the dose-response on the kidney work was

1 appropriate. There was some question as to
2 whether there was sufficient evidence for a linear
3 no dose model based on the mode of action.

4 To some degree, it seems like the
5 literature assumes a mode of action and then, when
6 they find the potentially mutagenic metabolites,
7 basically stopped there with having established a
8 level of biological plausibility. They really
9 haven't shown that those -- that -- done the work
10 to show that that potential model is actually the
11 true one. And several, including Dr. Apte --
12 several panel members suggested that greater work
13 had to be done on that.

14 Now, again, we're not doing the
15 work, so the question is we can think that in the
16 field there should have been more work done. But
17 we can only really act upon the data that's there.
18 So there will be people who will follow me who
19 will talk about the mutagenicity of those
20 metabolites and the question as to whether or not
21 they can rise to large enough levels in the body
22 to have a mutagenic or genotoxic effect. But I'll

1 let the people who've -- who want to make those
2 statements elaborate.

3 **DR. KENNETH PORTIER:** Is that it,
4 Dr. Grant?

5 **DR. STEPHEN GRANT:** Yep.

6 **DR. KENNETH PORTIER:** Maybe I should
7 let Dr. Apte speak, or --

8 **DR. UDAYAN APTE:** Yeah. Okay.

9 **DR. PORTIER:** -- talk about --

10 **DR. UDAYAN APTE:** So yeah. So
11 thanks for bringing that back up. So the question
12 I had -- well, no. The comment I had I guess that
13 I made earlier was about the liver cancer mode of
14 action and can probably apply to liver and kidney.
15 The idea here is that the TCE's probably
16 metabolized in the liver, except to E1 dependent
17 metabolism most likely, into the metabolites, and
18 then one of the metabolites will be glutathione
19 conjugated, which goes into the kidney. And then
20 it's converted back to DCVC, which is a kidney
21 toxicant. And that's where the mutagenicity comes
22 from.

1 When it comes to liver toxicity mode
2 of action, what I felt was -- well, the EPA stand
3 is that it's not -- there's not sufficient data to
4 say what is the mode of action one way or the
5 other. There is some idea that it is PPAR-alpha
6 dependent. That may be something that needs to be
7 verified better because we all know that PPAR-
8 alpha dependent mechanisms are not of human
9 consequence.

10 However, we clearly know that there
11 is a human risk here. So in that case, what is
12 the mode of action? So we have to consider non
13 PPAR-alpha dependent mechanisms, and I think,
14 given the fact that TCE's known to induce DNA
15 synthesis, hypertrophy septal proliferation all
16 leading to hepatomegaly increase the liver to body
17 weight ratios, it suggests a cytotoxic mode of
18 action.

19 So generally in the liver when
20 chemicals produce injury -- liver injury, which
21 result in liver cells to die, there is a
22 compensation response to make up for the lost

1 cells. This cycle will continue over a period of
2 long exposure and then in the end giving away to a
3 cancer pathogenesis. And so that mode of action
4 should have been considered.

5 The other thing is non PPAR-alpha
6 dependent mechanisms refer to other nuclear
7 receptors as -- especially CAR, constitutive
8 adenosine receptor, as well as things like HNO4
9 Alpha and a balance of those. And so there are
10 some reports on this that I will find and forward
11 to the committee, but I think there is
12 insufficient analysis here to just say that it is,
13 you know -- there is no mode of action. I think
14 there is probably a mode of action in terms of
15 liver disease. Thank you.

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

17 Dr. Lash.

18 **DR. LAWRENCE LASH:** Yes. Hi. So my
19 comments had to do with the -- specifically with
20 the kidney and the linear non-threshold model. So
21 what I noted in my comment is that, you know,
22 among all the metabolites of TCE, really DCVC was

1 the only one that was identified as being a
2 mutagen. But however, there was a paper was
3 actually part of a -- well, it was covered in the
4 2011 IRIS review, but it was a 2010 paper I think
5 by Martha Moore -- It might have been earlier --
6 that compared, you know, mutagenicity among -- of
7 DCVC and other classic, you know, established
8 mutagens. And DCVC is pretty weak, but it is
9 definitively a mutagen.

10 So, I guess I'm not --what's
11 missing is that we know that there seems --
12 there's evidence for this other mechanism of
13 cytotoxicity and cycles of proliferation and
14 repair. And what we don't really -- there's
15 really no information on the relative
16 contributions and, because of the weakness of DCVC
17 as a mutagen, although it is definitively a
18 mutagen, we don't really know the contribution.
19 So I'm not sure the liner no-threshold model has
20 enough support.

21 So that was, you know -- I mean, on
22 the one hand it -- I guess it follows some

1 standard practice set forth in the 2005 guidance,
2 but it's just my concern that there's not really
3 enough supporting evidence that a genotoxic mode
4 of action for kidney as a target organ is
5 sufficient.

6 **DR. KENNETH PORTIER:** Dr. Bruckner.

7 **DR. JAMES BRUCKNER:** Back to liver,
8 I wonder if EPA could comment on the -- what they
9 see as the strength of evidence for the linear
10 mode of action for carcinogenicity in the liver
11 itself. Based in -- and why are they assuming
12 there's a linear mode of action?

13 **DR. STEPHEN GRANT:** Yeah. Can I --
14 this is Steve Grant. Can I jump in? There's a
15 real priority here, people. And that is we're
16 driving this off liver -- off kidney cancer.
17 That's where the mode of action is most important.
18 The question becomes you are then adapting that by
19 adding the other endpoints.

20 I don't know whether the mode of
21 action in the secondary endpoints is necessary.
22 It's certainly clear that there's other types of

1 cancers, and we're simply taking the kidney as the
2 paradigm and then adjusting for the fact that it's
3 not the only target site. I really don't want to
4 spend all afternoon arguing about the mechanism of
5 action in secondary sites unless the EPA feels
6 that the addition of those secondary sites is
7 central to the model.

8 **DR. KENNETH PORTIER:** Dr. Apte,
9 you're hand's still up.

10 **DR. UDAYAN APTE:** Yeah. I was just
11 -- that's a good point that Dr. Bruckner brought
12 up. But the question is what-- you know, what Dr.
13 Lash just said. If DCVC is a weak mutagen and
14 are, you know, are there enough concentrations
15 going to build up to cause genotoxic
16 carcinogenicity? And if not, then what is the
17 primary target? So driving the whole thing around
18 kidney is fine, as long as we are sure that there
19 is an explanatory mode of action. Otherwise,
20 we'll have to think about other target sites.

21 **DR. STEPHEN GRANT:** Well, if I may
22 again, remember what is said when I started. I

1 did not feel that there was proof of the -- that
2 model. I simply thought that they had assumed the
3 model and then, when they proposed this and showed
4 that there was a mutagen present in the
5 metabolites, that they basically said that's all
6 we need. And again, it's a question of we may say
7 that's -- they should have gone farther. We have
8 to evaluate what's they -- what's in the
9 literature.

10 **DR. KENNETH PORTIER:** Dr. Lash.

11 **DR. LAWRENCE LASH:** I'm -- yes. I'm
12 sorry. So I wasn't sure what the question was, I
13 guess. You're saying -- I mean, I agree that
14 there's definitely a genotoxic component, but we
15 really -- it could be very minor. Or it could be
16 dose dependent and have a, you know, only a
17 significant role at higher doses.

18 We just don't know. So how -- I
19 guess the question is how that affects the
20 modeling is what you're asking or -- I guess I'm
21 not sure precisely what the question is.

22 **DR. STEPHEN GRANT:** Okay. Dr. Grant

1 again. There's a big difference between
2 establishing the -- sorry, the inappropriate risk
3 in a linear no-threshold model than other models,
4 especially models that have a threshold. Because,
5 basically, if we have a linear no threshold, then
6 we've got dose -- we're assuming dose response and
7 that there will be diminishing effects as we
8 reduce the amount of the agent.

9 With a threshold model, well,
10 there's a point at which you go from something to
11 nothing, and you don't need to go any further
12 after that. Now, so that's the thing is that it
13 would be important -- if there was evidence for a
14 threshold model, it would be important to
15 establish that. But I don't -- and most of you --
16 both of you have, although again, in the case of
17 Dr. Apte's talking about liver, have indicated
18 that there's not enough information on other
19 possible mechanisms.

20 The real question is, if there is --
21 suggest -- and this is, I think, why the question
22 is here. Is there enough evidence to say that

1 there is a linear no threshold or mutagenic
2 genotoxic carcinogenic model and that other things
3 may be contributing but there's no -- but that's
4 speculation? There's no evidence for it.

5 **DR. KENNETH PORTIER:** Dr. Barone, do
6 you want to clarify?

7 **DR. STANLEY BARONE:** Sure. I want
8 to piggy-back on what Dr. Grant was saying. And I
9 think, to provide some background and context,
10 we've had the NAS. We've had the SAB comment on
11 the previous IRIS assessment's approach to a
12 mutagenic mode of action based upon
13 epidemiological evidence and other evidence for
14 kidney cancer and a mutagenic mode of action being
15 at least part of the component of that cancer dose
16 response.

17 The data is -- and we also had this
18 included in our previous assessment of TCE in
19 2015, our final assessment there. So we are
20 looking for your input on whether a mutagenic mode
21 of action -- whether the data supports a mutagenic
22 mode of action for kidney cancer. And it doesn't

1 have to be the sole mode of action. That's not
2 what -- that's not obligatory according to the
3 cancer guidelines. But if it's significant
4 enough, if you feel like we have new information,
5 we want to make sure -- we're asking the same
6 question again to a different panel.

7 We're trying to make sure that we've
8 got this right. The other part that Dr. Grant
9 also keyed off of was we're using human data,
10 we're using the kidney cancers, and we're
11 adjusting for the other tumor types, NHL and liver
12 cancer, not necessarily, again, to be protective
13 according to the cancer guidelines. We're looking
14 at inhalation unit risk and an oral subfactor for
15 all cancers. So those are adjusted.

16 The other aspect is the linear
17 extrapolation. So the linear extrapolation beyond
18 the dose-response data 20, that's what we're
19 trying to get at here. Is there a threshold below
20 the observed data? That is the theoretical
21 question. Our cancer guidelines indicate to us
22 that if we have evidence of a mutagenic mode of

1 action, then we would do a linear extrapolation.
2 If we have evidence for a non-linear
3 extrapolation, or a non-threshold dose response
4 based upon the cancer incidents or mechanistic
5 information, then we would do a different type of
6 model.

7 And then third, and we talked about
8 this last time with methylene chloride -- excuse
9 me, carbon tetrachloride, the other option that we
10 -- is the default approach. When we don't have
11 enough clarity about a mode of action, we default
12 to a linear threshold -- excuse me, a linear
13 default extrapolation. And so those are the
14 choices.

15 There was some discussion about
16 modes of action for liver, modes of action for
17 NHL, other -- possibly other cancer types. We've
18 had previous discussions and inputs on other modes
19 of action. We can bring more of that discussion
20 into the current draft -- I mean, into the current
21 assessment. But again, if you think that's going
22 to change our dose-response approach, that's what

1 this question is about. We'd like your
2 justification for that.

3 **DR. STEPHEN GRANT:** Okay. So Dr.
4 Grant again, and I think that the answer is we're
5 not impressed with the evidence for a mutagenic
6 mechanism for kidney, per se, as that it's been
7 proven and it's the only -- it's the major
8 mechanism and the -- perhaps the only mechanism.
9 But we do fall back on that the -- that we --
10 there are -- there is at least one mutagenic
11 metabolite, and that is a known mechanism of
12 cancer. There are other mechanisms of cancer that
13 we would like to see investigated, but so far
14 there's no evidence for them. So there's no
15 reason to go from something that has weak evidence
16 to something that is basically speculative.

17 And I think all of us know that
18 probably, I mean, genotoxicity is still toxicity.
19 So if you have a small dose, you've mutagenized
20 greater dose you kill and that killing causes
21 stimulation of stem cells and inflammation. And
22 you can't discount the fact that both of them are

1 happening at the same time with the same dose.

2 But the difference here is there is suggestive
3 evidence for linear no threshold and no evidence
4 for anything else as far as I'm concerned.

5 **DR. KENNETH PORTIER:** Thank you, Dr.
6 Grant. Dr. Bruckner, your hand went up and then
7 it went down. And I didn't know if you wanted to
8 comment.

9 **DR. JAMES BRUCKNER:** Yeah. Let me
10 ask the question once more. I understand that
11 kidney cancer is the driving force here. I guess
12 I want to ask Stan Barone how does that impact --
13 or why do you -- or are you assuming that a linear
14 mode of action for NHL and for liver cancer? And
15 how does that influence -- does that influence
16 your overall risk assessment?

17 **DR. STANLEY BARONE:** Again, the dose
18 response is still based upon the kidney data, the
19 human data. It's not changing the dose response -
20 - the slope of the function.

21 **DR. JAMES BRUCKNER:** Okay. Thank
22 you very much.

1 **DR. KENNETH PORTIER:** Any additional
2 comments? Dr. Jacobs from EPA, you wish to
3 clarify.

4 **DR. KEITH JACOBS:** Yes. Just an
5 additional clarification. So the dose-response is
6 actually affected by the other tumor sites, and
7 this is all described in the IRIS assessment. We
8 can only model the data from the kidney, and, as
9 has been said, that's clearly the strongest
10 effect.

11 But in order to get a POD,
12 essentially, that is protective all tumor sites,
13 the relative potency was kind of compared from a
14 few other studies. And that is used to
15 essentially increase the overall IUR and OSF. So
16 the slope is not necessarily affected, but the IUR
17 and OSF do change because we are adding in
18 additional -- relative contribution of the other
19 tumor sties. So the POD overall is affected by
20 those.

21 So I guess the question for the
22 committee would be, if there's question about the

1 mechanism for the other sites, would there be any
2 alternative approach for accounting for those
3 sites in our derivation otherwise, if we were
4 going to do anything alternative?

5 **DR. STEPHEN GRANT:** Well, Dr. --

6 **DR. KEITH JACOBS:** But as we have it
7 --

8 **DR. STEPHEN GRANT:** -- this is Dr.
9 Grant again --

10 **DR. KEITH JACOBS:** -- as we have it
11 --

12 **DR. STEPHEN GRANT:** The question is
13 does the mechanism at the other sites affect how
14 you would add it to the model? Is there some
15 assumption there that they are also occurring by a
16 common mechanism?

17 **DR. STANLEY BARONE:** Again --

18 **DR. STEPHEN GRANT:** But is that
19 necessarily for the --

20 **DR. STANLEY BARONE:** It is not. It
21 is not according to our cancer guidelines. There
22 -- we could have --

1 **DR. STEPHEN GRANT:** But then I think
2 we can put aside the fact that there clearly is
3 liver cancer by whatever mechanism. Clearly is
4 non-Hodgkin's lymphoma, and EPA is making an
5 effort to incorporate those into the model by
6 using the best data to create the dose-response.

7 **DR. KENNETH PORTIER:** It sounds more
8 pragmatic than mechanistically supported. Dr.
9 Bruckner. Hello? Dr. Bruckner, you're muted
10 again.

11 **DR. JAMES BRUCKNER:** Okay. Can you
12 hear me now?

13 **DR. KENNETH PORTIER:** Yes.

14 **DR. JAMES BRUCKNER:** Okay. I'm
15 quite satisfied now. I just wanted to see how
16 those affect one another, how they're integrated,
17 and whether there's any net effect in the end.
18 And my question's answered.

19 **DR. KENNETH PORTIER:** Thank you.
20 I'll turn to Dr. Grant. Do you have sufficient
21 information to put --

22 **DR. STEPHEN GRANT:** Yes. I do.

1 DR. KENNETH PORTIER: -- together
2 the panel response?

3 DR. STEPHEN GRANT: Again --

4 DR. KENNETH PORTIER: Good.

5 DR. STEPHEN GRANT: It's -- if I can
6 make a general comment, one of the things that I
7 found --and it's becoming even more clear in this
8 panel -- is that the assumption that the open
9 scientific literature has all of the information
10 for these things seems to be rather naïve. And
11 again, several times we've called upon EPA to use
12 some mechanism to generate data, but in fact it's
13 probably worse than that. We need to incentivize
14 the scientific community to provide us with the
15 kind of data we need to make these assessments.

16 And just a statement but we just
17 can't expect the average -- a scientist doing an
18 investigator-initiated study is necessarily
19 producing the sorts of data that we need for our
20 uses.

21 DR. KENNETH PORTIER: You know, Dr.
22 Grant, it's been my experience, at least on the

1 Science Advisory Panel and the SIPRA, that
2 scientists read these reports and they identify
3 the gaps in knowledge and then attempt to pursue
4 those gaps. So since this is fairly new under
5 TSCA getting these kinds of committee reviews, I
6 suspect we'll see, moving forward, scientists
7 reading these reports and identifying those gaps,
8 one of which we just discussed. Turning to Dr.
9 Barone or one -- oh, Dr. Johnson, you had a
10 comment.

11 **DR. MARK JOHNSON:** Yes. So I would
12 just like to add -- ask a quick question -- ah, I
13 can't talk either, a quick clarifying question.
14 So did -- I'm assuming -- and I didn't get this
15 from the report -- that the EPA assumed a non-
16 threshold linear response from points of departure
17 for all three cancer types and summed them up. Is
18 that correct?

19 **DR. KENNETH PORTIER:** Dr. Barone or
20 Dr. Jacobs?

21 **DR. STANLEY BARONE:** This is Stan
22 Barone. No, that's not correct. The data that

1 was used for the dose-response for the point of
2 departure for tumors was the Charbotel study, the
3 meta-analysis. That is human data. It was based
4 upon the slope of the cancer data for kidney
5 cancer. The adjustments to that POD were made
6 upon -- made based upon an additivity of the NHL
7 tumors and the liver cancers. And then the linear
8 extrapolation, the model fits were from that point
9 of departure to zero.

10 **DR. MARK JOHNSON:** Okay. So NHL was
11 not included in that calculation.

12 **DR. STANLEY BARONE:** It was
13 included.

14 **DR. MARK JOHNSON:** Just like liver
15 tumors, correct?

16 **DR. STANLEY BARONE:** Yes.

17 **DR. KENNETH PORTIER:** I -- so let me
18 see if I can restate that. The point of departure
19 -- the initial point of departure was attained
20 from the Charbotel kidney cancer data. Then, that
21 point of departure was adjusted for liver and NHL.
22 And then that point of departure and a linear

1 extrapolation to zero used to produce the actual
2 value used. Right? Is that how -- I was trying
3 to make sure I kind of could see the mechanisms
4 and I'm thinking, Dr. Barone, is that right?

5 **DR. STANLEY BARONE:** Yes. Yes. I
6 think you captured it. And that is discussed in
7 the dose-response section of the evaluation.

8 **DR. MARK JOHNSON:** All right. Thank
9 you.

10 **DR. KENNETH PORTIER:** Okay? Dr.
11 Grant, I think we've done this one. And I want to
12 thank you at this point for taking on 5.1 to 5.5
13 or 5.2 to 5.5. Those were tough -- those were
14 really tough questions that we've had to address.

15 **DR. STEPHEN GRANT:** I have to thank
16 Dr. Bruckner because I actually demurred on 5.1,
17 and that's why he did 5.1. And now he's going to
18 pick up 5.6.

19 **DR. KENNETH PORTIER:** Okay. Let's
20 move on to 5.6. Dr. Bethel.

21

CHARGE QUESTION 5 (5.6)

DR. HEIDI BETHEL: Question 5.6, please comment on EPA's application of the PBPK model to the dose-response analysis for all endpoints. Was the selection of dose metrics and percentile output selection appropriate when considering the sensitivity, uncertainty, and variability of the data?

DR. KENNETH PORTIER: Dr. Bruckner had the lead on this one. Dr. Bruckner? Did we lose Dr. Bruckner from the call? Nope. He's there. We're not hearing you, James. You must still be muted somehow. Still not hearing you. There you are. Nope. We lost him again. Dr. Grant, you're still unmuted. Dr. Bruckner, keep trying. Hmm. Hello? I hear somebody in the background. And the only person I see unmuted is Dr. Bruckner, so somehow --

UNIDENTIFIED MALE: Dr. Portier, Dr. Bruckner is connected and that was him. I feel like he's just experiencing some trouble on his

1 end with muting, so we'll go ahead and email him
2 some assistance.

3 **DR. KENNETH PORTIER:** Okay. Why
4 don't we go ahead and take a 10-minute break at
5 this point and return at 3:10. Okay? Let's go
6 ahead and take a short break here, and we'll
7 reconvene at 3:10. Hopefully, we'll get Dr.
8 Bruckner's connection fixed at that point.

9
10 (BREAK)

11
12 **DR. KENNETH PORTIER:** Okay. Let's
13 reconvene. Yes. So we had read into the docket
14 question 5.6 on human health hazards relating to
15 the PBPK model, and I was turning to Dr. Bruckner
16 for comments. Dr. Bruckner.

17 **DR. JAMES BRUCKNER:** I'm here. Can
18 you -- and I'm muted when necessary. We have that
19 fixed now.

20 **DR. KENNETH PORTIER:** Yep. I can
21 hear you. Please proceed.

22 **DR. JAMES BRUCKNER:** Okay. Okay. I

1 guess the first thing is, with the modeling -- the
2 PBPK model that's used, I don't see any problems
3 with the model or with its use. My primary
4 concern is with the discussion in the document and
5 the way it's written. I'd like to see it a little
6 bit more user friendly or friendly for people who
7 don't really know much about modeling and what
8 it's used for.

9 So just looking back at some of
10 Harvey Clewell and Mel Anderson's early papers,
11 I'd like to see a couple of those papers
12 referenced. The only thing that's referenced
13 here is U.S. EPA 2006 and 2011 E. When you go
14 back and look at those, those are really detailed
15 accounts of the -- sort of the history, the
16 harmonization, the evolution of PBPK modeling, all
17 the things that were added and brought into
18 congruence. But if someone doesn't know much
19 about modeling or what its use -- its utility is,
20 how it can help reduce uncertainties and protect
21 them, they really, I think, won't understand too
22 much here.

1 So I was just going to recommend
2 that some additional references, some of these --
3 and I'll send the references for some of Mel's and
4 some of Harvey's papers. But also, you might just
5 include something like a simple model structure.
6 Perhaps, talk a little bit about input parameters
7 in terms of just the physiology and the
8 biochemistry that determines the -- if absorption
9 and the dose-symmetry of the chemicals.

10 And then just talk a little bit
11 about how, if you have a study which you're using
12 as a point of departure, that you can do a kinetic
13 study to determine what type of exposure produced
14 those tissue or blood levels. And then, with your
15 human model, then you can actually determine what
16 conditions the humans would be exposed to, to
17 produce that, and then go from that to how do you
18 simply determine human equivalent concentrations.
19 So if that makes sense, it's just a bit more of an
20 explanation of what it is, what it can be used
21 for, maybe a little bit about its limitations, but
22 just how it's used to actually end up with your

1 human equivalent concentrations, just a clearer
2 explanation.

3 What's here is good if you have a
4 PhD or even a J.D. and you can look at EPA policy
5 and guidelines. But it doesn't do much for me
6 even, you know, after 25 years now of modeling of
7 trichloroethylene. It sort of leaves me not
8 really knowing what it's really all about.

9 So that's my primary suggestion.
10 The modeling's great. I don't see anything wrong
11 with the model. It's been evolving now for 30
12 years, and I think it's, you know, it's
13 appropriately used in this assessment.

14 **DR. KENNETH PORTIER:** Thank you, Dr.
15 Bruckner. And this is Ken Portier. I'd like to
16 reiterate some of those things. I was able to
17 look at all of the PBPK model components that were
18 sent as part of the supplemental material. And I
19 think EPA did a good job of kind of combining that
20 and putting that all together in one space.

21 When you do look at the code files
22 though, I will encourage you to encourage

1 technical staff to continue to add comments. I
2 think the rule of thumb is you have twice as many
3 comments as you have actual active code in these
4 programs, and that's what we need to be able to
5 see to understand exactly what, you know -- to be
6 able to follow the code without necessarily
7 running the program itself. I did try to run a
8 couple of the components, and I was able to run
9 and replicate the output files. So I think that
10 was great.

11 Dr. Bruckner and others in this
12 question, one of the things I wanted to make sure
13 we talked about was the selection of dose metrics
14 and the percentile output selection and whether
15 that was appropriate. It, you know, it sounds
16 like that was okay. I'm seeing some hands going
17 up, so maybe I'll let Dr. Bruckner address that.
18 And then I'll turn to Dr. Morris. Dr. Bruckner

19 **DR. JAMES BRUCKNER:** Sure. In terms
20 of dose metrics, I don't think you can really do
21 better than what EPA's done here. In most cases,
22 other than kidney effects with DCVC, you can't

1 really be more specific than that. Whether it's -
2 - if it's liver toxicity or if it's toxicity --
3 reproductive toxicity or whether it's effects on
4 the immune system, about the best you can do is
5 perhaps look at either metabolism by one specific
6 pathway, GSH or P450, or look at total metabolism.

7 And I've looked at this, you know,
8 these types of questions for 10 or 15 years now.
9 I don't think we're any further along than we were
10 15 years ago. So I'm happy with the dosimeters
11 that are used.

12 It's the only question I have is, if
13 you're looking at effects on the fetus, think I
14 read that we're -- actually this modeling, what
15 happens or what -- the dosimetry is in the
16 maternal. And I'm wondering if that couldn't be
17 extended based on some of the PBPK models that
18 Jeff Fisher and others have done, if you couldn't
19 extend that a bit to actually looking at dosimetry
20 within the fetus itself. So I guess that's a
21 question I have for the EPA people who are here
22 now.

1 **DR. KENNETH PORTIER:** I see Dr.
2 Morris and Dr. Lash have their hands up. Dr.
3 Morris.

4 **DR. JOHN MORRIS:** Yeah. Actually, I
5 put in about four pages of comments, but I'll just
6 summarize them all here. I agree with what was
7 said before. I think this is a good model and is
8 being used appropriately. And so I don't, you
9 know -- I have a lot of comments, but they mainly
10 deal with the discussion of the model and the
11 discussion of the uncertainties.

12 And I think that discussion of the
13 uncertainties really should be a lot more robust.
14 And that probably would help in the comments I
15 made before about making this easier for the
16 reader to understand. So that's really where I'm
17 coming from on this, not that the model is
18 invalid. I have a couple of questions about the
19 model which, you know, just need to get put in the
20 text to rationalize what was done.

21 The first is that the model doesn't
22 have a nose, and I think that needs to be

1 discussed. That decision and then the
2 uncertainties introduced into that need to be
3 addressed. The real problem is that lower airway
4 delivery vapors and exercising mouth breathing
5 humans is very, very different than what you see
6 in this sedentary nose breathing rat. So that
7 just needs to be discussed and acknowledged, and
8 maybe you can argue around why that's not relevant
9 for this paper. But it's relevant for a lot of
10 papers. So I think that's a weakness that needs
11 to be acknowledged.

12 Another that I was sort of curious
13 about is the respiratory tract has got P450
14 metabolism, but, if I read it right, it doesn't
15 have any glutathione transferase metabolism. And
16 there's a lot of GSTs in the respiratory track and
17 even more in the nose. So I thought that was sort
18 of curious, and that needs to be discussed along
19 with the possible uncertainties.

20 One thing that I was a little
21 frustrated is -- I think it was mentioned before -
22 - is I couldn't find the breathing parameters.

1 And, I mean, I did look through all those
2 thousands of pages in the preceding documents, and
3 it looks like they've got breathing parameters for
4 the general public. But I couldn't find the
5 breathing parameters in the occupational setting.
6 And usually, in my experience, what's assumed in
7 the workers is that they're breathing more and
8 they're breathing through their mouth.

9 So that -- first off, that needs to
10 be explicitly stated, and then the uncertainties
11 introduced need to be discussed. I mean, I
12 thought, you know, maybe using the HEC99 would
13 sort of cover that, but the problem is in the
14 workplace what you've done is introduced a
15 systematic error. And I would venture to guess
16 that the HEC99 among workers is very different
17 than the HEC99 among the general public. So I
18 think that really needs to be discussed.

19 Also, I think the validations need
20 to be just discussed a little bit with respect to
21 two things. We're using this, especially in the
22 occupational settings, for multiple exposures.

1 And I went through all the validation figures in
2 the preceding documents, and it didn't look like
3 there was much validation of multiple exposure
4 scenarios. There were a couple of papers, but
5 there were some problems with those papers which I
6 put in my written review. So I just think that
7 needs to be discussed, you know, whether they're
8 confident in extending this model to a different
9 exposure scenario.

10 And by the same token, I didn't see
11 anything in the validation about altered breathing
12 parameters like what you might see in the
13 occupational settings. So this represents a
14 significant extension of the model, and some
15 discussion about whether it's been validated
16 under, you know, exercise breathing conditions
17 would really be useful. And I do have thoughts
18 about using the model for concentration times
19 time, but why don't we hold off on that until we
20 get to the end.

21 **DR. KENNETH PORTIER:** Thank you, Dr.
22 Morris. I heard at least six recommendations out

1 of that, so thank you. Dr. Lash.

2 **DR. LAWRENCE LASH:** Hi. Can you
3 hear me? Hello?

4 **DR. KENNETH PORTIER:** Yes.

5 **DR. LAWRENCE LASH:** Oh. Okay.
6 Great. So I just have a very brief comment
7 because it's relevant here, but then I have --
8 it's more relevant for question 5.8. As --
9 because it doesn't impact -- I didn't really have
10 much issue with the dose metrics and all. But
11 just when the sections that -- the two sections
12 that are noted go over, you know, the different
13 target sites, and they talk about reproductive
14 toxicity. There's -- the document misses a whole
15 bunch of studies on female reproductive toxicity.
16 And I think one of them mentions a LOAEL of 475
17 milligrams TCE per kilogram bodyweight, and I'm
18 not sure that's correct.

19 And so -- but I have -- it doesn't -
20 - it's not going to -- because it's not a very
21 sensitive endpoint, I don't think it's going to
22 impact the calculations here. But I think in

1 terms of correctness, it comes up in more -- I
2 think it's more relevant -- I have comments on
3 that -- more relevant for charge question 5.8.
4 But that's all I wanted to say.

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

6 Dr. Morris, your hand's still up. Did you have
7 more comments?

8 **DR. JOHN MORRIS:** Only when we get
9 to concentration times time. I would mention here
10 that I have no problems with the dosimetrics that
11 they picked, but I would have been more
12 comfortable if they'd provided a little bit more
13 justification for them, you know, just a couple of
14 sentences rather than one brief sentence. But the
15 choices themselves seem pretty straight forward to
16 me.

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

18 Dr. Bruckner, I'm reminded that Dr. Kissel made a
19 comment about how the model handled skin, and I
20 don't know if that'll need to be repeated in this
21 section or not. And if Dr. Kissel's on, he may
22 want to re-make that comment now. I mean, if the

1 model doesn't have a nose, it sounds like the
2 model has a simplistic skin.

3 **DR. JOHN KISSEL:** This is John
4 Kissel. I'm not sure we're talking about the same
5 model. Are we talking about the Poet TCE model?

6 **DR. KENNETH PORTIER:** Dr. Bruckner,
7 is that the one we're talking about?

8 **DR. JAMES BRUCKNER:** Right now, I
9 can't remember. I need to look back at John's
10 email to be sure, which I still have.

11 **DR. KENNETH PORTIER:** I thought
12 there was just the one PBPK model here.

13 **DR. JOHN KISSEL:** Well, it may be
14 the same. I was making a generic comment about
15 PBPK models typically teach -- treat skin as well
16 mixed boxes, as continuously stirred tank
17 reactors, which is not how skin actually behaves.
18 And so the numerical value of the permeability
19 coefficient that you get out of a PBPK model may
20 deviate from the numerical value that you would
21 get if you did a simple in vitro skin test. But
22 I'm not sure -- I thought -- I thought I saw a

1 comment somewhere that the pharmacokinetic model
2 was being used for the toxicity doesn't even have
3 a skin box, which is why I'm asking if it's the
4 same model.

5 **DR. KENNETH PORTIER:** And that's
6 probably what Dr. Lash wants to point out. It
7 probably doesn't have a skin model. Dr. Lash?

8 **DR. LAWRENCE LASH:** Yes. Yes. Hi.
9 I'm sorry. Yeah. I was just saying that it's
10 probably similar to the issue with the female
11 reproductive tox, that it's not going to impact
12 the calculation because it's a much less sensitive
13 endpoint is, I think, the point.

14 **DR. KENNETH PORTIER:** Dr. Barone,
15 you wanted to add some clarification here?

16 **DR. STANLEY BARONE:** Yes. The model
17 is actually an EPA model that you were provided
18 the code for and the documentation for. As Dr.
19 Bruckner indicated, this model has had a long
20 history. It does come out of -- the original
21 model comes out of Wright Patterson Air Force Base
22 and work of Mel Anderson and Harvey Clewell. It

1 incorporates work from (inaudible) Chu (phonetic)
2 at EP- -- when he was at EPA and the lead for the
3 IRIS assessment.

4 It incorporates comments from the
5 NAS and SAB peer reviews to the previous TCE
6 assessments. So this model has been around for
7 some time. It does have a probabilistic component
8 to it. It does not -- does not have a skin
9 compartment. And as Dr. Morris pointed out it
10 does not have a nose -- you know, nose
11 compartment.

12 **DR. KENNETH PORTIER:** Thank you.
13 Dr. Lash, your hand is still up. Okay. Anyone
14 else want to comment on the PBPK model? Dr.
15 Morris.

16 **DR. JOHN MORRIS:** I -- yeah. I
17 guess I'll just throw in my thoughts on
18 concentration times time and Haber's Law. I mean,
19 I think, you know, most of the dosimetrics that
20 were used in Table 3.5 were the total amount, like
21 the amount of TCE oxidized or total amount of TCA
22 produced. So you could run the model, you know,

1 under 24 hours to calculate what exposure
2 concentration would give you the same total amount
3 of dosimetric that would have been produced in the
4 three- or the six-hour exposure.

5 So you could make some sort of
6 model-based assessment of the appropriate
7 concentration times time extrapolation. And I
8 think that would be more based on science than
9 Haber's Law. So just food for thought.

10 **DR. KENNETH PORTIER:** Dr. Bruckner,
11 back to you.

12 **DR. JAMES BRUCKNER:** Yes. So I
13 wanted to ask Stan again to clarify why the
14 maternal modeling was done instead of fetal, since
15 the fetal models are available.

16 **DR. STANLEY BARONE:** We didn't -- we
17 did not include a fetal compartment in this
18 particular assessment.

19 **DR. JAMES BRUCKNER:** But I assume
20 you could have, just chose not to.

21 **DR. STANLEY BARONE:** That would be
22 additional work.

1 **DR. KENNETH PORTIER:** Stan, I always
2 worry when you're -- when you act -- give us short
3 answers. I'm always worried. Yes, of course it
4 would be more work. I think Dr. Bruckner's asking
5 is there a justification for not going there other
6 than the work?

7 **DR. STANLEY BARONE:** No. I'm sorry.
8 The actual fetal compartment is included for -- is
9 included for this particular effort. I'm
10 confusing my assessments because we did the
11 dosimetric -- we did the -- we did the work based
12 upon maternal exposure. We did not actually model
13 what the fetal levels were in the PBPK model.

14 So for cardiac defects, we were
15 looking at the maternal dose, internal dose. We
16 did not take it further into a more complicated
17 fetal compartment model, if that's what Dr.
18 Bruckner's getting at.

19 **DR. KENNETH PORTIER:** Dr. Morris,
20 your hand is still up.

21 **DR. JOHN MORRIS:** But it shouldn't
22 be.

1 **DR. KENNETH PORTIER:** Dr. Bruckner.

2 **DR. JAMES BRUCKNER:** That answers my
3 question. You decided not to go further.

4 **DR. KENNETH PORTIER:** So I guess it
5 begs the question whether the committee is okay
6 with that or whether we want to discuss whether
7 the fetal compartment should have been -- I mean,
8 the fetal levels should have been modeled and
9 somehow utilized in this. Dr. Bruckner, you
10 raised the question.

11 **DR. JAMES BRUCKNER:** I would think
12 it should be done since a model is available. And
13 I think this is one of the more controversial or
14 things of particular interest or the, obviously,
15 the fetal septal defects and valvular defects. So
16 I would advocate for it, but I wouldn't push too
17 strongly, I guess, at this point.

18 **DR. KENNETH PORTIER:** So a mild
19 recommendation.

20 **DR. JOHN MORRIS:** Yeah. I would
21 make the mild recommendation that it would be
22 preferable to do it if you could, but I would

1 raise the question of whether there really are
2 enough data to parametrize a fetal compartment and
3 any sort of data to validate it. So I think
4 those are issues that would have to be dealt with,
5 and perhaps they could just provide and
6 explanation for the decision one way or the other
7 in context of those factors.

8 **DR. KENNETH PORTIER:** You beat me to
9 my next question. Thank you. Dr. Bruckner, I
10 think at this point we've got a pretty good
11 discussion on 5.6. Do you have any closing
12 remarks before I turn to EPA for any final
13 comments?

14 **DR. JAMES BRUCKNER:** No. In view of
15 the work required for 5.1, I'm quite happy to end
16 it here.

17 **DR. KENNETH PORTIER:** Okay. Dr.
18 Barone, final comments?

19 **DR. STANLEY BARONE:** Yeah. To
20 follow up on Dr. Morris' comments, the reason for
21 not going into the fetal compartment pregnancy
22 model was based upon a lack of data for validation

1 for many of the parameterizations for specifically
2 TCE for that model. And that's principally it.

3 **DR. KENNETH PORTIER:** Thank you. At
4 this point, I think we're going to move on to
5 question 5.7. And while that is being scrolled
6 up, I will point out to the public, while the
7 committee agenda showed us ending at 3:30, as we
8 mentioned at the beginning, our timeframe for the
9 meeting is flexible. And it is my desire here to
10 complete question 7 before we quit for the day.
11 We have question 7 -- 5.7 and 5.8, which we're now
12 going to read into the docket. And this will
13 complete our day's work. So Dr. Bethel.

14
15 **CHARGE QUESTION 5 (5.7 AND 5.8)**

16
17 **DR. HEIDI BETHEL:** Question 5.7,
18 have the most scientifically robust critical
19 health effects and points of departures been
20 identified for TCE? Are there additional data
21 regarding other health effects for TCE that EPA
22 needs to consider? If data gaps exist in the TCE

1 database, how could the uncertainty about
2 sensitive health effects and critical windows of
3 exposure be better accounted for in the risk
4 characterization?

5 **DR. KENNETH PORTIER:** Go ahead and
6 read in question 5.8 as well, please.

7 **DR. HEIDI BETHEL:** Question 5.8,
8 please comment on any other aspects of the human
9 health hazard assessment that have not been
10 discussed, including the data quality evaluation
11 and the characterization of all assumptions and
12 uncertainties.

13 **DR. KENNETH PORTIER:** So Dr.
14 Bruckner. I think that's right. Yep. You have
15 it.

16 **DR. JAMES BRUCKNER:** That's it.

17 **DR. KENNETH PORTIER:** Please.

18 **DR. JAMES BRUCKNER:** I don't -- I
19 really don't have anything new for 5.7. I think
20 we've covered it in most of the last question. I
21 do have some comments on 5.8 though.

22 **DR. KENNETH PORTIER:** Dr. Barone,

1 did you want to clarify something? I see your
2 hand up.

3 **DR. STANLEY BARONE:** I'm sorry.
4 That -- I need to take it down.

5 **DR. KENNETH PORTIER:** Okay. Okay.
6 Does anyone else have comments on 5.7? I can see
7 Dr. Gilbert.

8 **DR. KATHLEEN GILBERT:** Yes. I'm not
9 absolutely positive that these comments belong
10 here, but I'll say them anyway. So it's talking
11 about critically -- critical health effects and I
12 think that, ultimately, we're going to find out
13 that developmental exposure to TCE is going to be
14 one of -- result in some of the most robust
15 effects. Now, we've always talked about the
16 cardiac malformations. I'm not going to discuss
17 those anymore.

18 But I'm a little concerned that
19 there was very little done in terms of
20 developmental immunotox. So they -- the EPA
21 states that the only identified study that
22 examined developmental immunotox, a Peden-Adams

1 2006, scored a low in data evaluation and a POD
2 could not be sufficiently derived. And as I
3 stated previously, the PBPK modeling is difficult
4 when exposure occurs in utero, during weaning, and
5 in -- during early life. However, as they noted,
6 this study exhibited one of the lowest PODs among
7 the developmental tox studies but was scored a low
8 for reasons mentioned.

9 This seems very inexplicable to me
10 and almost unacceptable, especially when compared
11 to the other immunotox studies of what I felt were
12 inferior quality that were nevertheless deemed of
13 medium quality and considered as key studies. So
14 we're asked to accept the fact that the criteria
15 used by the -- for -- EPA for assessing study
16 quality is appropriate. However, when faced with
17 such seemingly inappropriate manuscript ratings,
18 it calls this whole ability into question.

19 And, in any case, if they don't like
20 the Peden-Adams study well enough, there are other
21 animal studies that have documented developmental
22 immunotox at low dose TCE. And these provide

1 weight of evidence support for the validity of
2 this human hazard, which I think should be
3 included in the risk evaluation. So we've heard
4 just a few minutes ago about the issues with the
5 PBPK modeling, and I'm still not clear, if that
6 doesn't happen, does that mean you can't include
7 these studies in terms of determining a POD? And
8 I understand the difficulties associated with
9 looking at fetal levels under several different
10 conditions and including that and then going
11 forward of that in terms of weaning and post-
12 weaning. But it seems too important an endpoint
13 to leave out.

14 And then, the other question I have
15 for the EPA is what we're actually defining as
16 developmental toxicity. So does it only count if
17 it's manifest during early life such as pathology
18 specific or during infancy in childhood, or does
19 developmental tox refer to any toxicity that is
20 induced by developmental exposure but which may
21 manifest at any time during life? And that's
22 what's going to be true for some of these

1 immunotox endpoints.

2 I think that's where I am confused
3 about -- why they did not include the
4 developmental immunotox in the study. And is that
5 solely based on the difficulty with the PBPK
6 modeling? And what exactly they are defining as
7 developmental immune- -- developmental
8 immunotoxicity?

9 **DR. KENNETH PORTIER:** I saw -- I see
10 where Dr. Jacobs with EPA popped his hand up. Dr.
11 Jacobs, you want to clarify?

12 **DR. KEITH JACOBS:** Sorry, that was
13 actually a mistake or it's from before. But I am
14 currently looking up the details of our
15 evaluation, and I can provide that shortly once I
16 get it.

17 **DR. KENNETH PORTIER:** Okay. Let's
18 move on to Dr. Hossain.

19 **DR. MUHAMMAD HOSSAIN:** Hi. I have
20 additional comments regarding developmental
21 immunotoxicity following TCE exposure but that --
22 there are two studies that came out the last two

1 years. I think 2017 and '18. Those studies are
2 not included. So I think it was better included
3 as the developmental nervous system is more
4 vulnerable than the adult nervous system, which
5 could help for the evaluation of risk. So there
6 is one recent study that demonstrated that TCE at
7 very low dose, 0.25 micrograms, micrometer
8 concentration that is relevant to daily life
9 exposure in humans, decrease in neural progenitor
10 cells proliferations in differentiation, as well
11 as it also caused apotheoses cell death and
12 decrease of cell's bioavailability.

13 So I think this study should be
14 included for risk evaluation for developmental
15 neurotoxicity. I have the reference. I can send
16 it out later on. Another study demonstrated that
17 the prenatal exposure to 0 microgram, 10
18 microgram, and 100 microgram per milliliter TCE in
19 the drinking water causes inflammation but -- and
20 also deplete the glutathione depletion and caused
21 inter oxidative stress in the cerebral lung and
22 also altered the behavior of the mouse offspring.

1 So that could be very helpful for the risk
2 evaluation for developmental neurotoxicity.

3 And another thing, I think this is -
4 - it could be -- goes to the mode of actions maybe
5 mode of actions for dichloroethylene. It shows
6 that dichloroethylene depletes the glutathione
7 level in the brain. That could happen into the
8 other organs then lead to oxidative stress and
9 organ toxicity leading to cancer.

10 **DR. KENNETH PORTIER:** Thank you, Dr.

11 --

12 **DR. MUHAMMAD HOSSAIN:** That's all.

13 **DR. KENNETH PORTIER:** Thank you, Dr.
14 Hossain. Definitely get those citations over to
15 Todd so he can forward them to EPA and include
16 them on the website. Dr. Barone, I see your hand
17 up. Did you want to clarify something?

18 **DR. STANLEY BARONE:** Sorry. I was
19 talking while the mute was still on. One of the
20 points -- questions -- clarifying questions that
21 Dr. Gilbert asked about was, was developmental
22 toxicity defined as early exposure and effects at

1 any time in the lifetime of the progeny? And that
2 is correct. It does not have to be coincident
3 with a developmental occurrence.

4 It could be occurring later in life.
5 And in fact, that is part and parcel of the
6 considerations for developmental toxicity. And I
7 think Keith has some comments about the Peden
8 study that he can also offer as background.

9 **DR. KENNETH PORTIER:** I don't see
10 Keith's hand up. Dr. Jacobs.

11 **DR. KEITH JACOBS:** Yes. So I have
12 the overall summary comments from our evaluation.
13 So we had stated that actual doses were not
14 recorded and could not be calculated due to lack
15 of parental body weight data and lack of water
16 intake data. And then there was concerns over
17 sampling, lack of litter distribution data within
18 groups, use of pup as a statistical unit, and lack
19 of general health assessment in parental animals
20 and neonates.

21 **DR. KENNETH PORTIER:** Dr. Gilbert.

22 **DR. KATHLEEN GILBERT:** Well, I just

1 wanted to say that I appreciate Dr. Barone's
2 clarification in terms of what developmental
3 toxicity means to them. And I also appreciate the
4 comments from Dr. -- I'm sorry, the person we just
5 heard from concerning the problems with the Peden-
6 Adams study. But as Dr. Hossain also said, I
7 think we've -- there's enough evidence out there
8 that, aside from the cardiac defects, there are
9 issues associated with developmental toxicity,
10 whether that's immuno or whether that's neuro.

11 And I'm just -- and I'm -- there are
12 more papers besides the Peden-Adams that looked at
13 developmental immunotox. And I'm just a little
14 concerned that those other endpoints were kind of
15 discarded and we focused totally on the
16 controversial cardiac output. So I was just
17 curious --

18 **DR. KENNETH PORTIER:** So --

19 **DR. KATHLEEN GILBERT:** Go ahead.

20 **DR. KENNETH PORTIER:** Well, Dr.
21 Gilbert, I'm sitting here thinking that sounds
22 like a good recommendation, and I think you need

1 to add some of these additional references like
2 Dr. Hossain has pointed out and kind of give them
3 a -- point them in the direction you think they
4 need to go on this. I mean, you know, I don't
5 disagree with your assessment that it, you know --
6 in the draft risk evaluation they just haven't
7 provided a rich enough discussion in this area.
8 And I think it's up to us to help them, kind of,
9 fill it up.

10 **DR. KATHLEEN GILBERT:** Okay. I can
11 do that.

12 **DR. KENNETH PORTIER:** Yeah. Provide
13 that to Dr. Bruckner. Dr. Bruckner, your hand's
14 up. You're muted so --

15 **DR. JAMES BRUCKNER:** It was a --

16 **DR. KENNETH PORTIER:** There we go.

17 **DR. JAMES BRUCKNER:** It was a
18 mistake. It's like I'm looking for more work.
19 No. It wasn't up.

20 **DR. KENNETH PORTIER:** Well, I'm
21 about ready to ask anybody else on the panel
22 whether they have comments on question 5.7 that we

1 want to add in. And not seeing any, I'm going to
2 turn to EPA and say did you get a sufficient
3 thought response from the panel? Do you need any
4 -- do you have any clarifying questions other than
5 the discussion we just had?

6 **DR. STANLEY BARONE:** I think -- this
7 is Dr. Barone, Dr. Portier. Thank you for the
8 robust comments. Again, we heard earlier I think
9 about inclusion of exposure response arrays for
10 particular domains, including that into the hazard
11 characterization. We have identified quite a
12 number of studies -- developmental studies and
13 developmental endpoints that we carried forward to
14 dose-response, including developmental
15 neurotoxicity, developmental toxicity, and
16 developmental cardiac toxicity. And so there's a
17 number of endpoints that we've identified for
18 dose-response.

19 There were some additional studies
20 that were mentioned by, I believe, Dr. Hossain.
21 If those references could be sent to Dr. Todd
22 Peterson, the DFO, we'd be happy to look at those

1 and try to evaluate those as quick as we can,
2 given our timelines.

3 **DR. KENNETH PORTIER:** Okay. Dr.
4 Bruckner, let's move on to question 5.8.

5 **DR. JAMES BRUCKNER:** Okay. First, I
6 wanted to mention a little bit about
7 toxicokinetics in metabolism. I know this is not
8 a normal health effects document, but I was sort
9 of dismayed to see there's such little information
10 available on a number of these topics. First, in
11 terms of just metabolism and dosimeters and mode
12 of action, Larry Lash has been active doing lots
13 of things. But three things he's done is publish
14 review papers, one in 2014, one in 2016, one 2018
15 laying out sort of the state of the art on these
16 topics of the role of metabolism in cytotoxicity
17 and cancer. So I think those papers needs to be
18 referenced and more information needs to be given,
19 at least a summary what's in those papers.

20 Also, I saw something just from --
21 just the basic kinetics which would assume that
22 there's 100 percent absorption of inhaled

1 trichloroethylene. In my lab, we did a number of
2 studies. It depends upon the direction of
3 exposure and the concentration, but the numbers
4 are more from 50 to 60 or 70 percent.

5 I was a little surprised to see that
6 it assumed 100 percent of dermal absorption. I'm
7 not sure where that number came from. So I would
8 just urge to have a little bit more broad,
9 comprehensive discussion of the state of the art
10 in terms of just metabolism and kinetics and how
11 that impacts dosimeters that are chosen and
12 modeled.

13 I was also a little concerned --
14 there was one, sort of, an overstatement I saw
15 that says that animals and humans exposed to TCE
16 consistently experience liver toxicity. I think I
17 saw the same thing with kidney toxicity. These
18 are really overstatements. Let me give you just
19 an example.

20 Kurt Flossen (phonetic) did, you
21 know, a classic study back in the '60s in which he
22 looked at the dose of trichloroethylene and some

1 other solvents that would be required to produce
2 liver entry as shown by increases in serum
3 enzymes. He found that he had to give an LD50
4 almost of trichloroethylene before he got any
5 increase in liver enzymes. There've been suicide
6 attempts. In one case, 70 milliliters of
7 trichloroethylene was ingested, and there was no -
8 - there was kidney injury but no evidence of liver
9 injury.

10 Lots of other studies of
11 occupational exposures were -- I guess my question
12 -- or my problem is that only in extremely high
13 exposure concentrations do you see, at times, a
14 little bit of scattered liver injury, not much.
15 Sometimes kidney injury, but the types of
16 exposures we're talking about here are certainly
17 not environmental levels. They're high
18 occupational exposure levels, usually on a chronic
19 basis.

20 So I guess I'm just concerned about
21 some of the blanket indictments of
22 trichloroethylene as begin a liver or kidney

1 toxin. And I'd like to see some of those, with
2 specific references, toned down a little bit just
3 in terms of magnitude of injury being dependent
4 upon dose and duration of exposure. So those are
5 my primary comments here.

6 **DR. KENNETH PORTIER:** Dr. Gilbert.

7 **DR. KATHLEEN GILBERT:** I just wanted
8 to comment on the whole liver toxicity thing. I
9 take your point that we should note that there are
10 dozens of papers coming out of other parts of the
11 world where TCE is still used quite often
12 occupationally. And there are many, many papers
13 that see hypersensitivity associated with some
14 level of hepatotoxicity, some sort of hepatitis
15 associated with TCE exposure in the workplace. So
16 I don't know that saying that TCE causes liver
17 damage -- certainly not always but it's certainly
18 not unusual either.

19 **DR. KENNETH PORTIER:** Dr. Lash.

20 **DR. LAWRENCE LASH:** Yeah. Hi. I
21 agree -- I agree with, you know, what was just
22 said. But I do agree with what Dr. Bruckner said

1 that there are a lot of cases where the statements
2 are a little too broad so that, you know, to say
3 that you consistently observe an effect kind of
4 implies something different than that -- under
5 appropriate conditions then a certain target organ
6 can always be identified or something like that.
7 You know, so I think those statements do need to
8 be refined. So I had a bunch of comments on this
9 section. Is this an appropriate time or did -- to
10 give them?

11 **DR. KENNETH PORTIER:** There's no
12 other time than now.

13 **DR. LAWRENCE LASH:** Okay. Great.

14 **DR. KENNETH PORTIER:** Go for it.

15 **DR. LAWRENCE LASH:** Well, I have a
16 lot of minor comments that are in my notes that
17 are, like, corrections. So I won't go through
18 those in detail. There are a couple of
19 misstatements about relative levels of enzyme
20 activities in different species.

21 I thought there was also -- in one
22 of the sections, page 210, that the issue of

1 gender and species dependent differences which can
2 actually be quite prominent needs to be discussed
3 better. And I think that goes to the same issue
4 that we were just talking about in terms of making
5 comments with the right -- you know, under the
6 right conditions. So okay. There was also with
7 regard to, there was a statement on page 212, 214.

8 There was a section that talks about
9 immunotoxicity and sensitization and actually to
10 me it seemed like they were two statements that
11 contradicted each other because one was talking
12 about immunosuppression and one was talking about
13 immuno-stimulation. I think it's just a case that
14 this -- the description needs to be more specific.
15 Then, and here's why I mentioned in section
16 3.2.3.1.5 reproductive toxicity, which is 214, and
17 I had mentioned earlier that there's several
18 studies, primarily done recently by Rita Loch-
19 Caruso at University of Michigan -- and I've been
20 a co-author on a couple of them -- that have to do
21 with female reproductive toxicity.

22 And so, as I said, they don't -- I

1 don't think they end up influencing hazard
2 identification or the risk calculations because
3 it's not -- in terms of the sensitivity. But I
4 think -- I know there's a couple of statements
5 where it says that there's no -- something like --
6 to the effect of that there's no consistent or
7 significant evidence of female reproductive
8 toxicity. And I don't think that's really
9 correct.

10 So I've given in my notes all those
11 references. And a couple are very recent, but
12 there's a couple -- one that's from 2016 that's
13 relevant and 2018. And then the other are like --
14 three are much more -- or four are much more
15 recent.

16 Let's see. Then -- all right. All
17 right. I've got a lot here. So this is -- some
18 of these are -- repeat some of the things said
19 earlier about the MOA for kidney cancer that, you
20 know -- I think, because of what's not known,
21 maybe the uncertainty needs to be increased. But,
22 I mean, we can say it's definitely mutagenic, but,

1 you know, how prominent the role of that
2 genotoxicity is in the mechanism is really not
3 clear.

4 One of things that struck me also
5 with regard to the liver, there's a fair bit of
6 discussion on PPAR-alpha, and that's really not
7 relevant for humans. I mean, that's been, you
8 know, considered pretty well established that
9 it's, for the most part, a rodent specific
10 responsive. So I think that needs to be, you
11 know, to be -- and also there was a statement in
12 that same section, 3.2.4.2.2 -- it says -- it
13 talks about, again, "the predominant mode of
14 action for kidney carcinogenicity involve the
15 genotoxic mechanism."

16 So that's not accurate. I mean, we
17 don't know that. We know that it contributes, but
18 I don't think we can say that it's predominant or
19 even that it -- even that it could even be
20 significant under all conditions.

21 Okay. Then, the last thing, which I
22 think this was kind of the only place that it was

1 relevant. And again, this goes along with -- a
2 bit with, you know, what Dr. Bruckner said in the
3 beginning about toxicokinetics and metabolism.
4 There -- and so it's not really discussed much in
5 here, in the document, and I think a lot of this
6 may go to the point that a lot of those issues
7 were spelled out -- and it might not be in terms
8 of the TSCA requirements as relevant. But I know
9 it's spelled out in detail in the, you know, the
10 IRIS document and in other types of documents.

11 But I want -- I thought this was the
12 place to comment here so that it's on the record
13 since there were comments made by Dr. James Bus on
14 Tuesday with regard to the glutathione pathway.
15 And so in his oral comments, he talked about the
16 importance and quantitative significance of the
17 glutathione conjugation pathway. And I think as
18 clearly stated here, it's this pathway that has --
19 and this is what the consensus of this pathway has
20 been directly associated with adverse kidney
21 effects.

22 I think that is not in dispute and

1 should not be in dispute because it's been gone
2 over and over again. He does -- he makes an
3 argument in his comments that previously reported
4 HPLC method used to detect formation of the
5 glutathione conjugate, namely DCVG, that it
6 overestimated product formation by several orders
7 of magnitude due to interference by an over
8 lagging peak. And he cites a paper that he's a
9 coauthor on from 2018 in *Toxicology Letters*.

10 And then he repeats a conclusion
11 that was promulgated and disproven more than two
12 decades ago that -- about metabolic flux of the
13 glutathione conjugation pathway not being
14 significant. And one of the points that is made
15 in the IRIS document, as well as, for example, in
16 the 2014 IARC Monograph as well as in -- Dr.
17 Bruckner mentioned a couple of reviews that I co-
18 authored with Yvonne Russen (phonetic) in 2014,
19 2016, 2018 that -- because -- and this is what's
20 unique about this pathway because the -- it forms
21 a highly reactive intermediate derived directly
22 from dichlorovinyl cystine, DCVC, that you can't

1 simply equate flux by looking at a stable end
2 product that might be recovered in the urine. You
3 know, whereas the P450 pathway metabolites are
4 chemically stable such as trichloroacetate,
5 trichloroethanol, and glucuronide. And that -- so
6 you really don't know just from that type -- those
7 types of measurements.

8 So anyway, the point I wanted to
9 make was that the -- first of all, the issues that
10 Dr. Bus raised were not even brought up in this
11 document so -- and it's not even -- I don't even
12 think it's really -- it's relevant. And that
13 these issues have all been addressed in -- as I
14 said in the -- in a review that I coauthored in
15 2000 in a special issue of *Environmental Health*
16 *Perspectives*, in the 2011 EPA IRIS document, and
17 the 2014 IARC TCE Monograph.

18 And with regard to the citation, the
19 recent publication that he coauthored with Zhang
20 et al. in *Toxicology Letters* -- and he talks about
21 the comparison between the methods that we used
22 have and then LCMS assay. I would note that in an

1 LMCA- -- LCMS assay developed by Russen and
2 colleagues that the two publication that I've
3 given in the -- provided here the reference by Kim
4 et al. is the first author 2009 -- that the rates
5 of DCVG formation that -- or DCVG concentrations
6 in different biofluids that they reported were
7 actually fairly close or, at most, only a couple,
8 you know, fold off of what we reported. So I
9 think that's been disproven.

10 And then -- and I think finally, I
11 mean, the main point I think for TSCA is that this
12 issue, which as I said has been resolved but it
13 really doesn't impact the TSCA hazard assessment.
14 But I thought that, since that was in the record,
15 the public comment, that I think it needed to be
16 addressed. So that was what I had to say.

17 **DR. KENNETH PORTIER:** Thank you, Dr.
18 Lash. Anyone else want -- have additional
19 comments on 5.8? Dr. Lash, I still see your hand
20 up. Dr. Barone?

21 **DR. STANLEY BARONE:** Yeah. I just
22 wanted to follow up on Dr. Lash's comments. I was

1 a little confused, and pardon me -- bear with me.
2 Dr. Lash, are you saying the public comments that
3 we received are not accurate about the metabolites
4 that we were speaking about -- the mutagenic --
5 potentially mutagenic metabolites, or are you
6 agreeing with public comments? It wasn't -- it
7 wasn't clear to me.

8 **DR. LAWRENCE LASH:** No. I -- well,
9 yeah. What I was saying is that they are not
10 accurate. We addressed this issue back in --
11 because there were differences in reported work
12 between Trevor Green -- some of his work in like
13 1997-98 and also then with what Yvonne Russen's
14 group published in 2009 with their LCMS methods.
15 And so what I'm saying is that we resolved the
16 issue and discussed it in the 2011 IRIS document
17 also in a -- the 2000 *Environment Health*
18 *Perspective* special issue on TCE as well as in the
19 IARC Monograph. So yeah. So I am saying that
20 it's incorrect, what was stated.

21 **DR. STANLEY BARONE:** So to help me
22 understand, so the metabolites -- mutagenic

1 metabolite which you said is weak or less potent
2 than some other mutagens is appropriate to be
3 considered for the kidney cancer.

4 **DR. LAWRENCE LASH:** Yes. I mean,
5 this is where you get into the issue of data gaps
6 and that. I've -- as I said, we do know, it's
7 been demonstrated and I think Martha Moore
8 probably did most of, you know, most of those
9 studies where -- quantified the mutagenic
10 potential with a variety of assays for -- of DCVG
11 and compared it to a lot of standard mutagens. So
12 for example, compared to a vinyl chloride or
13 something, it's quite weak. But it is clearly
14 mutagenic, whereas all the other key metabolites
15 from the other pathways, such as trichloroethanol,
16 trichloroacetate, dichloroacetate, were not
17 mutagenic by any of those assays.

18 So I think it -- one can conclude
19 that it is a mutagen, that there's clear evidence
20 for that but it's a rather weak mutagen. But then
21 the issue comes up. We do know that -- and
22 there's evidence in terms of, you know, a

1 different mode of action that involves non-
2 genotoxic mode that would involve -- you know,
3 cytotoxicity and repair. And, you know, these --
4 particularly when you have chronic long-term
5 exposures. You have these cycles of sublethal
6 injury and repair proliferation, and there's times
7 where there's de-differentiation and
8 redifferentiation. And you can get disruptions in
9 the regulatory process, and that's what's thought
10 to occur.

11 And so the relative contribution of
12 this mutagen -- mutagenic mode versus the -- this
13 non-genotoxic mode is really we don't know. I
14 don't think anybody directly addressed it. You
15 know, we do know, for example, that there is some
16 data even from human studies with the Von Hippel
17 Lindau gene, you know, some others, that there are
18 some evidence of genotoxic. But we just don't
19 know how -- quantitatively how important it is.
20 So that's my only point. Does that --

21 **DR. STANLEY BARONE:** Yes. Thank you
22 for that clarification. And if you have any

1 further thoughts, please include that in your
2 responses. We had discussed the information on
3 the Von Hippel gene studies previously in the IRIS
4 assessments.

5 **DR. LAWRENCE LASH:** Right.

6 **DR. STANLEY BARONE:** If you have any
7 other suggestions, please include those in your
8 remarks.

9 **DR. LAWRENCE LASH:** Sure. Okay.

10 **DR. KENNETH PORTIER:** I guess this
11 is last call for any comments on questions 5.8,
12 5.7. Dr. Bruckner, I'm sure you have excellent
13 notes, and you know where to find all these
14 commenters to get their notes. At this point,
15 I'll turn to EPA and ask are there any comments or
16 clarifying questions on anything we've discussed
17 today regarding question 5 on human health hazard
18 before I close the meeting? Dr. Barone.

19 **DR. STANLEY BARONE:** I don't think
20 we have any further clarifying questions at this
21 point. We do appreciate the panel's robust
22 dialogue. I think there's been a lot of good

1 suggestions. I appreciate you, Dr. Portier,
2 formulating those into actionable recommendations
3 that we can follow up on.

4 **DR. KENNETH PORTIER:** Yes. Okay. I
5 -- that's kind of the -- this ends the material
6 that I was hoping we would cover today and which
7 we have. I'll remind the panel and the public
8 that we reconvene tomorrow morning at 10:00
9 Eastern to discuss two more sets of questions: one
10 on the risk characterization and then kind of an
11 overall content and organization set of questions.
12 It looks to be another full day of discussion. At
13 this point, I'll turn it over to the DFO, Todd
14 Peterson, for any last comments. Todd.

15 **DR. TODD PETERSON:** Thank you, Dr.
16 Portier. You actually covered what I was going to
17 cover in closing your part -- remarks. So, this
18 day's session is not adjourned. Thanks all.

19
20 **(MEETING ADJOURNED FOR THE DAY)**
21

1 **OPENING OF MEETING - DAY 4**

2

3 **OPERATOR:** Good morning. Welcome to

4 the fourth day of this meeting series on the U.S.

5 EPA Peer Review of the Draft Risk Evaluation for

6 Trichloroethylene or TCE. Battelle is an EPA

7 contractor providing meeting support for this

8 series. This event is being recorded.

9 The host may use chat to share

10 announcements with all attendees, but attendees

11 will not be able to respond to chat. Panelists,

12 please send direct messages to the host or

13 panelist. I will now introduce Dr. Todd Peterson,

14 the Designated Federal Officer.

15 **DR. TODD PETERSON:** Good morning. I

16 am Dr. Todd Peterson, Designated Federal Officer.

17 It is my pleasure to open the fourth and final day

18 of this four-day online meeting for the Science

19 Advisory Committee on Chemicals, what we TSCA SACC

20 for short. This is the peer review of EPA's Draft

21 Risk Evaluation for Trichloroethylene.

1 This week's WebEx hosted meetings
2 have all gone very well. However, if you
3 encounter any problems with audio or video
4 transmissions today, I please refer you to the
5 internet link that's at the bottom of the slide
6 that's showing on the screen now. And you can
7 then access that for tips on getting back into the
8 session.

9 For members of the press, EPA media
10 relations staff are available to answer your
11 questions specifically about this meeting, so I
12 would ask that you please address all your
13 questions to Mr. Ken Labbe, and his email address
14 is L-A-B-B-E dot K-E-N at E-P-A dot G-O-V
15 labbe.ken@epa.gov. His phone number is (202) 740-
16 3370. And while it's the rare occasion, I just
17 used the chat box to all attendees, so this same
18 information is now posted for your viewing.

19 As noted in our announcements about
20 the SACC meeting, the agenda times are
21 approximate, and we will be starting today with
22 the charge questions as indicated on this day's

1 agenda. As noted yesterday, the chair at his
2 discretion may call for additional breaks during
3 the meeting today and adding a ten-minute break
4 here or there can be helpful for the committee.
5 And we have extra time on the agenda to
6 accommodate an additional break or two during the
7 meeting.

8 Overall, the committee's sessions
9 are going well, and I thank all of our peer
10 reviewers for your contributions to this meeting.
11 I now turn the meeting over to our chair, Dr.
12 Portier.

13 **DR. KENNETH PORTIER:** Good morning
14 and welcome to the committee and to the public to
15 Day 4 of this meeting. We'll begin the meeting as
16 we've done in the past by calling the role. Dr.
17 Anderson? Dr. Bennett.

18 **DR. STEVEN BENNETT:** This is Steve
19 Bennett.

20 **DR. KENNETH PORTIER:** Dr. Barton.

21 **DR. CHARLES BARTON:** Here.

22 **DR. KENNETH PORTIER:** Dr. Blystone.

1 DR. SHERI BLYSTONE: Good morning.

2 DR. KENNETH PORTIER: Dr. Bruckner.

3 DR. JAMES BRUCKNER: Present.

4 DR. KENNETH PORTIER: Dr. Cory-

5 Slechta?

6 DR. DEBORAH CORY-SLECHTA: I'm here.

7 DR. KENNETH PORTIER: Dr. Davies.

8 DR. HOLLY DAVIES: I'm here.

9 DR. KENNETH PORTIER: Dr. Doucette?

10 DR. WILLIAM DOUCETTE: Virtually

11 present.

12 DR. KENNETH PORTIER: Dr. Jimenez-

13 Gonzales?

14 DR. CONCEPCION JIMENEZ-GONZALEZ:

15 I'm here.

16 DR. KENNETH PORTIER: Dr. Gilbert.

17 DR. KATHLEEN GILBERT: I'm here.

18 DR. KENNETH PORTIER: Dr. Johnson?

19 DR. MARK JOHNSON: Hi, good morning.

20 DR. KENNETH PORTIER: Dr. Kaufman.

21 Dr. Kissel?

22 DR. JOHN KISSEL: Here.

1 DR. KENNETH PORTIER: Dr. Rowlands.

2 MR. ALAN KAUFMAN: Sorry, this is
3 Kaufman. I was on mute.

4 DR. KENNETH PORTIER: That's fine.
5 Dr. Rowlands?

6 DR. CRAIG ROWLANDS: I'm here.

7 DR. KENNETH PORTIER: Thank you.
8 Dr. Schlenk.

9 DR. DANIEL SCHLENK: Here.

10 DR. KENNETH PORTIER: I think Dr.
11 Anderson had class this morning, he'll be joining
12 us a little late. Dr. Apte.

13 DR. UDAYAN APTE: Here.

14 DR. KENNETH PORTIER: Dr. Cobb.

15 DR. GEORGE COBB: Here. I'm here.

16 DR. KENNETH PORTIER: Dr. Grant. I
17 don't see Dr. Grant online yet. There he is.

18 DR. STEPHEN GRANT: Double muting.

19 DR. KENNETH PORTIER: Where am I?
20 Dr. Hossain?

21 DR. MUHAMMAD HOSSAIN: Yes, I am
22 here.

1 DR. KENNETH PORTIER: Dr. Jenkins?

2 MS. ALLISON JENKINS: Here.

3 DR. KENNETH PORTIER: Dr. Lash?

4 DR. LAWRENCE LASH: I'm here.

5 DR. KENNETH PORTIER: Dr. Morandi?

6 DR. MARIA MORANDI: I am here.

7 DR. KENNETH PORTIER: Good morning.

8 Dr. Morris?

9 DR. JOHN MORRIS: I'm here.

10 DR. KENNETH PORTIER: Dr. Rosol?

11 DR. KENNETH PORTIER: I can see
12 you're unmuted. There we go.

13 DR. THOMAS ROSOL: I'm here.

14 DR. KENNETH PORTIER: Got it. Dr.
15 Vorhees.

16 DR. CHARLES VORHEES: Here.

17 DR. KENNETH PORTIER: Dr. Pessah was
18 called away and hasn't been able to participate,
19 but that ends the roll call. I will turn to Ms.
20 Bethel to introduce the EPA staff that are on the
21 call.

1 **DR. HEIDI BETHEL:** Good morning,
2 everyone. Thank you for attending today. This is
3 Heidi Bethel of the Environmental Protection
4 Agency. Today on the phone we have, I believe,
5 the majority of our team members. Dr. Keith
6 Jacobs is our primary team lead for the TCE
7 assessment. We have Stan Barone and Nhan Nguyen
8 who are our management leads. We also have on the
9 call today Franklyn Hall, Kara Koehn, Xiah
10 Kragie, Wen Lee, Sue Makris, Stephanie Sarraïno.

11 **DR. KENNETH PORTIER:** Thank you and
12 welcome to all of you. Yesterday we had I would
13 say a vigorous and rigorous discussion of the
14 human health hazard issues presented to us in the
15 Draft Risk Assessment for TCE. Today we're going
16 to be looking at risk characterization issues and
17 overall content and organization of the report.

18 **FOLLOW-UP ON PREVIOUS DAY DISCUSSION**

19
20 Before we move on to Charge Question
21 6, I wanted to open the discussion to any of the
22 committeemen member who might want to -- or who

1 have had new thoughts on yesterday's discussion on
2 hazard. Please, raise your hand so I can call on
3 you. Dr. Kissel.

4 **DR. JOHN KISSEL:** So this is not
5 about hazard, this is going back a day earlier.
6 But prompted by George Cobb's question, I went
7 looking for evidence of skin damage from
8 trichloroethylene; and turns out there's quite a
9 large literature that occupational dermatitis is
10 very prevalent, especially in Asia. A lot of the
11 literature is in Chinese, and I couldn't really
12 access it, but some of it has leaked through into
13 English language.

14 So there's lots and lots of evidence
15 that trichloroethylene does damage skin. That's
16 qualitative evidence. There's nothing in those
17 papers that I found that was helpful with respect
18 to predicting permeability. But the starting
19 point of assuming that trichloroethylene damages
20 skin is a reasonable starting point.

21 I had mentioned that I -- the one
22 thing I had discussed was a rat study from 1991,

1 which did side-by-side testing of neat compound
2 versus a pure substance -- or neat compound versus
3 a saturated compound. And there was a substantial
4 difference, which is a flag that skin damage is an
5 issue. That was a rat study.

6 Upon further searching, I did find
7 two human hand-immersion studies, one done in
8 Japan in the '70s and one done in the United
9 States in the '60s, in which volunteers put their
10 hands into liquid trichloroethylene. I have
11 obtained the Japanese study and it does permit
12 estimation of a flux, and that flux is
13 substantially greater than would be predicted
14 using the POD-derived permeability coefficient.
15 So that's confirmatory.

16 The second one I've requested from
17 my library, and it hasn't come yet. But I do
18 expect to ultimately get that, and I will provide
19 that information and sample calculations to EPA.

20 **DR. KENNETH PORTIER:** Thank you,
21 John, that's useful. Anyone else? Dr. Blystone.

1 **DR. SHERI BLYSTONE:** Yeah, just
2 following on Dr. Kissel's comments, this is one of
3 the reasons why I think having GHS classification
4 as part of the document would be useful, because
5 if you look at the GHS classification it is
6 categorized as a Category 2 skin irritant.

7 **DR. KENNETH PORTIER:** Thank you.
8 Anyone else have comments to add on any of the
9 earlier questions? Dr. Kissel, I see your hand's
10 still up. Okay, that's good material that will be
11 added to the committee's response to the previous
12 days' questions. At this point I think the
13 committee is ready to move forward with Charge
14 Question 6 on Risk Characterization, and I'll turn
15 it to Dr. Bethel to read the question into the
16 docket. Dr. Bethel?

17 ***CHARGE QUESTION 6 (6.1)***
18

19 **DR. HEIDI BETHEL:** Yes, thank you.
20 Question 6 on Risk Characterization. EPA
21 concludes that TCE poses a hazard to environmental
22 aquatic receptors, with invertebrates and fish as

1 the most sensitive taxa. Environmental risks were
2 assessed using Risk Quotients (RQs) and the number
3 of days that a concentration of concern (COC) was
4 exceeded.

5 EPA evaluated potential risks for
6 workers and occupational non-users, consumer
7 users, and bystanders/non-users. For non-cancer
8 effects EPA used a margin of exposure (MOE), which
9 is the ratio of the hazard value to the exposure.
10 For cancer, an inhalation unit risk (IUR) and oral
11 slope factor (OSF), that incorporate the combined
12 extra risk for all three cancer sites, was used to
13 evaluate chronic cancer risks for occupational
14 scenarios. Next slide, please? Oh, I think I
15 missed the last part.

16 EPA concluded that TCE presents an
17 unreasonable risk to workers, occupational non-
18 users, consumer users and bystanders, but not for
19 environmental receptors.

20 Question 6.1. Please comment on
21 whether the information presented to the panel
22 supports the conclusions outline in the draft risk

1 characterization section concerning TCE. If not,
2 please suggest alternative approaches or
3 information that could be used to further develop
4 risk estimates within the context of the
5 requirements stated in EPA's Final Rule,
6 *Procedures for Chemical Risk Evaluation Under the*
7 *Amended Toxic Substances Control Act.*

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

9 The importance of this question is underlined by
10 the fact that we've asked almost half the
11 committee to comment on this question. And the
12 lead on this is Dr. Vorhees, Chip?

13 **DR. CHARLES VORHEES:** Yes, I'm here.

14 All right so I got a lot of feedback, and so I
15 think what I'll do is be pretty literal about it
16 and read you most of the feedback that I got.
17 Every time you hear me say "comment" that means
18 it's a different person speaking. They're de-
19 identified, however. So the first -- so let me
20 start off with this one.

21 In general conclusions on the
22 environmental risk are consistent with the state

1 of the art. One can deduce that the EPA did not
2 find unreasonable risk to aquatic organisms in
3 surface water, but this needs to be more clearly
4 stated. There was some risks with RQ greater than
5 1 associated with specific facilities and species,
6 but this does not seem to translate to a solid
7 determination per mode of use given that several
8 facilities had risks with RQ greater than one. It
9 is recommended that EPA summarize the approach and
10 determination for each condition of use.

11 It is also concerning that the
12 emission pathways to ambient air from commercial
13 and industrial stationary sources were excluded on
14 a statutory basis. Even though it is expected
15 that most of the TCE will be removed in wastewater
16 treatment by volatilization during aeration it is
17 not appropriate to assume that ambient exposure
18 risks are effectively managed by the Clean Air
19 Act, particularly when coming from an aeration
20 basin.

21 A sensitivity analysis is
22 recommended for environmental risk assessment,

1 particularly for those values for which the
2 uncertainty is larger, e.g., chronic hazard
3 values, similar to what was done when large
4 variation was found on toxicity values for
5 different species.

6 A quantitative or semi-quantitative
7 uncertainty analysis is also recommended,
8 particularly in some of the model data for
9 environmental risk. The geographical
10 representations of the assessments, shown in
11 Figure 4-1 through 4-6, are good ways to represent
12 the risks; but since none of the monitoring
13 locations are downstream from facilities, the
14 conclusion of the "risk to aquatic organisms from
15 TCE exposure is more likely in areas near
16 facilities" needs to be accompanied with some
17 measure of uncertainty.

18 One concern of the methods is
19 related to the questions that arose publicly
20 regarding alleged changes to the EPA risk
21 evaluation. That claim that the draft provided
22 for interagency review identified fetal cardiac

1 malformations as the most sensitive endpoint used
2 to derive the points of departure for making
3 determinations of risk consistent with prior
4 reviews of TCE, a full discussion of the rationale
5 for excluding fetal heart malformations as
6 endpoints in contradiction of EPA's 2011 IRIS
7 evaluation is needed.

8 These allegations need to be
9 investigated as the mere suggestion that EPA
10 changed the first scientific evaluation, based on
11 pressures from non-scientific sources, could cast
12 a significant doubt on the scientific integrity
13 that EPA has worked so hard to maintain.

14 Comment. The information in Section
15 6 is based entirely on the conclusions drawn on
16 earlier parts of the document on exposure
17 assessment and health hazard assessment with dose
18 response. In my view the information presented in
19 these earlier portions of text, with the exclusion
20 of the comments provided above, supports the
21 conclusions that are given in the risk
22 characterization.

1 Comment. Risk Characterization,
2 Page 275, Lines 329 to 333; in this section the
3 EPA considers volatilization rates not to
4 contribute to exposure to terrestrial organisms.
5 However, I wonder about soil invertebrates and
6 burrowing mammals in functionally confined spaces
7 exposed to TCE through vapor intrusion from
8 contaminated underground sources. Certainly this
9 is considered in other EPA regulations, e.g.,
10 CERCLA for human health concerns, and more robust
11 justification or assessment is needed to dismiss
12 such exposures for these organisms.

13 Comment. EPA identified six health
14 effect domains for non-cancer risk and dose
15 response analyses: liver, kidney, nervous system,
16 immune, reproductive system and development. EPA
17 identified three domains for cancer: renal,
18 hepatic, and non-Hodgkin lymphoma, but I'm
19 concerned about the Johnson cardiac malformation
20 data.

21 These data can be used for hazard
22 identification but should not be used for dose

1 response consideration because of study design
2 problems, replications failure, et cetera. While
3 the controversy between the methods of fetal
4 dissection are important scientifically, it is
5 unsettled science and cannot be resolved in the
6 DRE, therefore should not be relied upon for POD
7 determination.

8 Comment. Consistent with the
9 requirements of TSCA, Section 4 outlines potential
10 human health effects for each use that involves
11 TCE exposure. The section comprises an extensive
12 array of clear and well-organized tables that list
13 for each occupation, each endpoint, for both
14 inhalation and dermal exposure listing the
15 benchmark MOE, worker MOE with and without the use
16 of PPE. Standard criteria are used to calculate
17 MOE values. Determination of these values and
18 their comparison with the benchmark MOE values,
19 which is used to reach the conclusions about
20 whether unreasonable risks exist for each use, are
21 clearly described and logically presented.

1 Comment. EPA adequately identified
2 and addressed both cancer and non-cancer endpoints
3 of heart toxicity, liver toxicity, kidney
4 toxicology, immunotoxicity, and neurotoxicity and
5 reproductive and developmental toxicity. However,
6 exposure to TCE during pregnancy reported to cause
7 severe cardiac defects in offspring, Johnson et
8 al., 2003, but a recent Charles River study 2019,
9 with similar doses, was unable to reproduce the
10 same effects on cardiac development. I think the
11 Johnson study is still useful for risk evaluation,
12 but further clarification is required.

13 Comment. EPA should consider
14 carefully the likelihood that appropriate PPE is
15 used in occupational scenarios in general and in
16 some specific scenarios. For example, the
17 likelihood of PPE use in commercial use
18 categories/subcategories/OES, particularly
19 respiratory protection, is so low that EPA should
20 consider not presenting these risks.
21 Alternatively, these risk estimates could be
22 presented in a separate subsection/table that

1 describes very clearly and specifically why EPA is
2 presenting risks with PPE for these categories
3 despite the Agency's declared belief that the use
4 of appropriate exposure controls in these cases is
5 unlikely.

6 EPA needs to consider evaluating
7 non-cancer chronic risks for consumers. First,
8 the Westat survey is unlikely to capture the full
9 range of high-frequency users. High-frequency
10 users may be a small fraction of the population
11 for some consumer products. To capture them, a
12 survey would require oversampling the users of
13 these products.

14 Second, TCE concentrations will
15 remain elevated for some time after use of a
16 product. Third, a product stored in the house or
17 garage may continue emitting a low level, and once
18 the container is opened contributing to indoor air
19 concentration, so users and bystanders are likely
20 to be chronically exposed at varying
21 concentrations.

1 Okay, that's the feedback I got.
2 And also, I did want to -- I asked Dr. Gilbert if
3 she would also be willing to comment on this
4 section since the immunotoxicity is also relevant
5 here.

6 **DR. KENNETH PORTIER:** Dr. Gilbert?

7 **DR. KATHLEEN GILBERT:** Well, I know
8 I said I would but having thought about it some
9 more, it's not clear to me what I could say today
10 that's not just a rehash of what we said
11 yesterday, unless we want to go into that again.

12 **DR. KENNETH PORTIER:** No, I don't
13 think we want to rehash the hazard discussion in
14 the characterization. I think a lot of the
15 uncertainties in exposure and hazard carry over
16 into characterization. Dr. Lash, you have your
17 hand up.

18 **DR. LAWRENCE LASH:** Yes, I do. So I
19 just to make a point. One of the comments said
20 about with the calculations for plus or minus use
21 of PPE, and I think one of the comments was that
22 the EPA should take into account that certain

1 industries or certain businesses are fairly
2 unlikely to use PPE even though they're required.
3 I think that's really two separate issues, so I
4 think the tables as they're presented with plus or
5 minus PPE and with the different levels of
6 protection, I think that's appropriate.

7 And then there could be if there is
8 actual data not anecdotal information but actual
9 information on the lack of appropriate use of PPE,
10 then that could be included in a separate section.
11 But I think the way the tables are I think it's
12 appropriate to calculate the risk with or without
13 use of PPE, so that's what I just wanted to
14 comment.

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

16 Dr. Morandi. Dr. Morandi, I see you're still on
17 mute.

18 **DR. MARIA MORANDI:** Sorry. I wanted
19 to address a comment from Dr. Lash. The comment
20 about reconsidering estimating risk with PPE was
21 for certain uses not consumer uses -- or I'm
22 sorry, industrial uses -- not across the board.

1 And this refers more specifically to the category
2 that includes commercial use, because there is
3 absolutely no evidence that I can think of that
4 PPE is used in this type of commercial uses. And
5 EPA recognizes in the document that they have a
6 very low level of confidence that this is the
7 case.

8 So it seems to me that this is a
9 little bit somewhat deceiving in the sense that as
10 somebody looks at these tables -- and frequently
11 many people don't look at the footnotes or go back
12 to the text -- that they may assign to the
13 estimates of risk with PPE for these particular
14 categories the same level of (inaudible) as for
15 the rest. So the comment was geared to suggest
16 EPA either not include those risk estimates with
17 glove protection for those particular categories
18 or have them separate from the rest of the table
19 and comment more specifically about those. So I
20 wanted to clarify that.

21 **DR. CHARLES VORHEES:** Dr. Morandi,
22 could you send me that comment, because while you

1 were talking the system cut me off, and I've had
2 to dial back in, so could you just send that
3 clarification over to me?

4 **DR. KENNETH PORTIER:** Dr. Morandi --

5 **DR. MARIA MORANDI:** I didn't write
6 it down as I was speaking, because I thought that
7 the comments have been clear but probably not in
8 the recent comment. But I'll send it to you.
9 I'll write it out and send it to you.

10 **DR. CHARLES VORHEES:** Okay, thank
11 you.

12 **DR. KENNETH PORTIER:** Also, Chip,
13 some of this can be pulled off of the audio
14 transcript which should be available by tomorrow
15 or Monday morning.

16 **DR. CHARLES VORHEES:** Okay.

17 **DR. KENNETH PORTIER:** Anyone else
18 want to comment on 6.1? I know we had a lot of
19 names on there, but I know you got a lot of
20 comments. Dr. Cobb.

21 **DR. GEORGE COBB:** So, Ken, is this
22 the point where we want to talk about this

1 fugacity stuff again, or is this not the point for
2 that?

3 **DR. KENNETH PORTIER:** I'm looking at
4 it. It's either this one or 6.3, where we talk
5 about calculation of risk derived from different
6 exposure data sources.

7 **DR. GEORGE COBB:** So I'll defer to
8 you. Whenever you want to do it, we can do it.

9 **DR. KENNETH PORTIER:** Let's go ahead
10 and do it now.

11 **DR. GEORGE COBB:** Okay, so that
12 means that I would need the folks from the Agency
13 to pull that slide of mine up and please bring up
14 the small table rather than the large one. While
15 I have the mic, I will say that a comment I've
16 made before is that this environmental assessment
17 is only for aquatic receptors, and it's only for
18 direct releases into aquatic systems. So whatever
19 statement the EPA would like to make about any
20 lack of risk has to be constrained both to the
21 limited exposure scenarios and to the limited
22 organisms that have been assessed. This

1 explicitly, not just stating that in conditions of
2 use, but explicitly aquatic receptors exposed from
3 direct releases to the aqueous environment alone.

4 I want to go back to the discussion
5 that we started on Monday and didn't quite get
6 through, or maybe my thoughts weren't clear. What
7 you're looking at is the EPI Suite, which is used
8 to estimate environmental partitioning of TCE.
9 And the top row there is the default which EPA
10 used. And those are the outputs that EPA
11 obtained: 35 percent going to air, 54 percent
12 going to water, 10 percent to soil and a quarter
13 of a percent going to sediment. And the
14 persistence was 147 hours in those compartments.
15 So that's basically what that is.

16 What I'd like to point out is that
17 in this scenario, the water has 163 percent or
18 1.63 times as much in the water as was released to
19 water. So that's the first thing.

20 Now the next thing is from my
21 perspective, and Bill Doucette and I talked a
22 little bit about this, that if you look back in

1 the problem formulation document, those values of
2 1,000 kilograms per hour being released to each
3 compartment are actually higher than what's
4 happening. And so we go back through that data
5 and found as best we could the amounts that EPA
6 has in the problem formulation, because it's
7 almost impossible to dig out of the Draft Risk
8 Assessment what those releases look like.

9 And that's what's in that next box
10 down there, that's problem formulation. And then
11 I just scale that a third a third a third up there
12 where it says scaled default. The second row says
13 scale default. That's just those numbers in that
14 next line divided up into three equal parts. The
15 point being there no matter what input values you
16 put in the fugacity as long as the ratios are the
17 same, the ratios and the output are the same. If
18 you put one, one, and one in those values -- those
19 inputs, you get the same percentage out, so that's
20 just the demonstration of that for the committee.

21 So let's go down to the rows 3 and
22 4, which is a problem formulation. So I've gone

1 through the problem formulation, and the releases
2 to air turn out to be 214 kilograms per hour if
3 you just assume constant release based on what the
4 reported releases were there. I did the same
5 thing for water and soil. Now there were two
6 different values given for water. So I used the
7 lowest value for release and the highest value for
8 release that the Agency had in the problem
9 formulation. Please note how small those numbers
10 are going into water.

11 And it looks like you have a small
12 partitioning into water there. It does look very
13 small but if you look at the ratio of what was
14 released directly to water to what ends up in
15 water, you end up with 130 times as much in the
16 low-release scenario and 8 times as much in the
17 high-release scenario.

18 Then if we go to the next grouping,
19 the last two boxes, I said, well, the soils maybe
20 those are buried in landfills. Let's just take
21 that 5.7 out, and that changes the ratios a little
22 bit in the air and water but not enough to matter,

1 and you get the similar outputs across the bottom.
2 What I'd like to point out is taking the soil out
3 doesn't really change the outcome. You get 109
4 times as much in water in the low-release
5 scenarios and 7.3 percent in the low -- excuse me
6 -- in the high release to water scenario.

7 So the point here is whatever the
8 Agency is doing is by this fugacity modeling is
9 underestimating risk by at least a factor of eight
10 and maybe a factor of 100 based on this kind of
11 modeling.

12 The last thing I'd like to say about
13 this is nowhere in this EPI Suite can you get
14 masses. It does not tell you what the masses are
15 anywhere, so there's no way to obtain masses that
16 are in the environment at the outcome. And that's
17 simply a limitation of the way that EPI Suite
18 model is set up.

19 So with that, maybe Bill has
20 something he'd like to say, or we can open it up
21 for further thoughts.

22 **DR. KENNETH PORTIER:** Dr. Doucette?

1 **DR. WILLIAM DOUCETTE:** Yeah, this is
2 Bill Doucette. George and I have talked about
3 this over a while through email over the past
4 couple days, and I thought he did a great job of
5 presenting that.

6 The other thing that I think could
7 be done is in addition to the fugacity model,
8 obviously, you can download a model that would
9 provide masses and concentrations from the Trent
10 University essentially Don Mackay's old group is
11 still doing modeling. And you can actually
12 download an Excel version of this model that
13 allows you to change all the input and also look
14 at more detailed output. And I think that would
15 be something that would be very easy for EPA to
16 implement in the next couple of environmental risk
17 assessments.

18 The other thing that I wanted to
19 bring out 00 and I was hoping to show some
20 calculations but I had a little bit of difficulty
21 running one of the models because of the Visual
22 Basic component of it -- but it would be really

1 useful to do a sensitivity analysis with this sort
2 of model or the STP model or the volatilization
3 model looking at variability within physical
4 chemical properties. I just did a couple of quick
5 calculations, and I can provide that information
6 just looking at variation in log KOC for example.
7 And it does change the outputs. It does change
8 the distribution.

9 And what would be nice is just to be
10 able to say if there's a factor of two or a factor
11 of ten variability in one of these key physical
12 chemical properties, how much does that influence
13 the model output and would that change the way EPA
14 characterized the risk? And I think that's
15 probably where I'll quit with that. Thank you.

16 **DR. KENNETH PORTIER:** Dr. Grant.

17 **DR. STEPHEN GRANT:** Hello, I
18 apologize if I'm repeating myself here if Dr.
19 Vorhees did that already, but I was distracted by
20 students while he was giving the rundown. So I
21 just want to repeat something that I said the

1 other day. It's something that's bothered me
2 about the PPE.

3 We wound up getting to the point
4 where EPA is consistently presenting with and
5 without PPE, but I'm concerned about the fact that
6 those are not a step 1 and step 2, those are step
7 1 and step 5, so I'll just read the paragraph that
8 I've provided for inclusion here. While risks are
9 provided with and without PPE, it is inappropriate
10 to provide these two possibilities as the universe
11 of possibilities. Protective equipment is easily
12 described and can be easily quantified with some
13 simple but usually unsupportable assumptions.

14 However, the hierarchy of control
15 stipulates that PPE should only be invoked after
16 structural and administrative controls. No
17 effects of PPE should be invoked unless structural
18 and administrative controls have first been
19 required and their effects demonstrated.

20 **DR. KENNETH PORTIER:** Thank you, Dr.
21 Grant. Before I go on -- Dr. Jimenez-Gonzalez,
22 one minute -- I wanted to ask Dr. Cobb to explain

1 again how we interpret that box all the way on the
2 right. What are you really saying when you say
3 109 mass fraction from input? I'm having a hard
4 time interpreting that. Everything else I can
5 follow but then I get to the point, and I'm
6 missing it.

7 **DR. GEORGE COBB:** So, Ken, just to
8 cut right through it all, if you take the
9 percentage in water -- so basically, that 109 is
10 saying that there's 109 times more in water than
11 you started with. And you're putting 100.006
12 kilograms per hour into water, and you're putting
13 214 kilograms per hour in from air. Let's just go
14 to that bottom box, to the 109, and when you're
15 done, you have 99.6 in the air and 0.3 in the
16 water. Well, that point -- the fact of the 214 is
17 all that there is, so 0.3 times 214 is a whole lot
18 bigger than 0.006, and so that's what the 209 is,
19 is 0.3 times the sum of whatever's in that big
20 box, the green box divided by the 0.006. Does
21 that clear that up?

1 **DR. KENNETH PORTIER:** Well, I think
2 when you write this up, you'll need to add those
3 equations so I can look at that. I'm still having
4 a struggle. I mean the bottom line is that
5 there's more in the water. What's "when"? Is
6 that an hour later, a day later? What's the
7 timeframe for this?

8 **DR. GEORGE COBB:** Ken, that's at
9 equilibrium. That's when the system comes to
10 equilibrium.

11 **DR. KENNETH PORTIER:** Whenever that
12 is.

13 **DR. GEORGE COBB:** Well, that's
14 assuming the system comes to equilibrium, and the
15 half-life or the persistence time, I forget which,
16 is 147 hours, so that might be a hint to when that
17 is. But these are the equilibrium values with the
18 inputs that the Agency is saying we have. Now
19 it's possible that if there was a summation -- and
20 this is one of things I suggested -- if there was
21 a summation of all of the water inputs from all of
22 the TRI data or the estimates where there aren't

1 TRI data, that percentage that was thought to be
2 released to water could increase. And that may
3 make the increase over -- the increase that's
4 partitioning in from air less.

5 But my point here is if you have as
6 much being released to air as is being released to
7 air and as little as the Agency is saying is being
8 released to water, the equilibrium drives the TCE
9 into the water.

10 **DR. KENNETH PORTIER:** That was the
11 point I was trying -- I think you were trying to
12 make is that under this model with the way it's
13 parameterized and organized and given the
14 characteristics of TCE at equilibrium, the TCE
15 comes out of the water and goes -- I mean, comes
16 out of the air and goes into the water. And it's
17 not a release from the water. It's the water
18 becomes more of a sink. Is that correct?

19 **DR. GEORGE COBB:** That is correct.
20 And it may be counterintuitive but remember how
21 large those releases to air are. And my point
22 here is even if you're not going to assess the

1 risks from inhalation, you can't assume that that
2 compartment has zero TCE in it. You can't. To
3 put a maybe improper current scenario on it, you
4 can't assume that there's zero people who have
5 coronavirus simply because you simply haven't
6 tested them.

7 **DR. KENNETH PORTIER:** Yeah, you need
8 to look in the water. Okay, I think when you
9 write this up, I'm going to be communicating with
10 you to make it clear. And I think also you need
11 to think in terms of what's the implications of
12 this? And I think you've just mentioned one, and
13 that is you can't assume that the TCE is released
14 from the water if the conditions of this model are
15 correct. And it may be that the conditions or the
16 assumptions under which this model is run are
17 incorrect for TCE. That's what I'm trying to
18 figure out.

19 But I think we can stop this at this
20 point. Anyone else want to address issues with
21 this analysis? I see Dr. Jimenez-Gonzalez's hand

1 up and Dr. Morandi. Well, I'll ask Dr. Jimenez-
2 Gonzalez.

3 **DR. CONCEPCION JIMENEZ-GONZALEZ:**

4 Yeah, and my comment is linked to what is being
5 shown here and what Dr. Grant said earlier on in
6 terms of the sensitivity and uncertainty
7 assessment. It's interesting when we give
8 comments on the models, because anyone who has
9 done any modeling knows that all models are wrong,
10 some models are useful. And they become useful
11 when we know how far apart we are, how sure we are
12 that we're modeling something close to reality.
13 And the table is a good example of that.

14 One additional recommendation in
15 terms of sensitivity, sometimes when you have this
16 type of parametric model, and some *Monte Carlo*
17 simulation might give you a sense of what's the
18 distribution of your sensitivities and your
19 uncertainties as well depending on how you use
20 that. So that will be my two cents in there and
21 also in terms of this mass balance of the model
22 maybe it's an opportunity to revise the parameters

1 and look at them through the sensitivity
2 assessment plans.

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

4 Dr. Morandi?

5 **DR. MARIA MORANDI:** A question to
6 George for clarification, because I am not
7 familiar with this model. So are these
8 equilibrium, the equilibrium is it calculated or a
9 closed system or an open system? In other words
10 what I'm trying to find out is in a real-world
11 situation, I thought we agreed that TCE from air
12 could partition into the water, I don't have any
13 problem with that.

14 But I was trying to think in terms
15 of a real situation with the actual input or
16 outflow from some company going into the water and
17 also emitting to air; well, the air emissions,
18 obviously, would be dispersed. And how and how
19 much and so forth depends on a number of other
20 considerations in terms of almost any situation.

21 So I was trying to think about how
22 would this actually work in the actual situation.

1 Because the amount that goes to air that's fine,
2 but that is dispersed through air to a large
3 extent. It's not that it's constantly in
4 equilibrium with, or in an equilibrium condition
5 with the water, so will you explain that a little
6 bit, George?

7 **DR. GEORGE COBB:** So that's a really
8 good question and if I get any of this incorrect,
9 Bill, chime in, please. These models are open
10 systems. At least laterally they're open systems.
11 They're in essence tubes of air and water and soil
12 and sediment that are in appropriately scaled
13 contact. And there's flow or advection into each
14 compartment at given rates. And you can in the
15 more sophisticated models you can change those
16 rates, and you can change the compartment sizes.
17 I'm not sure that EPI Suite allows that.

18 I did not do that simply because
19 this is the only tool EPA has used. And I wanted
20 what I was doing to be directly comparable to what
21 EPA was doing and the rationales they were using.

1 But the short answer to your
2 question is these models allow air and water in.
3 It allows sediment deposition and that to remove,
4 once the sediments are buried, to remove materials
5 from the system. And so you have air in, water
6 in, air out, water out are the big transfers that
7 are going on.

8 **DR. MARIA MORANDI:** Okay, so that
9 answers my question, because in other words it's
10 essentially a dynamic procedure that takes into
11 account the dynamics in each one of the
12 compartments. And that is what I was asking.

13 **DR. GEORGE COBB:** That is correct.

14 **DR. MARIA MORANDI:** Okay.

15 **DR. GEORGE COBB:** Yeah, another term
16 for some of this modeling is chemodynamic
17 modeling. And that's the reason those fugacity
18 inputs in the green box there on the left are in
19 kilograms per hour, because there's air moving
20 across that and water moving across that system.

21 **DR. MARIA MORANDI:** Okay.

1 **MR. WEN-HSIUNG LEE:** This is Wen
2 Lee. Is it okay I can provide some input?

3 **DR. KENNETH PORTIER:** Please, you're
4 with EPA, correct?

5 **MR. WEN-HSIUNG LEE:** Yes, very
6 quick, because I'm an EPI Suite developer, the
7 project manager, and also the fate assessor for
8 this. Because that all the estimation is -- all
9 the discharge will go to wastewater treatment.
10 And wastewater treatment in aeration entry the
11 dominate effect is a Henry's Law Constant and this
12 is 10 minus 3. It means that whenever have a --
13 enters the surface of water -- between water and
14 air, that all the tendency go to air is very
15 quick. So it's a aeration will dominate. It will
16 be -- will lose 80 percent in volatilization.

17 And so the one use is with regards
18 to model is more that a higher partition
19 coefficient is not an open system, because the air
20 if you are in the real situation, the air part is
21 the -- they will diffuse to air, so the air
22 concentration is decreasing. And that's the

1 reason why it's only a very short, the half-life
2 in a river. Because river have always provide
3 with new unlimited fresh air.

4 So this is where we control by the
5 Henry's Law Constant, which is very, very, very
6 high, and for all the -- you have more extension
7 aeration you will all go diffused to air. So
8 that's a reason we do not use this model to
9 calculate the total water. Water is not a sink in
10 this -- particular for this case. Thank you.

11 **DR. KENNETH PORTIER:** George and
12 then Dr. Kissel.

13 **DR. GEORGE COBB:** So look, you're
14 continuing to refuse to accept the fact that
15 there's TCE in the air. You can't say there's no
16 TCE in the air. Your entire assumption is all the
17 TCE is leaving the water because there's none in
18 the air, and that is not correct. That is untrue.

19 **MR. WEN-HSIUNG LEE:** No, we're not -
20 - in the --

21 **DR. GEORGE COBB:** So is the point of
22 this whole exercise.

1 **MR. WEN-HSIUNG LEE:** The estimate we
2 have some -- the two-release site is a little bit
3 higher -- is all the river, the receive water body
4 is river in the -- is river is allow mixing. So
5 that's the particular for this starting. We used
6 the two side.

7 That's a receiving water body is the
8 river and -- no I'm sorry. It's a wastewater
9 treatment first. They all have a NPDES permit, so
10 they need to discharge the public wastewater
11 treatment. And we always -- all were reduced 80
12 percent and will go discharge mixed with other
13 (inaudible) and they go into the river. So that's
14 the total quantity for the reduced 80 percent, so
15 that's the exposure assessors using that.

16 **DR. GEORGE COBB:** Yes, but if 138 to
17 130 times as much as you are releasing is
18 partitioning back in from air, it doesn't matter
19 how much you're taking out by wastewater
20 treatment. And so this is making my point,
21 really, for needing monitoring data because if you
22 don't have robust monitoring data, we could argue

1 this all day long. It really depends on the
2 assumptions of your model input, and we're
3 assuming things that we don't really know.

4 **DR. KENNETH PORTIER:** And we're not
5 going to argue this all day long. Dr. Kissel?
6 John, I see you unmuted, but we don't hear you.
7 Could your phone be muted?

8 **DR. JOHN KISSEL:** Yep, that was it.
9 Sorry, I don't know why my phone was muted. But
10 okay, so I argued for fugacity modeling quite a
11 long time ago because exactly what we're seeing
12 here is that these models are capable of giving
13 you insights that you would not otherwise pick up.
14 And what the -- but basically chemicals released
15 to the environment move downhill on thermodynamic
16 pathways. And if that means that something that
17 you think of as volatile and has a high Henry's
18 constant is dumped into the air from the
19 wastewater treatment plant, if it reaches contact
20 with a surface water body that's relatively clean,
21 then the gradient will be toward that surface
22 water body, and the reverse process will happen.

1 And that's why you do models, because your brain
2 kind of fails sometimes when you're trying to
3 explain very complicated things.

4 And so I think this discussion is an
5 excellent illustration of why adding this modeling
6 to the overall mix is very worthwhile. And I
7 don't agree that -- and this actually makes
8 perfectly -- sense to me.

9 I've done fugacity modeling for
10 quite a long time, and the processes are two-way
11 processes. And it just -- all that matters is
12 which one is higher thermodynamically at any given
13 time. And I don't find this at all
14 counterintuitive that material would partition
15 back into water from air, especially if you have -
16 - if you dump something into the air that doesn't
17 photolyze quickly so it's going to be maintained
18 at relatively high fugacity in the air column for
19 a while, then you would expect it to partition
20 back. And there are examples of things dumping
21 into air contaminating water.

1 The PFAS scenario in West Virginia
2 was ultimately determined to be discharges to air
3 which were then rained back into the ground which
4 wound up in the ground water, and then people
5 drank that. So people on the other side of the
6 Ohio river from the discharges were getting
7 contaminated water from air releases from the
8 chemical plant. And this is an excellent
9 illustration of why we want to do transport and
10 fate modeling.

11 **DR. KENNETH PORTIER:** Thank you,
12 John. Any additional comments? I think this is a
13 good point. I'm not quite -- I'm not quite sure
14 where this -- this may go back in the fate and
15 transport discussion when we write up the report.
16 Host, can you bring back up the question? Let's
17 just make sure we have -- I'll talk to -- I'll
18 turn to Dr. Vorhees and say do you feel like you
19 have enough discussion to answer this question?

20 **DR. CHARLES VORHEES:** Yeah, I think
21 if anybody's added clarifications -- Dr. Lash
22 added a clarification. And Dr. Morandi if she's

1 going to send me a clarification, yeah, then I
2 think I can put these comments together.

3 **DR. KENNETH PORTIER:** And I'll turn
4 to EPA, and do you have any clarifying questions
5 on the panel response to Question 6.1? We may
6 still have questions on the fugacity modeling but
7 --

8 **DR. STANLEY BARONE:** This is Stan
9 Barone, no further questions or comments.

10 **DR. KENNETH PORTIER:** Okay, last
11 call for any comments. Dr. Kissel, I still see
12 your hand up. And it's down. Okay, let's move on
13 to Question 6.2.

14 ***CHARGE QUESTION 6 (6.2)***

15
16 **DR. HEIDI BETHEL:** Question 6.2.
17 EPA presented overall human health risk
18 conclusions from Section 4.5.2 based on risk
19 estimates for the endpoints that it believes are
20 best representative of acute and/or chronic
21 scenarios (see Question 5.3 - immunosuppression

1 for acute exposure and autoimmunity for chronic
2 exposure).

3 Please comment on EPA's approach
4 including any alternative considerations for
5 determining and presenting risk conclusions
6 including the risk summary tables (Table 4-54 and
7 4-55).

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

9 **DR. CHARLES VORHEES:** Okay, so
10 you're going to hear in the comments that I've
11 received that some of the discussion issues that
12 have gone on yesterday continue to weave their way
13 through the feedback to this one.

14 So the first commenter says, as
15 noted in my previous responses to questions, my
16 comments relative selection of best representative
17 responses focus on the goals of this exercise and
18 on the basis of exclusion of congenital heart
19 defect data. Greater transparency might be
20 warranted in the rationale for selecting "best
21 representative responses" since risks are
22 characterized for all potential responses, the

1 need for the "best" ones to be explicitly
2 separated out isn't clear.

3 I don't necessarily disagree with
4 the decision to exclude the congenital heart
5 defect data due to weaknesses in that data set.
6 But I do think that greater
7 explanatory/transparency is needed to justify this
8 decision. Is the basis of this decision that the
9 data had considerable uncertainty? More than one
10 sentence of support should be provided. Also, at
11 least to this reader there is a disconnect between
12 the decision to exclude the congenital heart
13 defect data and the large amounts of text given to
14 support the decision to use these data in the
15 earlier text. This lack of balance doesn't make
16 sense.

17 Comment. Page 259 lines 25 and 26,
18 exactly what toxicity values for acute exposures
19 range from 7.8 to 33.9 milligrams per liter,
20 median lethality values, EC₅₀, NOELs, LOELs? What
21 is the basis for using the geometric mean?

1 The following sentence discusses
2 chronic values for fish and invertebrates. What
3 do these values represent? More explanation is
4 needed.

5 Comment. The DRE spells out the
6 human health risk conclusion based on the key
7 studies the Agency used in Tables 4-55 and 4-56
8 using benchmark values. These tables include use
9 of the Johnson data that are fraught and should
10 not be used for human health risk conclusions.

11 Comment. The human health risk
12 conclusions are summarized for both inhalation and
13 dermal exposures for different occupational
14 exposure scenarios at both high end and central
15 tendency exposure levels. MOE values for acute
16 and chronic non-cancer effects and cancer
17 estimates are given. Additionally, each table
18 divides these risk calculations between workers
19 with and without use of PPEs. Risk estimates that
20 indicate increased risk versus the benchmark
21 values are shaded gray.

1 These tables provide a clear summary
2 of the risk conclusions. This section then
3 presents a similar summary table of human health
4 risks for presumed consumer exposures. Criteria
5 for the types of exposures are clearly explained.

6 Comment. Worker Table 4-54 and
7 consumer Table 4-55 risk summary tables adequately
8 present the details of the benchmark values for
9 dermal and inhalation exposure. But oral exposure
10 may also occur when a respirator is not used and
11 people touch their mouth. EPA should add
12 benchmark values for the route of oral exposure if
13 such data are available.

14 Comment. The tables present good
15 summaries of risk conclusions. Although there is
16 some formatting problems that need correction, the
17 links to the summary tables for OEFs are useful.
18 For ONUs exposure based on worker's central
19 tendency exposures, it would seem that the
20 exposure and risk for ONU is the expected high
21 end, i.e., Table 4-54 the upper limit not the
22 central tendency.

1 Okay, that's the feedback I've got
2 so far.

3 **DR. KENNETH PORTIER:** Okay, we'll
4 open the discussion. Do we have any panel members
5 who wish to comment or add to their comments on
6 Question 6.2? Dr. Gilbert.

7 **DR. KATHLEEN GILBERT:** I'm not
8 positive these comments belong here or in Question
9 7, but I'll say them here. So I'm appreciative
10 that the immunotoxicity endpoints were chosen as
11 representative of the acute and chronic toxicity.
12 However, the focus this time on immunotox made it
13 clear to me that the EPA needs to be challenged to
14 improve their evaluation of immunotox in the draft
15 risk evaluations. This is evident from some of
16 the terms that they used to describe immunotox
17 including allergic respiratory sensitization and
18 sensitization/hypersensitivity. I know these
19 terms are used in the literature a lot but they're
20 not specific and they're not really that useful.

21 And the other issue that makes it
22 clear is that the selection of the studies that

1 they used to look at the dose response -- I think
2 those were listed in Table 3-11. And some of the
3 comments, I think it was from Dr. Jacobs yesterday
4 when we were discussing the Peden-Adams study, and
5 I understand his point of view, so when selecting
6 the key studies or when evaluating the merits of
7 the study, they are interested in details and
8 statistics, sufficient documentation dosage,
9 document how groups are randomized, standardized
10 methodology, I think those are all important.
11 However, they're only a part of what makes a good-
12 quality paper.

13 We also need to know whether the
14 choice of the methodology and the model makes
15 sense for the question asked, whether the proper
16 controls were included so that the reader can
17 assess whether the immune assay actually worked,
18 the proper interpretation of data, and the
19 legitimacy of conclusions.

20 So I would like to -- my suggestion
21 would be to the EPA is to explain whether all of
22 these consideration are taken in account when they

1 are selecting key studies and if not, I think they
2 should be. So I would like to recommend that
3 their selection process for immunotox studies
4 should be more carefully described or improved.
5 That's all.

6 **DR. KENNETH PORTIER:** Thank you, Dr.
7 Gilbert. And I'd say -- those are good points,
8 and then they may be better discussed in the
9 hazard section than in the risk section, because
10 what you're saying is when we're looking at the
11 hazard, we need to do a better job on that -- so
12 that they get proper consideration in looking at
13 the overall hazard.

14 Dr. Barone, you had a clarifying
15 statement or question? You're unmuted. I mean
16 you muted it again and you were unmuted.

17 **DR. STEVEN BENNETT:** Sorry, I'm
18 sorry. That was one of the clarifications I
19 wanted to get at. The other clarification was
20 when Dr. Vorhees was reading the comments, a
21 number of us heard comments about the eco risk
22 estimates which are mixed in. This Question 6.2

1 is about the acute and chronic scenarios for human
2 health so if you could take those comments on eco
3 and put them into the appropriate responses for
4 the charge questions, it would be most helpful
5 rather than mixing them in with human health.

6 **DR. CHARLES VORHEES:** Okay, I'm
7 happy to do that.

8 **DR. STANLEY BARONE:** Thank you.

9 **DR. KENNETH PORTIER:** This is Ken
10 Portier, and I'm looking at Table, what is it, 5-
11 54, and it's a huge table. And for clarification
12 point of view I'd almost like to see one table for
13 occupational worker inhalation and some discussion
14 on that and one table for occupational worker
15 dermal and maybe even split out the with and
16 without PPE, because a lot of our discussion has -
17 - and some of the discussion we had day before
18 yesterday and talking about exposures kind of
19 thinks of PPE versus non PPE as kind of two use
20 classes rather than a continuum within a use
21 class.

1 And I'm wondering if a separate
2 table or separating a table of risk for no PPE
3 from a table of risk with PPE offers an
4 opportunity for a different kind of discussion in
5 the risk characterization section? And it's just
6 a thought. Again, it's kind of risk communication
7 and how you see things. The same thing with
8 putting the ONUs with the workers, it's kind of --
9 they kind of get lost, because the worker has four
10 lines and the ONU has two lines of which one line,
11 the high end, is typically missing so with that
12 that ONU kind of gets lost. But maybe the
13 occupational people have a better justification
14 for why it's better to have it in one table. Dr.
15 Morandi.

16 **DR. MARIA MORANDI:** Yes, I think
17 this is the first time that I disagree with Dr.
18 Portier since I remember. But I like to have them
19 together, because I think it makes it easier to
20 compare, in other words to compare across the
21 board and also to compare across all the different
22 conditions of use, compare workers to ONUs.

1 Except that if you put them in
2 different tables -- and there are some instances
3 in this document where that has been done for
4 other reasons, for other purposes -- then you have
5 to flip back and forth if you have to have a quick
6 comparison of the value.

7 So again, I feel that if there is a
8 lot of information on the tables in doing it this
9 way, but I think it also facilitates to do
10 comparison of values much more than having
11 separate table. That's all.

12 **DR. KENNETH PORTIER:** Dr. Morandi,
13 my feelings are not hurt. You can disagree with
14 me all you want. Dr. Davies.

15 **DR. HOLLY DAVIES:** Hi, I was also
16 going to say I like having everything together,
17 because it makes it easier to see all at once
18 especially since this is where EPA is pulling out
19 whether it sees unreasonable risk so you can see
20 all the numbers together. I was going to suggest
21 if you wanted to see individual, those could be
22 separate tables as a compromise.

1 **DR. KENNETH PORTIER:** Dr. Grant.

2 **DR. STEPHEN GRANT:** Yeah, I would
3 have to agree that there's no reason why in a
4 document like this the data should be presented
5 only once. It probably can. It's useful to
6 reiterate it in different context so that it's --
7 if it's making a different point.

8 The only other thing I would add --
9 and I mentioned that as soon as we talked about
10 those two, I'd like to bring up the point again
11 about total risk should be based on aggregate
12 exposure. So those scenarios where there is both
13 significant inhalation and dermal risk, we're
14 really not doing a good job of risk assessment if
15 we don't add those together for people who are
16 going to experience both methods of exposure.

17 **DR. KENNETH PORTIER:** Dr. Grant,
18 that's a point that the committee has continued to
19 bring up and include in its report. But I'm glad
20 you mentioned it, because this is the proper place
21 to add it, Dr. Vorhees, into the discussion.

1 **DR. CHARLES VORHEES:** Yeah, I'll put
2 it in.

3 **DR. KENNETH PORTIER:** Good. Anyone
4 else want to comment on this? When it gets down
5 to the risk conclusions when you've made your
6 arguments on hazard and you've made your arguments
7 on exposure, it's kind of putting it together, and
8 the risk is what the risk is.

9 The only other thing I could think
10 of as I looked at these table is to somehow
11 indicate the certainty or uncertainty that goes
12 along with these estimates. And so the tables
13 don't really provide that. These are one number,
14 a risk, 1.2 for an MOE. But we don't have the
15 kind of uncertainty, and I'm hoping at some point
16 we get there.

17 Any additional comments on this from
18 the panel? I'm not seeing any. I'll turn to EPA.
19 Do you have any clarifying questions or comment?

20 **DR. STANLEY BARONE:** Not at this
21 time, Dr. Portier. This is Dr. Barone.

1 **DR. KENNETH PORTIER:** Good. I have
2 11:15, and I think this may be a good point to
3 take a midmorning break, so let's take 15 minutes
4 and reconvene at 11:30 Eastern.

5
6 [BREAK]

7
8 **DR. KENNETH PORTIER:** Okay, let's
9 reconvene, please. So any additional thoughts on
10 Question 6.2 from the panel? Please raise your
11 hand. Not seeing any and having confirmation from
12 EPA that they've had no questions on our
13 discussion, why don't we move on to Question 6.3?

14 ***CHARGE QUESTION 6 (6.3)***
15

16 **DR. HEIDI BETHEL:** Question 6.3.
17 Please comment on the calculation of risk derived
18 from different exposure data sources (modeling
19 tools and monitoring datasets) and how they
20 account for variability in environmental and human
21 exposure. Please provide specific recommendations
22 as needed for improving the risk characterization

1 and references to support any recommendations.

2 See Section 4.

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

4 Dr. Vorhees?

5 **DR. CHARLES VORHEES:** Yes, in
6 response to Dr. Barone's suggestion that the
7 comments be divided by environmental risks versus
8 human health risks, I've resorted these. So we'll
9 start with the environmental risk comments.

10 The first comment is the draft
11 ignores the human health implications of TCE
12 releases to the environment such as air emissions
13 and contaminated ground water and drinking water
14 using a statutory basis. This is not acceptable
15 in the frame of risk assessment as it assumes
16 these potential exposures are appropriately
17 managed, excluding risks to the general
18 population. In addition, some sub-population
19 could be exposed to different pathways.

20 Comment. This charge question
21 focuses on either modeling tools or different
22 datasets are used to calculate risk to the

1 environment or human exposure. A summary table,
2 Table 4-5, Page 280, lists the most sensitive
3 endpoints for human health. Because many
4 exposures are expected to be acute -- actually
5 this is -- this should be on the next one --
6 especially for exposure from consumer uses, a
7 similar table as this one but focusing on acute
8 exposure scenarios should also be presented.

9 The draft employs the use of
10 protection factors for use of personal protective
11 equipment, which is contrary to OSHA's hierarchy
12 of control. As the current COVID-19 pandemic
13 painfully shows the world, the adequate use of PPE
14 is not going to be assumed as many enterprises are
15 finding themselves with significant low stock of
16 basic PPE. This reviewer will again strongly
17 discourage the application of PPE protection
18 factors.

19 The EPA states that it cannot be
20 ruled out that consumers at high-end frequency of
21 use could be at risk given the uncertainty in the
22 extrapolation from continuous studies in animals.

1 But EPA did not develop risk estimation, because
2 this risk is expected to be unlikely. It is
3 recommended that the EPA develop uncertainty
4 factor and/or sensitivity assessments to determine
5 how unlikely this may be, particularly as the
6 current study is not accounting for background
7 water and ambient exposures.

8 Comment. I think the risk
9 characterization is clear and transparent. The
10 tables clearly present the risk estimate with
11 colored highlighting indicating the responses of
12 concern.

13 Comment. The calculated values are
14 correct based on data in Table 4-5, page 280.
15 However, as noted above, the Johnson cardiac
16 malformation data need to be removed from this
17 part and subsequent parts.

18 Comment. Monitoring data are
19 unlikely to control for the full range of
20 variability in occupational exposures, because the
21 TCE monitoring data are not representative of OES.
22 Few workers monitored, and typically low number of

1 samples available, sampling done over relatively
2 short periods of time, data collected at one or
3 few sites, and/or samples collected for purposes
4 other than for exposure sampling all are
5 relatively small and/or large but are also
6 potentially biased convenience samples.

7 Therefore, it is unlikely that risks based on
8 these estimates capture the variability in
9 exposures.

10 On the other hand, deterministic
11 modeling can be used to derive, e.g., using *Monte*
12 *Carlo* approaches, robust exposure estimate
13 distributions. And these distributions are likely
14 to include the full range of variability in
15 exposure. EPA should continue exploring modeling
16 given the continuing limitations in available
17 monitoring data or invoke its statutory authority
18 to request these data.

19 That's the feedback I've got so far.

20 **DR. KENNETH PORTIER:** Thank you, Dr.
21 Vorhees. Dr. Schlenk.

1 **DR. DANIEL SCHLENK:** Yeah, I just
2 wanted to -- I've made some of these comments
3 already in terms of Question 2 and 3, but I just
4 wanted to put them here, because it specifically
5 asks for recommendations for characterization. I
6 agree with Dr. Portier's assessment of
7 characterization. It should primarily an
8 assessment of the uncertainties that are present.
9 Obviously, the exposure assessment and the effects
10 assessments are in different sections for hazard.

11 In terms of uncertainty analysis, I
12 think, again, I say this for every panel we've
13 been on, but there needs to be a better statement
14 on the ecological side for uncertainty. To
15 disregard various receptors based upon the
16 modeling, again, assumes that that model is valid.
17 So consequently, there needs to be a better
18 statement of uncertainty for particularly the
19 effects side.

20 Recommendations, I would say, for
21 that would be to assume worst-case scenario in
22 those uncertainty evaluations. And I've mentioned

1 this before but particularly if water is going to
2 be a fate component, then wastewater dominated
3 streams should be the worst-case scenario, and a
4 focus particularly on the monitoring data should
5 be in those locations.

6 Likewise, on the effects side, the
7 uncertainty there is, again, almost all the
8 studies that are present are primarily acute in
9 nature. There was one chronic, which was growth,
10 but there was limited vertebrate reproduction, and
11 very limited vertebrate development that I saw
12 anyway in terms of some of the studies that were
13 provided. Consequently, I think there's a
14 significant uncertainty there as well.

15 And then I already mentioned the
16 fact that, again, inhalation exposure,
17 particularly at worst-case scenarios streams
18 primarily for shore-based vertebrates such as
19 birds and other mammals that are located within
20 discharge sites would be predominate.

21 My recommendation on the exposure
22 side also would be to utilize NPDS data,

1 particularly for discharge sites. That is the
2 worst-case scenario, particularly in a wastewater
3 dominated stream it is discharge dominated. So
4 consequently, those discharge numbers,
5 particularly in areas of the southwest, I would
6 think would be a fairly good target to provide for
7 a worst-case scenario and to address uncertainty.
8 That's all I got.

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

10 Anyone else wishing to comment on this? This is
11 Ken Portier. I was just looking at Section 4 and
12 trying to identify quickly where the uncertainties
13 in PPE kind of factor in, are highlighted. And I
14 guess if you look at the occupational exposure
15 considerations, there's air concentrations,
16 there's an underlying section, there's an
17 underlying section on averaging times.

18 I guess I'd kind of like to see an
19 underlying section in 4.3.2.1 where you talked
20 about the PPE considerations. And I know that's
21 discussed in the exposure section but kind of
22 carried through to the characterization. There's

1 dermal absorption consideration, and then there's
2 confidence in risk estimates. So it's almost like
3 PE and environmental control considerations are
4 not mentioned in the risk characterization.

5 Anyone else? Dr. Vorhees, you got
6 all that?

7 **DR. CHARLES VORHEES:** Yeah, if Dr.
8 Schlenk and you can send me those additional
9 comments, I'll put them in.

10 **DR. KENNETH PORTIER:** I'll try.

11 **DR. CHARLES VORHEES:** Okay.

12 **DR. KENNETH PORTIER:** I'm giving
13 people a chance a chance to think about this one
14 more time. I guess at this point I can turn to
15 EPA and say do you have any -- oh, Dr. Bennet, I
16 see your hand's up.

17 **DR. STEVEN BENNETT:** Yes, I thought
18 I'd jump into this. I'm not sure if this is the
19 right question, but I was posing this question as
20 all panel. It's in reference to the pepper spray.
21 And I think with the dichotomy in the discussion
22 between the developmental effects versus the acute

1 immunotoxicology to a toxicity piece, that
2 decision pathway is critical with respect to
3 pepper spray and consumer uses. It was the
4 different endpoints, where if you look at the --
5 if you use the congenital heart defects, it does
6 not -- it is below the margin of exposure, but it
7 does not when you look at the immunotoxicity.

8 And I think it's a good point to
9 have a discussion around that. I'm certainly not
10 the expert on the toxicology piece, but I think in
11 the highlight this is the -- that is the one
12 consumer use that does not present criteria. And
13 I think it'd be appropriate to have a conversation
14 around that with a little bit more detail.

15 **DR. KENNETH PORTIER:** Thank you.
16 Any additional comments. Dr. Schlenk, your hand's
17 up. And it's down. Dr. -- yeah, good, Dr.
18 Barone?

19 **DR. STANLEY BARONE:** This is Stan
20 Barone, no further comments or clarification's
21 needed. I think your latter comments were really
22 helpful.

1 **DR. KENNETH PORTIER:** Okay, let's
2 read into the docket 6.4, and let's go ahead and
3 do 6.5 at the same time. Dr. Bethel?

4 **DR. HEIDI BETHEL:** I'm here. I'm on
5 the wrong page, 6.3 and 6.4 is that right? No.

6 **UNIDENTIFIED MALE:** No, 6.4.

7 **DR. KENNETH PORTIER:** Yes, 6.4 and
8 6.5, please.

9 ***CHARGE QUESTION 6 (6.4 AND 6.5)***
10

11 **DR. HEIDI BETHEL:** Six point four
12 and six point five -- 6.4. Please comment on
13 whether the risk evaluation document has
14 adequately described the uncertainties and data
15 limitations associated with the methodologies used
16 to assess the environmental and human health
17 risks. Please comment on whether this information
18 is presented in a clear and transparent manner.

19 Question 6.5. Please comment on the
20 clarity and validity of specific confidence
21 summaries presented in Section 4.3.

1 **DR. KENNETH PORTIER:** Dr. Vorhees on
2 Question 6.4?

3 **DR. CHARLES VORHEES:** Okay and for
4 the environmental risks I got one comment. The
5 uncertainties of environmental risk
6 characterization are summarized clearly in Section
7 4.3. The section on environmental hazard
8 identification has a more detailed account of the
9 uncertainties and limitations than the one
10 summarized in 4.3. So it's recommended to
11 consider expanding this section or cross
12 referencing to the section describing the
13 uncertainties of the environmental hazard
14 identification.

15 Comments on the human health risks,
16 occupational exposure limitations are also clearly
17 explained. It is concerning that the EPA did not
18 find enough reasonably available data to determine
19 complete statistical distributions for air
20 concentrations for workers exposed to TCE.
21 Similar uncertainty and variability is found for
22 the ONU and consumers.

1 It is recommended that EPA use its
2 statutory authority to request some limited
3 studies to consider in the assessment,
4 particularly given the draft determination of
5 unreasonable risk. The report states that
6 "certain inputs to which model outputs are
7 sensitive, such as zone volumes and air flow
8 rates, were not varied across product use
9 scenarios." But I did not see a sensitivity
10 assessment.

11 If a sensitivity assessment was
12 performed, it would be good to accompany the
13 discussion of the sensitivity of the model with
14 the numerical estimation. If no sensitivity
15 assessment was done, it is recommended that it be
16 performed.

17 Comment. I think the uncertainty
18 and data limitation section of the document lacks
19 balance, is incomplete, and should be expanded.
20 Over two pages of text are devoted to the exposure
21 assessment, and only one short paragraph is given
22 to human health hazard. There are numerous

1 uncertainties/data limitations to the health
2 hazard. Simply referring to Section 3.2.6 without
3 highlighting the specific issues of greatest
4 uncertainty/limitation is not adequately
5 transparent.

6 What's the point of having a full
7 section on uncertainty/data limitations if the
8 reader is simply referred to earlier text? The
9 cited Section 3.2.6 inadequately addresses the
10 uncertainty/data limitations of PBPK modeling
11 approaches.

12 Comment. In Table 4-5-2 the effects
13 that stand out are immune and congenital heart
14 defects. The cardiac effect is based on a study
15 from Johnson with no corroborating data from any
16 other lab. Moreover, Dr. Johnson was part of the
17 study with TCE given by gavage and did not find
18 cardiac defects found previously. See Fisher.
19 Therefore, the cardiac defects should be brought
20 forward for POD determination.

21 Comment. Discharge question focused
22 on how well uncertainties and data limitations are

1 described. Each category of potential uncertainty
2 is clearly explained, and equations that are used
3 are clearly highlighted in the document. Although
4 the concerns and issues with congenital heart
5 defects as a non-cancer endpoint as based on the
6 Johnson study are described elsewhere. It is
7 completely ignored in this short summary.

8 Additional mention of the issues and
9 concerns and how EPA dealt with this endpoint
10 should be mentioned in the sections where it is
11 discussed in more detail and referenced.

12 Comment. EPA adequately addressed
13 acute neurotoxicity of TCE such as CNS depression,
14 but there is uncertainty for developmental
15 neurotoxicity. There is a study demonstrating
16 that prenatal exposure to 0, 10, and 100
17 micrograms per milliliter TCE in drinking water
18 causes neuroinflammation, glutathione depletion,
19 and oxidative stress in the cerebellum and altered
20 locomotive behavior in mouse offspring. This
21 study should be added to the report for

1 developmental neurotoxicity. And this person
2 gives the citation.

3 Comment. The summary of
4 uncertainties is too limited. The text directs
5 the reader to Section 2.3.1.3 for details. One
6 would expect to see a complete summary of
7 uncertainties in this section. A table format
8 would help, two columns, one listing variables
9 parameters and the other the uncertainties.
10 That's it.

11 **DR. KENNETH PORTIER:** Any additional
12 comments on -- Dr. Davies.

13 **DR. HOLLY DAVIES:** Yes, I just want
14 to mention I didn't see the -- for consumer
15 exposures to include that the Westat surveys from
16 1987 and some product formulations and use
17 patterns have changed as one of the uncertainties.

18 **DR. KENNETH PORTIER:** This is Ken
19 Portier. As I was listening to what Dr. Vorhees,
20 the comments Dr. Vorhees was giving, I started
21 thinking about how uncertainties are handled in
22 this document. So we have uncertainty discussions

1 in the exposure component. We have uncertainty
2 discussions in the hazard component. And then we
3 put them together in the risk characterization,
4 and then the question becomes does the risk
5 characterization just recapitulate what we've
6 already discussed, or is it should that
7 uncertainty discussion have a different
8 characteristic? What should we see in the answer
9 -- the discussion in the risk characterization?
10 And as I'm turning to people like Dr. Davies and
11 Dr. Morandi and asking when you're reading the
12 risk characterization or when a professional wants
13 to focus on that risk estimate, what do they want
14 to see in the way of an uncertainty discussion?
15 Do they want to see what we see in the exposure
16 and the hazard discussions, or should that be a
17 different kind of discussion? Anyone? Dr.
18 Morandi.

19 **DR. MARIA MORANDI:** Well, this is a
20 standing issue because, obviously, the derivation,
21 the risk characterization uncertainties derive
22 from the chain of uncertainty that were into the

1 exposure assessment and risk characterization. So
2 it is difficult to think about the overall
3 confidence under risk characterization.

4 And as a separate discussion of
5 uncertainties on the risk characterization that
6 are independent of the uncertainties on exposure
7 and (inaudible). So it is a difficult question.
8 And I haven't actually come to some decision about
9 how to do this.

10 And you are correct that all the
11 uncertainties that are described, although not in
12 enough detail, tend to recapitulate, you know, who
13 has been said before rather than be sort of a
14 separate global description of the uncertainties
15 in risk, so it's a tough question. I just wanted
16 to give my opinion not a solution to the problem.

17 **DR. KENNETH PORTIER:** Dr. Johnson?

18 **DR. MARK JOHNSON:** Yeah, for me it's
19 you have your uncertainties that you've kind of
20 alluded to in your hazard ID section. You have
21 your uncertainties that you allude to in your
22 exposure section and then when you put them

1 together in risk characterization, you'd like to
2 see at least some kind of a quantitative or semi-
3 quantitative idea on when putting those two
4 together, what you have.

5 And I've seen it before where they
6 would have a high, medium, and low semi-
7 quantitative relationship on degree of uncertainty
8 that one would have in that -- and I wouldn't call
9 it a risk estimate -- hazard estimate, or actually
10 even a little more precise than that insofar as
11 with degree of order of magnitude the authors
12 would think that giving these uncertainties would
13 have to influence that hazard estimate.

14 So there's a couple ways you could
15 go about it. But you also want to explain why you
16 believe your risk estimate is off that much, at
17 least the hazard characterization section.

18 **DR. KENNETH PORTIER:** Yeah, I guess
19 -- this is Ken Portier. I guess I was thinking in
20 terms like propagation of air or a kind of
21 propagation of uncertainty. If you indicated high
22 uncertainty in exposure and high uncertainty in

1 your hazard, you'd almost want to say there's high
2 uncertainty in this risk estimate. But that may
3 not help the person reading that value of risk,
4 1.2, to be able to think about what's my action
5 based on that risk? We would want that risk
6 estimate to somehow inform future decision making
7 over and above the numerical value that we
8 provide.

9 Dr. Davies, I see your hand's up.

10 **DR. HOLLY DAVIES:** I was going to
11 say something similar to Maria about no good way
12 of handling this. I really like Mark's semi-
13 quantitative ideas when you put it together. What
14 I'd be looking for is the, as Mark was talking
15 about, a semi-quantitative, the biggest risk or
16 the most known uncertainties, kind of what are the
17 highlights in this section rather than repeating
18 everything.

19 For me this is part of the whole
20 issue that I brought up before of how the risk
21 assessment is spread out over so many hundreds of
22 pages, so when someone's reading this risk, they

1 don't necessarily remember what would happen in
2 the hazard. They don't remember what happened in
3 the exposure, because it was so far back in the
4 document and so that just to kind of bring forward
5 the most important ones.

6 **DR. KENNETH PORTIER:** This is Ken.

7 I was looking back -- looking forward in the
8 Chapter 5, where we had a risk determination, and
9 I seem to remember in earlier reports in the final
10 unreasonable risk discussion there was something
11 like an uncertainty statement that went with it,
12 but we've kind of lost that as we've moved
13 forward. So I think it does need to be in Chapter
14 4. I hear -- it may be an open question for us.

15 Dr. Morandi, Dr. Johnson, I still
16 see your hand's up. Did you want to add into this
17 discussion?

18 **DR. MARIA MORANDI:** Well, what Mark
19 was saying in a way when EPA assigns the overall
20 confidence to the estimate is a way of getting
21 around to what he was saying. But I don't think
22 that decision, because it's not clear, again, how

1 that confidence level was arrived at considering
2 all the issues of the uncertainties across the
3 whole process.

4 And we were discussing these prior
5 reviews and also in this one earlier this week.
6 And I think that EPA needs to consider this an
7 issue that they may want to bring to the committee
8 sometime so there is an approach that could be
9 used to deal with this issue.

10 And I agree with you that for a
11 reader that is reading the document and looking at
12 the overall risk characterization number and
13 seeing these uncertainties, the uncertainties kind
14 of fall by the wayside, you know, we are more
15 focused on the numbers. So the issue is also how
16 to communicate it so that that uncertainty, if it
17 is part of what the reader considers just below
18 the number, because the numbers grab your
19 attention mainly; and most people would not -- or
20 do not -- focus on the uncertainties that are
21 around that number. That's all I wanted to say.

1 **DR. KENNETH PORTIER:** Dr. Johnson,
2 did you want to add in?

3 **DR. MARK JOHNSON:** Yes, sir. I
4 would just add that in the end what we have are a
5 set of numbers, a set of numbers. And they're all
6 not created equal. We know that. What the
7 uncertainty analysis helps us to do when we put
8 these together is give the decision makers some
9 kind of idea of how much confidence that we have
10 in the data that are designed to provide these
11 numbers that are calculated to provide these
12 values. And so I think that's important, because
13 the decision makers in the end need to know that
14 these numbers are not created equal.

15 **DR. KENNETH PORTIER:** Yeah, and
16 that's kind of what I was trying to get at is, is
17 there a way? And we may not be able to answer
18 that question today, but I think that's what
19 Question 6.4, to me, was trying to get it. Does
20 it describe, does it -- the limitation not just
21 the data limitations but the integration or the
22 limitations in integrating all of the information

1 and data that we have into a risk number. And I
2 recognize that it's become multidimensional
3 problem that we're trying to come down to a one
4 number or one classification, and those are always
5 extremely difficult problems.

6 Dr. Morandi, your hand's still up.

7 **DR. MARIA MORANDI:** Yes, I just
8 wanted to add that I agree with what Dr. Vorhees
9 is saying, but it could require, again, going
10 through a process of how to assign some sort of
11 rating, even it's an quantitative through each one
12 of the type of uncertainties and then come up with
13 a set of scores perhaps that could be applied to
14 the risk characterization. But this is going to
15 require some thinking on the part of EPA and with
16 contributions, probably, from the committee.

17 **DR. KENNETH PORTIER:** And we have
18 another topic for a future consultation. Dr.
19 Jimenez-Gonzalez?

20 **DR. CONCEPCION JIMENEZ-GONZALEZ:**
21 Yeah, just link to that. When you don't have
22 enough numerical data and you probably -- I don't

1 know -- if you cannot do a *Monte Carlo* simulation
2 with enough confidence, one of the options is
3 precisely as Dr. Morandi was saying, do some sort
4 of ranking. You can even -- one of the things
5 that is done often as well is to do a RAG
6 assessment with amber, green depending on the type
7 of confidence that you have in the data to
8 generate some sort of a heat map to get a sense.

9 And in some sections the EPA had
10 done something towards that, but it will be useful
11 to have some more structured way looking at that.
12 And hence, that we have been talking both about
13 sensitivity and uncertainty, because you can have,
14 let's say, a one to five scale, a relative scales,
15 you can have an area that has very low certainty
16 or high uncertainty, but when you marry that with
17 a sensitivity assessment, you can make a
18 determination like might have a lot of
19 uncertainty, but it doesn't impact the final
20 answer as much. It's not too sensitive to the
21 final answer. That's why those two things need to

1 go hand in hand to make -- to guide the decision
2 makers.

3 And on the other hand you can have
4 something that has medium uncertainty but high
5 sensitivity so you can make a determination, okay,
6 I need to go and look for better data to increase
7 the uncertainty, because I can go from one
8 conclusion to the opposite very quickly if I
9 change assumptions, or I change the data I am
10 using.

11 **DR. KENNETH PORTIER:** You know,
12 that's an excellent point. I hadn't thought
13 through the uncertainty sensitivity kind of
14 integrating those two together. Dr. Davies?

15 **DR. HOLLY DAVIES:** Hi. I was also
16 thinking about the confidence summaries and how
17 they assign kind of high, medium, low without a
18 lot of background of exactly how they came to
19 that. And I realized when I was reading this
20 again yesterday that it's just kind of relative.
21 It's not really absolute. And summarizing
22 everything which is really hard to do as we've

1 been talking about and just thinking more about
2 how the whole thing is a gradient so looking, for
3 instance, at consumer uses sometimes they took
4 other uses, but they didn't have specific data.
5 They used similar data. And that seemed really
6 reasonable.

7 And then there's other estimates
8 that just kind of fell below the line where they
9 said we don't have enough data to do this. And so
10 it's all just relative, and it's kind of just
11 adding to the discussion on it's hard to do.

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

13 Dr. Anderson.

14 **DR. HENRY ANDERSON:** I was just
15 going to add into that. I mean one of the things
16 I always had trouble with these is well what how
17 to do we expect this to be used? I mean it's an
18 interesting descriptor, but it's hard to then take
19 this and to -- when we say we have high
20 confidence, that's good.

21 If it's moderate or low confidence,
22 then one of the issues would be well, how would we

1 -- what needs to be done to raise our level of
2 confidence, and what would it take to change that,
3 which would then be into what are the key
4 components that go into it that could be changed?
5 So is it we just need some additional data? Is
6 that potential to develop that data in the short
7 term or what?

8 So at what point -- if we say it's
9 very low, then one can say well, it's our
10 confidence is so low you really can't make a
11 decision based on this particular data. But if
12 it's medium or high, what does that mean in terms
13 of next steps, or where do we go from here?
14 That's the challenge I have. It's interesting. I
15 think it helps support recommendations we may have
16 for what can be done to improve our confidence,
17 but we tend not to go in that direction. It's
18 just a summary of it and sort of leaves -- it
19 leaves the general public questioning as to well,
20 so how does this impact the process or the next
21 steps?

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

2 Dr. Jimenez-Gonzalez, your hand's still up. Dr.
3 Johnson.

4 **DR. MARK JOHNSON:** Yeah, where I've
5 seen this done successfully is where it's actually
6 presented in some sort of table or even the table
7 that's already there, where you assign a high,
8 medium, and low level of confidence and then a
9 descriptor as to why. You have a medium level of
10 confidence because of a variability and
11 uncertainty associated with a exposure model or in
12 the range of toxicity information for different
13 species used to being extrapolated to human health
14 or whatever. You need some kind of explanation of
15 why you assigned it that category. You just can't
16 do that and then let it go.

17 **DR. KENNETH PORTIER:** Dr. Jimenez-
18 Gonzalez, your hand's still up. It strikes me
19 that this conversation has drifted into Question
20 6.5, and that maybe I should ask Dr. Hossain if he
21 has any additional comments on clarity and the

1 validity of specific confidence summaries
2 presented in Section 6.3, Dr. Hossain?

3 **DR. MUHAMMAD HOSSAIN:** Yeah. I have
4 received some comments from two panel members, and
5 those comments are summarized. And if I missed
6 something, just I request to other panel member to
7 bring it up.

8 Most panel members concurs the
9 confidence summaries are clearly presented for
10 most of the exposure scenarios and endpoint
11 outcomes. But they found it is sometimes
12 difficult for the readers to follow up as the
13 details are cross referenced to other sections.

14 The main concern is about congenital
15 heart defects as the developmental endpoint. Two
16 members believe that due to the numerical
17 uncertainty and lack of sensitivity assessment,
18 Johnson's 2003 data should be removed.

19 Now I want to move it to other panel
20 members for further discussion.

21 **DR. KENNETH PORTIER:** Does anyone
22 want to add to the discussion on 6.5? Dr.

1 Jimenez-Gonzalez, I still see your hand up.

2 Anyone else? Dr. Morandi.

3 **DR. MARIA MORANDI:** I just wanted to
4 say that we kind of discussed some of these issues
5 for the prior question. And this, in my mind, is
6 a standing problem we are trying to eventually
7 resolve of how to link all those uncertainty
8 issues through the whole process and starting from
9 theory to that final confidence level however it
10 is expressed by medium, low or as a score.

11 And I think going through that
12 process in which you actually specify clearly what
13 the sources of uncertainty is in detail and, you
14 know, guiding through ranking for each one of
15 those sources of uncertainty, then it makes it
16 clear how you arrive at that confidence level.

17 I also think that maybe the high,
18 medium, low may be a little narrow in terms of the
19 range available for assigning confidence that
20 perhaps having a score with increased gradients of
21 confidence, degrees -- I'm sorry, degrees of

1 confidence may be more informative and more useful
2 to the reader. That's all I wanted to say.

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

4 **DR. HOLLY DAVIES:** Hi, I was going
5 back. I was opening up the slides from the first
6 day, because the slides have a nice summary. They
7 don't rankings, but I assume these are the ones
8 that the Agency thought were the most important
9 like slide 48 for consumer exposure gives the most
10 important uncertainties -- oh, thank you, whoever
11 is putting those up -- and strengths and
12 confidence.

13 So this has a nice summary, and I
14 think what I would like is both the longer
15 discussion that's currently there but with some of
16 the improvements you've suggested but also a
17 summary of this is what we think are the biggest
18 strengths that affect the confidence, these are
19 the uncertainties and limitations, the most
20 important ones that affect our confidence. I
21 think adding a summary and, as I said before,

1 sometimes the slides have really good summaries
2 that we don't see in the Draft Risk Assessment.

3 **DR. KENNETH PORTIER:** Good point.

4 Any additional comments? Not seeing any
5 additional comments, I think I'll turn to EPA and
6 ask whether they have any clarifying comments or
7 questions on 6.4 or 6.5 discussing uncertainties
8 and the clarity and validity of confidence
9 summaries.

10 **DR. STANLEY BARONE:** Not at this
11 time.

12 **DR. KENNETH PORTIER:** I think we've
13 had a good discussion, but we haven't quite
14 reached conclusion on this issue. And I think
15 we'll continue to discuss it moving forward.
16 Let's move on to Question 6.6 and see if we can
17 get through that before we break for lunch.

18 ***CHARGE QUESTION 6 (6.6)***
19

20 **DR. HEIDI BETHEL:** The Frank R.
21 Lautenberg Chemical Safety for the 21st Century
22 Act states that "potentially exposed or

1 susceptible subpopulations" or PESS be considered
2 in the risk evaluation process.

3 Question 6.6. Has a thorough and
4 transparent review of the available information
5 been conducted that has led to the identification
6 and characterization of all PESS? Do you know of
7 any additional information about PESS that EPA
8 needs to consider? Has the uncertainty around
9 PESS been adequately characterized?

10 **DR. KENNETH PORTIER:** And we asked
11 Dr. Hossain to lead this discussion. Dr. Hossain?

12 **DR. MUHAMMAD HOSSAIN:** Yes, I
13 received several comments on this section, and I'm
14 going to read them.

15 The issue of potentially exposed and
16 susceptible subpopulation, PESS, is always a
17 difficult one to address. It is DRE does a great
18 job of explaining why the information is in
19 several sections and tying the multiple sections
20 together. There is no mention of UFs which is a
21 departure from earlier DRE.

1 It is good to see the Agency not
2 relying on UFs to cover PESS. There are three
3 sections entertain PESS, the Section 2.3.3
4 explains PESS in TSCA and mentions that EPA
5 identified PESS during problem formulations but
6 does not say what they were. It includes a useful
7 distinction of why that is included in this
8 section and ties it to the other section. In this
9 section EPA addresses the potentially exposed or
10 susceptible subpopulations identified as relevant
11 based on greater exposure.

12 EPA also added here subpopulations
13 identified as relevant based on greater
14 susceptibility in Section 3.2.5.2. In this
15 section the list workers and professional non-
16 user, consumers, product users and bystanders
17 associated with consumer use at best with more
18 exposure.

19 EPA quantified age, genders and
20 people of reproductive age using census data. EPA
21 stated there excess exposure under all condition

1 of use, but the Agency did not aggregate
2 exposures.

3 Section 3.2.5.2 also summarize risk
4 in TSCA and therefore the problem formulation
5 without saying what risks were identified
6 previously. Again, there is a helpful statement
7 on why risk is described here and tying to it
8 other section. In this section EPA addresses the
9 potentially exposed or susceptible subpopulations
10 identified as relevant based on greater
11 susceptibility.

12 EPA identified lifestage, gender,
13 genetic polymorphisms, race, ethnicity,
14 preexisting health status, and lifestyle factors
15 or nutrition status as factors affecting
16 biological susceptibility in Section 2.3.3.

17 In this you also identified pregnant
18 women, especially older women, as likely to be
19 more susceptible subpopulation. This section also
20 lists several variations that may affect
21 susceptibility to TCE including CYP polymorphisms,

1 GST metabolism and tumor suppression. These
2 important details are not given.

3 EPA should provide more of the
4 details to support the conclusion data the
5 HEC₉₉/HED₉₉ is sufficient to account for the
6 susceptible subpopulations.

7 In Section 4.4.1 the
8 characterization summary; in this summary they
9 presented in 4.4.1 should be more detailed. It
10 does not repeat the definition they applied to the
11 problem formulation or tie this section to the
12 other section.

13 However, the use of 99th percentile
14 output of the PBPK model these values are expected
15 to be predictive of particularly susceptible
16 subpopulations, such as pregnant women, but no
17 part of discussion is made. So a more definite
18 statement about the availability or lack of
19 availability of actual data supporting any of
20 these conclusions, expectations should be made.

1 Overall, EPA clearly and adequately
2 described assumption and uncertainties about the
3 use of -- oh, that's all. That's all I received.

4 **DR. KENNETH PORTIER:** Thank you.
5 Any additional comments on this? Dr. Apte?

6 **DR. UDAYAN APTE:** Yeah, hi. This is
7 Udayan Apte. I mentioned some of these comments
8 before about liver toxicities. And I wanted to
9 get them on record here as well.

10 There is a significant change in the
11 demographic, disease demographic in the United
12 States in the last 10 years or so, 20 years or so.
13 Over 30 percent of the population is now
14 considered obese or overweight. These people have
15 significantly higher amounts of fat in their
16 bodies as well as in their liver. And TCE and
17 other solvents which are soluble in fat they can -
18 - these people can possibly have a significantly
19 distinct toxicodynamic profile.

20 Also, it turns out that CYP2E1, the
21 metabolizing enzyme, is affected in obesity and
22 overweight people. So this would change the way

1 we look at TCE and possible endpoints, especially
2 liver and kidney endpoints, because kidney again,
3 will depend on the liver metabolism.

4 And so I think EPA right now -- at
5 least my review of literature, I did not see any
6 studies that EPA could have used. So this is sort
7 of a suggestion for the future work where specific
8 studies or specific information needs to be
9 generated or used if it is present for risk
10 assessment, keeping in mind that a large section
11 of U.S. population is now more susceptible because
12 of underlying conditions such as non-alcoholic
13 fatty liver disease or NASH stemming from the
14 obesity.

15 So I wanted to just put that point
16 there which is going to become significant public
17 health issue. And it will come back to the table
18 some point in time. Thank you.

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

20 Okay, hands are up. Dr. Davies.

21 **DR. HOLLY DAVIES:** Hi, I wanted to
22 mention two things. One was that throughout the

1 PESS sections the Agency is referring to gender,
2 which is a social construct, when I think they
3 really are referring biological sex differences,
4 and so that language should be changed.

5 The other one was a recommendation
6 where they state in section -- on the hazard
7 section in 3.2.5.2, where they performed a
8 population analysis to systematically estimate
9 uncertainty and variability across several
10 metabolite factors, but none of the details are
11 given. So it'd be good to see more of that. It
12 was nice to see that they had done the analysis
13 but just wanted more details behind it and what
14 exactly they did.

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

16 Dr. Bruckner.

17 **DR. JAMES BRUCKNER:** The NRC
18 published a really nice comprehensive overview of
19 susceptible populations and factors that influence
20 carcinogenicity and toxicity of both TCE and
21 perch. So I'll send in that reference. That
22 might be referenced there.

1 **DR. KENNETH PORTIER:** So, Dr.
2 Bruckner, while I have you here I -- something I
3 thought of as Dr. Apte and Dr. Hossain were
4 speaking with regards to the PBPK models, they're
5 run with randomly chosen paraments. But I was
6 specifically thinking of people with abnormal
7 kidney or liver functioning and whether the
8 simulations that would run reasonably cover
9 individuals with those health conditions, or
10 whether at some point they should have considered
11 looking at those functioning parameters in the
12 PBPK models and run specific scenarios for
13 individuals that have abnormal values. You
14 understand what I'm saying?

15 **DR. JAMES BRUCKNER:** I sure do. I
16 think that would be a good idea just to run those
17 and see what the net effect is on your dosimetry.
18 I think that's an excellent idea. I haven't seen
19 that done too much.

20 **DR. KENNETH PORTIER:** Well, I think
21 that the belief is that if we do the big *Monte*
22 *Carlo* with 10,000 or 100,000 simulations, you're

1 covering the tails of the distribution. But
2 that's the tails of normal functioning
3 individuals.

4 Now you get into the PESS discussion
5 and thinking what Dr. Apte's saying, now you're
6 starting to talk about individuals with slightly
7 abnormal functioning. You got a hepatitis A
8 infected 65-year-old, their liver is not going to
9 be the same as a 40-year-old construction worker.
10 But that 65-year-old may still be in the workforce
11 being exposed. And are these upper-bound 95, 99
12 percent values reasonably covering those workers
13 or not? And in my mind, I can't really do the
14 integration fast enough to think about whether
15 that is fair. Dr. Bruckner?

16 **DR. JAMES BRUCKNER:** No, I think you
17 hope you're catching some of those in the tail,
18 but you really don't know what the net effect is
19 or whether it's a significant effect in that
20 population. I agree with you.

1 **DR. KENNETH PORTIER:** Okay. I think
2 Dr. Gilbert's next and then Dr. Anderson then Dr.
3 Morandi. Dr. Gilbert.

4 **DR. KATHLEEN GILBERT:** Hi, yes, so
5 we talked about women and reproductive years being
6 one of the most susceptible populations which, of
7 course, implies that we're actually talking about
8 fetal exposure. And I just need some
9 clarification from the EPA on this point, because
10 I couldn't quite find it in the report, and that
11 may be totally my fault. So the EPA selection of
12 the immunological endpoints for determining risk
13 from acute and chronic were derived from adult
14 exposure. It's not clear that developmental
15 exposure studies were given appropriate weight.

16 The EPA states that aside from the
17 congenital heart defects, EPA did not identify any
18 repeat dose experimental studies in animals or
19 humans, epidemiological studies that would
20 contribute significant additional information for
21 this hazard. Then EPA on page 215 goes on to
22 describe numerous papers including studies from

1 Camp Lejeune that associated developmental TCE
2 exposures to various developmental outcomes in
3 humans such as spontaneous abortion, developmental
4 neurotox, and childhood cancers.

5 There are also, of course, several
6 animal studies demonstrating long-term immune
7 effects from TCE exposure. So I just want to get
8 from the EPA what kind of a conclusion did you
9 come to in terms of the role of developmental TCE
10 exposure in the risk assessment?

11 **DR. KENNETH PORTIER:** So, Dr.
12 Gilbert, we could also turn that around for this
13 report and say it's unclear, right?

14 **DR. KATHLEEN GILBERT:** Yes.

15 **DR. KENNETH PORTIER:** And then make
16 a recommendation that they should clarify this. I
17 did notice as I was reviewing the 2011 IRIS
18 report. There's a lot more discussion on this in
19 the IRIS report than occurs in this report. And
20 some of that discussion could have been carried
21 over into this DRE.

1 And I kind of had a similar question
2 like all of this -- the IRIS report is extremely
3 dense for TCE even for an IRIS review. And I
4 guess some of the discussion just didn't make it
5 here.

6 Let me see if Dr. Barone wants to
7 jump in on this. I see your hand's up, Dr.
8 Barone.

9 **DR. STANLEY BARONE:** Yes, so in our
10 overview slides we mentioned the PODs and the risk
11 estimates we developed for developmental
12 endpoints. And beyond cardiac we had
13 developmental morbidity. We had also
14 developmental neurotox being included in our
15 characterization of different developmental
16 endpoints that we did dose response and included
17 in our risk estimation in the appendix. So we
18 have considered other developmental endpoints.

19 Again, about that with regard to
20 both the hazard and the risk characterization,
21 we're looking for information that the committee
22 feels would indicate that PESS potentially exposed

1 or the most susceptible are possibly outside the
2 normal range. And I think Dr. Bruckner was sort
3 of getting at this with his previous comment.

4 If the committee or the public has
5 information that would quantitatively inform the
6 variability or the potential response being
7 outside the factor of ten or if something else is
8 informative for our approach of using the HEC₉₉ or
9 the PBK approach, HEC approach that we used if the
10 committee thinks there's other things that we
11 should include quantitatively, that would be most
12 helpful.

13 **DR. KENNETH PORTIER:** Dr. Gilbert,
14 did that answer your question? Maybe not.

15 **DR. KATHLEEN GILBERT:** Pretty much.

16 **DR. KENNETH PORTIER:** Okay, good,
17 thank you. Dr. Anderson.

18 **DR. HENRY ANDERSON:** I've mentioned
19 this previously, and it's sort of unusual with
20 this compound the impact that alcohol consumption
21 has on symptoms which can be pretty significant in

1 individuals who consume quite a bit of alcohol on
2 a regular basis or before or after an exposure.

3 I don't know how that fits. It's
4 not really an illness. It doesn't necessarily
5 reflect liver disease but if you want to talk
6 factor of ten, that's a group that if you use
7 symptoms and concern about how you're feeling and
8 the flush that some of these people get, I don't
9 know where that fits in, but I think that's a
10 fairly substantial group of individuals that could
11 be impacted here and would probably be outside
12 your factor of ten that if you have over and above
13 the alcoholic liver issue, but I would just say
14 the consumption of alcohol. And I think you can
15 estimate that in the population.

16 But I think that's a group that is
17 worth at least mentioning. I think it is
18 mentioned in a couple of places that this is an
19 issue, but certainly in the workplace that becomes
20 problematic for some workers.

21 **DR. KENNETH PORTIER:** Dr. Morandi?

1 **DR. MARIA MORANDI:** Now, I just
2 wanted to mention that with respect to PESS that
3 they seem to be considered one at a time. And at
4 least in terms of health conditions that people
5 can have multiple health conditions. And so when
6 I read the statement to the fact that the PBPK
7 model would probably cover 99 percent of all
8 variability, I find it to be or have a little bit
9 of an overstatement because of that risk.

10 **DR. KENNETH PORTIER:** And this is
11 Ken Portier. I think my point about utilizing the
12 PBPK model to kind of support or not support the
13 10X factor I think you probably can get some
14 medical professionals, physiologists to tell you
15 what the liver, kidney condition is of an
16 alcoholic, Dr. Anderson, or of an overweight
17 diabetic individual in their 50s who might be
18 still working or in the occupational workforce to
19 be able to run some limited scenarios and show
20 that they either do fit into that HEC₉₉, or they're
21 considerably outside of it.

1 And what we've learned, to Dr.
2 Gilbert's point, the model -- I think at least the
3 animal models have a maternal component. I think
4 I heard it has a fetal component, but it wasn't
5 used. And that's another open question that to
6 what extent can that model be used to explore the
7 extent to which we can look at some of those
8 issues? Now I think the immuno stuff is very
9 difficult at this point, but some of the other
10 more standard toxicity stuff is covered in that
11 model.

12 Dr. Gilbert, your hand's still up.

13 **DR. KATHLEEN GILBERT:** Sorry.

14 **DR. KENNETH PORTIER:** Dr. Jimenez-
15 Gonzalez, your hand's still up. She may have
16 stepped out of the room and forgot to put her hand
17 down.

18 **DR. CONCEPCION JIMENEZ-GONZALEZ:**
19 Yeah, I'm here, but I am here and forgot to put it
20 down, sorry.

1 **DR. KENNETH PORTIER:** Oh, okay. Any
2 additional comments? Dr. Bruckner, your hand's
3 up.

4 **DR. JAMES BRUCKNER:** I just wanted
5 to emphasize one more time that Jeff Fisher
6 (phonetic) and some others have the models there
7 if the EPA wanted to actually predict or simulate
8 what fetal levels of TCE or its metabolites might
9 be. The model's there, the validate model is
10 available.

11 **DR. KENNETH PORTIER:** Dr. Morandi,
12 your hand's still up.

13 **DR. MARIA MORANDI:** Yes, a
14 clarification question for EPA. I notice that now
15 this document the term that is used for risk
16 through this particular section and also the
17 previous one is "extra risk" instead of "excess
18 risk" which is a term that I was more familiar
19 with. And I was wondering if that's a terminology
20 that TSCA has adopted that is different from the
21 usual terminology.

22 **DR. KENNETH PORTIER:** Dr. Barone?

1 **DR. STANLEY BARONE:** That is not a
2 strictly a TSCA terminology. The models actually
3 -- we have two approaches, excess risk and added
4 risk, and they're slightly different approaches,
5 but virtually we get very similar answers, very
6 similar statistical outputs.

7 **DR. MARIA MORANDI:** Okay.

8 **DR. KENNETH PORTIER:** Any additional
9 comments on PESS? Not seeing any, I'll turn to
10 EPA at this point. Any clarifying questions or
11 comments?

12 **DR. STANLEY BARONE:** This is Dr.
13 Barone. No, not at this time. Again, thank you
14 for the robust dialog.

15 **DR. KENNETH PORTIER:** Okay, I'm
16 looking ahead at what additional questions we have
17 and at our timeline. We're supposed to break at
18 lunch at 1:00 Eastern. We have two more questions
19 on the risk characterization. I think we'll go
20 ahead and read those into the docket and start the
21 discussion. We have about 25 minutes left before
22 our lunch break. We may actually be able to

1 address these two. This is Question 6.7 and 6.8.
2 Ms. Bethel? I see you're muted, but we don't hear
3 you, so your phone's probably muted.

4 **DR. HEIDI BETHEL:** Hello, can you
5 hear me?

6 **DR. KENNETH PORTIER:** Now we hear
7 you. Now we hear you.

8 **DR. HEIDI BETHEL:** Okay perfect.
9 Sorry about that, too many mute buttons.

10 ***CHARGE QUESTION 6 (6.7 AND 6.8)***
11

12 Question 6.7 and 6.8. The EPA
13 characterization of human health risk from
14 inhalation exposure to workers includes risk
15 estimates both with and without respirator use.
16 EPA also characterized exposure scenarios in which
17 respirator use was unlikely.

18 Question 6.7. Please comment on
19 whether EPA has adequately, clearly, and
20 appropriately presented the reasoning, approach,
21 assumptions, and uncertainties for characterizing

1 risk to workers and occupational non-users using
2 personal protective equipment.

3 Question 6.8. Please comment on any
4 other aspect of the environmental or human health
5 risk characterization that has not been mentioned
6 above.

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

8 Dr. Hossain, comments on Question 6.7?

9 **DR. MUHAMMAD HOSSAIN:** I received
10 some comments from few members. Those I combined,
11 and I'm telling you those. Most of the members
12 agreed that overall EPA clearly and adequately
13 describes assumptions and uncertainties about use
14 of PPE for risk characterization for worker and
15 occupational non-user, but not with persistent
16 emphasis.

17 Other issues are while this are
18 provided with and without PPE, it is inappropriate
19 to provide these two possibilities as the universe
20 of possibilities. Protective equipment is easily
21 described and can be easily quantified with some
22 simple but easily inseparable assumption.

1 However, the hierarchy of control
2 stipulates that PPE should only be involved after
3 structural and administrative controls. No
4 effects of PPE should be involved unless
5 structural and administrative controls have part
6 been required and their effect demonstrated.

7 EPA should explain with full
8 transparency and clarity why EPA has to provide
9 exposure and risk estimate with use of PPE in all
10 cases despite the evidence of poor adherence to
11 such use and EPA's own (inaudible) of considerable
12 uncertainty about the proper use of PPE in many
13 scenarios.

14 One member said that as the current
15 COVID-19 pandemic is painfully showing the work
16 that adequate use of PPE is not going to be
17 assumed as many enterprise are finding themselves
18 with significantly low stock of basic PPE. It is
19 (inaudible) strongly discourage that application
20 of PPE protection factor.

21 Finally, all of the assumptions are
22 clearly explained and seem logical to me. Other

1 panel members should add their comments on the
2 validity of assumptions made by the EPA at this
3 time. Thank you.

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

5 Any additional comments or clarifications of
6 comments from the panel? The PPE issue does not
7 go away the more we get into these discussions.
8 I'm not seeing any additional comments, which is
9 not unusual when we get there was the end of the
10 set of questions, because the committee tends to
11 answer things earlier on.

12 Dr. Hossain, why don't we go ahead
13 and take in Question 6.8. Are there any additional
14 comments?

15 **DR. MUHAMMAD HOSSAIN:** Okay. I am
16 going to read 6.8, and I did notice it that many
17 comments here, and it's some that are
18 recommendation for EPA.

19 However, the fundamental objectives
20 need to be more clearly and explicitly stated.
21 Issues of questions of the following need to be
22 more emphasis.

1 Number 1, what is the most sensitive
2 endpoint for each exposure route and use both
3 acute and chronic cancer and non-cancer endpoint?
4 Number 2, limitations and data gaps need to
5 presented in a more highlighted and obvious
6 manner. Number 3, area of controversy should be
7 highlighted.

8 Although the EPA may come to a
9 conclusion that they conclude to be consistent
10 with their policy or published guidelines, clear
11 acknowledgement of limitations and lack of
12 consensus and where appropriate EPA's uncertainty
13 factor need to be incorporated. That's all.

14 **DR. KENNETH PORTIER:** Thank you. As
15 you were talking, I was looking at the discussion
16 just prior to Table 4-54, the Occupational Risk
17 Summary table, page 358. And I think you're right
18 in the sense that they don't point to the lowest -
19 - the highest risk or the lowest value in the
20 summary. They just present the table and allow
21 the user to look through, and there's no way to
22 find the highest risk without scanning one, two,

1 three, four, five, six, seven, eight, nine, ten,
2 eleven, twelve pages of output. So it was a good
3 point somebody picked up on. I hadn't thought
4 about that.

5 Any additional comments? Dr.
6 Jimenez-Gonzalez?

7 **DR. CONCEPCION JIMENEZ-GONZALEZ:**

8 Yes, thank you. In one of the points that caught
9 my eye as the presentation, the technical
10 presentation happen early on is that in the
11 technical presentations, and I'm going to call as
12 lines 13, 23, 24, 27 it is very clear the risk
13 characterization conclusions that the Agency came
14 to after looking at the different evidence.

15 I wish something like that had been
16 used in the manuscript. It took me a little bit
17 to go back and forth and when I saw the
18 presentation, I think those slides 13, 23, 24, 27
19 really do a good job summarizing their
20 conclusions. And my recommendation will be to
21 mimic something like that in the report to make it
22 clear.

1 DR. KENNETH PORTIER: Thank you.

2 Dr. Kaufman?

3 MR. ALAN KAUFMAN: Yes, actually
4 nothing really new here. I just wanted to
5 reiterate that I think we've talked about this
6 earlier. There are two issues that bother me.
7 One is the fact that we've got some susceptible
8 subpopulations that you wouldn't normally think
9 of. And I think the best example is probably
10 someone who is either an alcoholic or is, let's
11 say, a heavy social drinker on a regular basis
12 that is exposed to TCE in an occupational setting.

13 And then also just the idea of the -
14 - I don't think it was adequately addressed that
15 there's significant potential for cumulative risk
16 here. I think you've got potential to be exposed
17 through drinking water, through consumer exposures
18 and at the same time still be exposed as either an
19 occupational user or an ONU. And I don't think
20 that's adequately been covered in the risk
21 assessment so risk evaluation rather.

1 And I think we've covered it before
2 but I just wanted to emphasize that those two
3 issues cause me some concern. Thanks.

4 **DR. KENNETH PORTIER:** Thank you.
5 Any additional comments? I'm not seeing any.
6 I'll turn to EPA, any comments on the panel
7 response?

8 **DR. STANLEY BARONE:** Not at this
9 time. This is Dr. Barone.

10 **DR. KENNETH PORTIER:** Thank you.
11 I'm showing about a quarter to one Eastern Time.
12 And I'm going to ask Dr. Davies whether we have
13 substantial responses to Question 7 that we should
14 take our lunch break and come back or whether we
15 could reasonably complete Question 7 in, say, a
16 half hour's discussion and then just be able to
17 end the meeting and free up afternoons for
18 everyone? Dr. Davies.

19 **DR. HOLLY DAVIES:** I have a lot of
20 responses for Question 7 including people who have
21 made new tables and figures, so it seems to me
22 like it would take a little more than -- take more

1 than half an hour. But it always depends on how
2 much people are going to talk and want to comment
3 on it.

4 **DR. KENNETH PORTIER:** Yeah, and they
5 may feel better about talking after lunch than
6 before lunch. I really don't want to rush this,
7 because the Question 7 on the overall content
8 organization is often, I think, where the
9 committee can really help EPA in its risk
10 communication task.

11 So I think at this point I'm going
12 to go ahead and call the break for lunch, and we
13 will plan to come back from lunch at 1:45. Why
14 don't we take a slightly longer break, and we will
15 come back from lunch at 1:45 and probably spend
16 one hour completing Question 7. And we may be
17 ending earlier today. So at this point, we'll
18 break and return at 1:45 Eastern. Thank you.

19
20 [BREAK FOR LUNCH]
21

1 **DR. KENNETH PORTIER:** Good afternoon
2 on the East Coast and a continued good morning for
3 those of you on the West Coast. We're going to
4 reconvene for the TSCA SACC Committee review of
5 the TCE Draft Risk Evaluation. I notice that most
6 of the panel has returned. We'll do a quick roll
7 call just to establish who's actually on the call.
8 Dr. Anderson?

9 **DR. HENRY ANDERSON:** Yes, I'm here.

10 **DR. KENNETH PORTIER:** Dr. Bennett.

11 **DR. STEVEN BENNETT:** I'm here.

12 **DR. KENNETH PORTIER:** Dr. Blystone.

13 **DR. SHERI BLYSTONE:** I am here.

14 **DR. KENNETH PORTIER:** Dr. Barton.

15 **DR. CHARLES BARTON:** Here.

16 **DR. KENNETH PORTIER:** Dr. Bruckner.

17 **DR. JAMES BRUCKNER:** Here.

18 **DR. KENNETH PORTIER:** Dr. Cory-
19 Slechta. I don't see -- Dr. Davies.

20 **DR. HOLLY DAVIES:** I'm here.

21 **DR. KENNETH PORTIER:** Dr. Doucette.

22 **DR. WILLIAM DOUCETTE:** Present.

1 DR. KENNETH PORTIER: Dr. Jimenez-
2 Gonzalez.

3 DR. CONCEPCION JIMENEZ-GONZALEZ:
4 Here.

5 DR. KENNETH PORTIER: Dr. Gilbert.

6 DR. KATHLEEN GILBERT: I'm here.

7 DR. KENNETH PORTIER: Dr. Johnson.
8 That's right, Dr. Johnson is going to be out this
9 afternoon. He'd already informed us. He may
10 return before the end of the conversation. Dr.
11 Kaufman. Dr. Kaufman? Dr. Kissel.

12 DR. JOHN KISSEL: Here.

13 DR. KENNETH PORTIER: Dr. Rowlands.

14 DR. CRAIG ROWLANDS: Here.

15 DR. KENNETH PORTIER: Dr. Schlenk.

16 DR. DANIEL SCHLENK: Here.

17 DR. KENNETH PORTIER: Dr. Apte.

18 DR. UDAYAN APTE: I'm here.

19 DR. KENNETH PORTIER: Dr. Cobb.

20 DR. GEORGE COBB: I'm here.

21 DR. KENNETH PORTIER: Dr. Grant.

22 DR. STEPHEN GRANT: I'm here.

1 DR. KENNETH PORTIER: Dr. Hossain.
2 DR. MUHAMMAD HOSSAIN: I am here.
3 DR. KENNETH PORTIER: Dr. Jenkins.
4 MS. ALLISON JENKINS: I am here.
5 DR. KENNETH PORTIER: Dr. Lash.
6 DR. LAWRENCE LASH: I'm here.
7 DR. KENNETH PORTIER: Dr. Morandi.
8 DR. MARIA MORANDI: Here.
9 DR. KENNETH PORTIER: Dr. Morris.
10 DR. JOHN MORRIS: Here.
11 DR. KENNETH PORTIER: Dr. Rosol.
12 DR. THOMAS ROSOL: Here.
13 DR. KENNETH PORTIER: Dr. Vorhees.
14 DR. CHARLES VORHEES: Here.
15 DR. KENNETH PORTIER: So I think Dr.
16 Kaufman I see him dialed in.
17 MR. ALAN KAUFMAN: I am here.
18 DR. KENNETH PORTIER: Good. I think
19 that's everyone then.
20 DR. DEBORAH CORY-SLECHTA: This is
21 Deborah Cory-Sclechta. I'm here as well.

1 **DR. KENNETH PORTIER:** Oh. Now,
2 there you are. Yes, I see you logged in. Thank
3 you, Deborah. Okay, I think we're ready to move
4 onto Question 7 unless someone really has a
5 comment for Question 6. Dr. Kaufman, your hand is
6 up. Is that a new hand or a legacy hand? If
7 you're speaking, I see you as still muted. Okay,
8 Dr. Bethel, let's go ahead and read in 7.1 and
9 7.2.

10 ***CHARGE QUESTION 7 (7.1 AND 7.2)***

11
12 **DR. HEIDI BETHEL:** Question 7.
13 Regarding overall content and organization. EPA's
14 Final Rule, *Procedures for Chemical Risk*
15 *Evaluation Under the Amended Toxic Substances*
16 *Control Act* stipulates the process by which EPA is
17 to complete risk evaluations under the Frank
18 Lautenberg Chemical Safety for the 21st Century
19 Act.

20 It is important that the information
21 presented in the risk evaluation and accompanying

1 documents is clear and concise and describes the
2 process in a scientifically credible manner.

3 The peer reviewers' critical focus
4 should pertain to recommendations of the technical
5 information's usefulness for intended users and
6 the public.

7 Questions 7.1. Please comment on the
8 overall content, organization, and presentation of
9 the TCE draft risk evaluation. Please provide
10 suggestions for improving the clarity of the
11 information presented.

12 Question 7.2. Please comment on the
13 objectivity of the underlying data used to support
14 the risk characterization and the sensitivity of
15 the Agency's conclusions to analytic decisions
16 made.

17 **DR. KENNETH PORTIER:** Okay, and I've
18 asked Dr. Davies to lead the discussion on this
19 topic. Dr. Davies.

20 **DR. HOLLY DAVIES:** Hi, so I wanted
21 to take these one at a time. I've gotten a lot of

1 great responses from the associates and other
2 committee members.

3 So starting with 7.1 on the general
4 content organization and presentation, committee
5 members comments were on areas that were easy to
6 read and offered suggestions to improve the
7 clarity. Some of our previous recommendations
8 also apply to this Draft Risk Evaluation. So the
9 Draft Risk Evaluation follows the established
10 organization of the previous series. And, as we
11 mentioned in regard to the previous series, there
12 is not consensus on the committee to whether this
13 is the easiest format to follow. And there were
14 also still comments on how much information to
15 include in the main body of the report versus the
16 appendices, the supplemental documents, and other
17 references.

18 So one example is Section 1.3 on
19 regulation and assessment history does not have
20 enough details in the main report and instead
21 refers to other documents in Appendix A. And a
22 specific recommendation is to add concise summary

1 tables that highlight previous hazard assessments
2 and risk assessments such as the IRIS document,
3 ATSDR, NTP, IARC etcetera with their main
4 conclusions.

5 A similar comment is about including
6 GHS. The person who commented suggested adding
7 this to Section 1.1, which is the physiochemical
8 properties, and to add the GHS classification for
9 the substance as a reference in Section 1.1 where
10 we first talk about the characteristics of the
11 chemical, because GHS classifications provide a
12 standardized way to look at the hazards across
13 chemicals and the most common way to communicate
14 on hazardous chemicals to industrial users.

15 Another suggestion is to put this
16 with the other assessments since GHS is also an
17 assessment of the chemical.

18 There was a comment that EPA had
19 started adding links and tables to other tables
20 and that approach should be applied more broadly.
21 One person commented they appreciated the simpler
22 Table 5-1 with details after the table. This is

1 the table that we've commented on a lot in other
2 draft risk evaluations.

3 The next comment relates to the
4 slide, the second slide that I sent this morning
5 on IRIS 2011 Table 5-13. So this comment is that
6 when there's an existing IRIS review available --
7 and I was hoping that that slide could get put up
8 on the WebEx so everyone could see it. This
9 comment is that when there's an existing IRIS
10 review available for a TSCA chemical under review,
11 it's preferable to use the summary table formats
12 in the draft risk assessment that is the same
13 structure as the table in the IRIS report. So I
14 put this up since not everyone might have IRIS
15 open, but I assume that people do have the DRE
16 opened.

17 So this is compared to Table 3-7 and
18 3-14 with the dose-response analysis that has the
19 points of departure as HECs, HEDs, and uncertainty
20 factors. And the comment is that this more
21 clearly presented in the IRIS table rather than in
22 the way it's done in the DRE. So the

1 recommendation would be to use the IRIS format to
2 make it more clear.

3 Next comment, unlike in previous
4 DREs EPA chose to include the ONU exposure
5 estimates based on modeling or measurements in
6 Section 2, Exposures, but not the exposure
7 estimates based on worker central-tendency
8 exposures which are presented in Section 4, Risk
9 Characterization. This is problematic, because
10 the estimates for ONUs based on workers are also
11 exposure estimates although with different levels
12 of assumptions, uncertainty, and confidence, and
13 they should be included in Section 2 with the
14 appropriate justification description of
15 uncertainties, caveats etcetera.

16 Another comment on PPE, EPA should
17 provide more detailed discussion of PPE usage in
18 the main document instead of just referring the
19 reader to the NIOSH memorandum as EPA did for
20 carbon tet based on the same reference. And this
21 again, is part of the balance between how much
22 detailed information to present in the main

1 document versus the appendices and other
2 references.

3 Also presenting the PPE in Section 2
4 is organized awkwardly. PPE for dermal exposures
5 appears as part of Subsection 2.3.1.3.5, modelled
6 dermal exposures, while for inhalation exposures,
7 it's presented in the next subsection, 2.3.1.3.6,
8 Consideration of Engineering Controls and Personal
9 Protective Equipment which discusses respirators,
10 but inhalation exposures are described in other
11 sections, 2.3.1.2.1 through 2.3.1.2.4 well before
12 the dermal exposures.

13 So the recommendation would be to
14 present either the presentations of dermal
15 inhalation presentations made separately for each
16 route of exposures or there should be a separate
17 subsection that discusses exposure controls and
18 prevents both types of PPE. And I can't remember
19 what question it was, but I know we had a robust
20 discussion of PPE and ways to be consistent in a
21 more detailed discussion.

1 There is referencing, constant
2 referencing to documents in the docket instead of
3 providing the citation to the document. So the
4 citations to the document in docket is non-
5 standard, so the recommendation would be to cite
6 original sources instead of referring to the
7 docket.

8 Another comment on the
9 presentations, commenter who likes the
10 presentation of uncertainty in overall confidence
11 in the table format such as Table 2-26, Summary of
12 overall confidence and inhalation exposure
13 estimates. If the descriptions are systemized
14 better than in this table, it would be a good
15 model to follow for summarizing uncertainties and
16 confidence throughout the DRE including
17 summarizing the potentially exposed and
18 susceptible subpopulations.

19 In the beginning of the specific
20 Section 2.2.6.2.2 it's not clear what "cleansed
21 data set" means. and so it's a suggestion to
22 enhance the clarity with a reminder of the

1 definitions and the reasons for filtering and
2 cleaning are described. But the few paragraphs
3 after, it was the concept of cleansed data set was
4 introduced.

5 On Table 2-3, Summary of EPA's
6 estimates for the number of facilities for each
7 OES, the estimation of the number of facilities
8 could be enhanced by adding a sense of
9 uncertainty.

10 Figure 2-4, the choice of a tornado
11 graph does not seem to be the best one to promote
12 clarity. So it's suggested that pie charts or
13 section bar graphs may better illustrate the
14 point. The report mentions in Section 2.2.5
15 surface water concentration maps, but we don't see
16 them. Color coding was provided, but we don't see
17 where the maps are or the immediate reference.

18 Section 5.1.3 is not clear on the
19 final risk determination. From Section 4.1 one
20 can deduct that the EPA did not find unreasonable
21 risk to aquatic organisms in surface water, but
22 there was some risk with RQ above 1 associated to

1 specific facilities and species. But there's not
2 a summary of either in the final risk
3 determination, so we'd more clarity and summary on
4 that.

5 So there's a few recommendations on
6 presenting the manufacture and use of TCE. And
7 these are slides that I sent earlier that I think
8 I called them slide 7 -- Question 7 slides. So
9 this I repeated the Table 1, so we can see which
10 one we're talking about.

11 So the first two recommendations are
12 on graphics. One is this using a bar graph
13 instead of a table for the production volume just
14 to show the -- you can see it more clearly. And
15 on the next slide is a graphical depiction of
16 percent volume of uses to see where, again, a
17 graphical presentation of where the TCE uses are.

18 So the second one is about our
19 recommendation or previous recommendations to
20 include more information on the chemical
21 manufacture, uses, and releases, which we refer to
22 as the mass balance approach. And I think this

1 connects to what Dr. Cobb was talking about this
2 morning with better understanding where the TCE
3 is. And this is the table that's the next one.

4 So putting the COUs evaluated in
5 this DRE in context of all manufacturing uses and
6 releases will make it easier to understand. And
7 this is a consolidation of -- an expansion of
8 several tables in the problem formulation main
9 report and appendices. So some of us had started
10 making a table with possible entries to give an
11 idea.

12 And the only -- my last part on 7.1
13 is that people have typos that we'll send for EPA
14 to correct. So I put the mass balance last,
15 because I thought that might have more discussion,
16 the mass balance and the other ways of presenting
17 Table 1-2. So that's everything I have so far on
18 7.1.

19 **DR. KENNETH PORTIER:** Thank you,
20 Holly. This is Ken Portier. I kind of started
21 the discussion a counseled weeks ago on this issue
22 of mass balance, because we've brought it up a

1 number of times, and the concept is balancing
2 manufacturing and import against uses, recycling
3 and disposal. And there's a good discussion in
4 the DRE but at the end of the day you don't have a
5 good feeling for, well, how much of it is used in
6 processing, how much of it is really recycled?
7 There's amounts, but you don't get to see it all
8 in one picture here.

9 Now we recognize, and we had a lot
10 of conversation about how difficult it may be to
11 complete this table for many chemicals. And in
12 fact, the point was made that with available data
13 it may not be easy to pull out domestic
14 manufacturing from input -- imports. And we
15 understand that and, in some situations, you may
16 just have a total. But part of this came up as I
17 was thinking about as EPA moves forward with more
18 and more chemicals, the industry is going to look
19 at these DREs for suggestions of what kind of data
20 they need to prepare for their chemical when it
21 comes up.

1 And our first recommendation should
2 be we need to know what's manufactured and where
3 it goes. So kind of industry get your act
4 together and provide EPA a table like this so that
5 we get the picture of where quantities go.

6 And then the other issues were back
7 on the physical chemical properties table that Dr.
8 Davies showed first, Table 1-1, to make sure that
9 we have all the physical chemical properties of
10 the chemical in front of us and, hopefully, with
11 references that are fairly recent. When I've
12 looked at the physical chemical property data,
13 some of this data is 40, 50 years old. And
14 understanding how measurement methodology has
15 changed in the last century, I would think that we
16 would have some better measurement methodology for
17 many of these physical chemical properties.

18 And then I asked members of the
19 committee to suggest or at least identify whether
20 that list on Table 1-1 is the complete list or
21 whether certain components are missing because in
22 the last two or three evaluations we'd go to

1 properties that the panel wished to see, physical
2 chemical properties that they would have wished to
3 have seen but didn't see on the table.

4 And I think there were a couple of
5 suggested -- I know Dr. Kissel had suggested some
6 for dermal, and there may have been one other.
7 I'm hoping some of you will raise your hand and
8 mention that. But that's where this mass balance
9 table comes from and where the physical chemical
10 properties discussion has come from. Dr.
11 Doucette.

12 **DR. WILLIAM DOUCETTE:** Yeah, just to
13 follow up on your comment on Table 1-1, and I
14 tried to put a couple of comments in various
15 previous reports and in this one on what I would
16 call a little bit of an over reliance on using the
17 EPI Suite program just because it was peer
18 reviewed. I don't have a particular problem on
19 the age of some of those references. These are
20 off -- or we've been evaluating what I would
21 consider legacy chemicals anyways, but the
22 database within EPI Suite is not complete. It

1 isn't always updated, and I think that the big
2 thing would be to just go back to that whole idea
3 of showing at least the reader some indication of
4 the variability associated with those.

5 We agonize over the biological
6 endpoints and the variability associated with it,
7 but we don't spend much time on the variability
8 associated with the physical chemical properties
9 and how that variability would influence the
10 outcome of the various environmental fate models.
11 And even something like a PBPK model requires
12 octanol/water partition coefficient or log D in
13 there and how much that might influence the model
14 outcome.

15 So, again, I don't think I'm worried
16 about the age of the references. I'm more worried
17 about the fact that EPA focuses on that database
18 only, even though there are many, many references
19 the EPA includes in the supplemental information.
20 It could be easily incorporated to provide
21 essentially a range. That's all I have.

1 **DR. KENNETH PORTIER:** Yeah, Dr.

2 Doucette, you just got me thinking one of the
3 reasons I looked at this table was I noticed in
4 the -- for original problem formulation some of
5 these parameter values are different than they
6 showed up in the DRE which means as EPA searched
7 the literature they found different and, I assume
8 they considered, better measurements and replaced
9 them in the document. But I think you're right.
10 Especially if they do the literature review, they
11 should be able to develop something like a
12 minimum, medium, maximum kind of value that would
13 be very useful for sensitivity analysis on a lot
14 of these other things as well.

15 Does anybody else have any comments?

16 Dr. Cobb.

17 **DR. GEORGE COBB:** Okay, I think I've
18 got my -- am I unmuted?

19 **DR. KENNETH PORTIER:** Yes.

20 **DR. GEORGE COBB:** Am I unmuted
21 there?

1 **DR. KENNETH PORTIER:** Yes, you are,
2 George. I can hear you.

3 **DR. GEORGE COBB:** Okay, my comment
4 is simply to echo what Bill said is that the
5 information that we're using for our models
6 determines the confidence we have in those
7 outputs. And I'll also say it is my understanding
8 that EPI Suite and all of the EPA models are not
9 being supported, which is a major issue for those
10 of us who are trying to teach students how to
11 model these things. But also it perhaps hampers
12 our friends in the Agency who were discussing this
13 matter about if the databases are not being kept
14 up by others, be that as contractors or Agency
15 employees.

16 **DR. KENNETH PORTIER:** Thank you.
17 Dr. Blystone.

18 **DR. SHERI BLYSTONE:** Yeah, I just
19 wanted to make a comment about the mass balance
20 side of things. Besides the confidential business
21 information, that might be an issue to get to
22 where the committee seems to want to go. There's

1 also I think fundamentally an issue to try to
2 balance production volume in a year to what is
3 used in that year, because it doesn't really work
4 that way. You have things like inventory. You
5 have recycling. So to account for every pound
6 that is produced in 2012, I don't know that that
7 is an easy exercise to do.

8 So I was the one that put the pie
9 chart in, but that was just based on text
10 information that was in the DRE to -- I think it's
11 better to get, overall, a picture of where is the
12 product going in its uses. And what seems to have
13 gotten missed in this conversation is that the
14 bulk, according to EPA's evaluation, 87 percent is
15 consumed in making another product. And that the
16 rest of these uses are, then, a small percentage
17 of the overall production volume.

18 And that was where I was trying to
19 go with the pie chart. I think that gives a
20 better picture for the reader to get a sense of
21 where is the product going, and where is most of
22 it going? Is it going into consume product? And

1 we might get to that in some other chemicals, but
2 where is it going in the end market? That might
3 be a little bit more practical to do than a true
4 mass balance. That's all.

5 **DR. KENNETH PORTIER:** Yeah, Dr.

6 Blystone, this is Ken Portier, and I guess I was
7 considering especially these -- you notice in the
8 total use and processing we have functional fluids
9 and solvent. And that makes up 85 percent of the
10 total uses for TCE. And that means that the rest
11 of these can only make up 14.4 percent. And that
12 at least gives the reader a feeling.

13 But EPA does do conditions of use
14 for each one of these and, again, in our
15 discussion of uncertainty, our discussion of
16 especially risk characterization is the bigger
17 picture. It'd be nice to know, while we don't
18 really have a good handle on apparel and footwear
19 risk but, by the way, those risks are less than 1
20 percent or less than 0.5 percent. I mean that's a
21 very small fraction of the total amount used.

1 But I don't really care if it's an
2 individual year or a five-year total or something
3 like that that the industry might feel more
4 comfortable providing and may feel comfortable
5 from a confidential business information of
6 consolidating. But I think if the industry
7 doesn't see us requesting this kind of stuff,
8 they're not going to be putting those kind of
9 reports together.

10 I can't believe they don't know the
11 answer to this. They just haven't provided that
12 answer to EPA, which means providing that answer
13 to the public to look at it. Dr. Blystone, your
14 hand's still up. I assume you want to argue.

15 **DR. SHERI BLYSTONE:** Not argue, just
16 again, marketing information tends to be a bit on
17 the confidential side so there is -- I'm not
18 saying it is or isn't in any particular case, but
19 there could be potential issues there.

20 And I also wanted to stress that I
21 believe EPA's objective or their mandate in this
22 is not to -- they have to review the risks of any

1 current uses or any uses identified by the
2 administrator regardless of whether it's only 0.01
3 percent of the production volume or not.

4 **DR. KENNETH PORTIER:** Yeah. Well, I
5 guess the other thing too, is I don't want to
6 leave out disposal and releases down at the
7 bottom, which to me is the real part that gets
8 translated into the next section on exposures.
9 And you notice I was not really able to fill in a
10 lot of that from the text in the material, so I
11 don't have a good feeling for how much of the
12 material is recycled or how much of the material
13 is disposed. In the past, we have seen some
14 recycled fractions. I don't think we've seen
15 disposal and release fractions that have been
16 very, very well. Dr. Bennet.

17 **DR. STEVEN BENNETT:** Yeah, this is
18 Steve Bennet. Yeah, I certainly echo some of
19 Sheri's comments as well, because I think in some
20 respects that exercise was done in some of the
21 earlier materials. If you look at the marketing
22 use report that information, some of it is in

1 there. But, again, that identifies a very large
2 portion of it as being -- it's used as an
3 intermediate, and we've not really talked about
4 that other than a couple comments.

5 And it really wasn't discussed at
6 all within the risk evaluation itself. Or to some
7 extent we've spent a lot of time dealing with
8 particular conditions of use where there's a
9 single product in some cases, so what are just a
10 very small number of products. And I'm certain
11 this is something that they would address when it
12 comes to the risk management piece, and something
13 the Agency would be obligated to put those
14 appropriate risks in context.

15 But I think it would be helpful for
16 a SACC panel or for a review or the public to have
17 a better understanding of where the risks and
18 where the emphasis should be put on to some extent
19 and to have the appropriate context.

20 **DR. KENNETH PORTIER:** Dr. Davies,
21 and then I see Dr. Kaufman's hand's up as well.
22 Dr. Davies.

1 **DR. HOLLY DAVIES:** One advantage
2 that I see about this is that it forces us to look
3 at all the estimates, because the TCE has to be
4 someplace. And if what we're estimating doesn't
5 add up to all the TCE out there, it shows that the
6 estimates are wrong. I think that's one reason
7 why it brought to mind for me what Dr. Cobb was
8 mentioning this morning about it has to be either
9 in the air or the water. You have to add up to
10 100 percent.

11 So I think going through this helps
12 see how good the estimates are because if
13 everything got added up and it was really far off
14 what we thought was out there, that would show
15 that something was missing and just, again, helps
16 us know where things are. And I also agree with
17 other comments on helping us with looking where
18 the risk is by seeing which ones are small uses or
19 small amounts.

20 **DR. KENNETH PORTIER:** Dr. Kaufman.

21 **MR. ALAN KAUFMAN:** Yeah, hi, thanks,
22 yeah, I just wanted to echo some of the earlier

1 comments. Although, I think we could probably
2 figure out a way to handle the CBI issue. I think
3 the, as Dr. Davies said, I think it's important to
4 try to at least roughly figure out where these
5 things are going.

6 But when I look at the top of the
7 table, what bothers me is that we're essentially
8 looking into the past. I mean, we're looking at
9 data that's five years old. And things change
10 pretty quickly.

11 I mean with California seemingly
12 bent on sticking every chemical on demand on the
13 Prop 65 list, including aspirin and Tylenol, there
14 are a lot of factors that are driving
15 manufacturers to eliminate some of these chemicals
16 or substitute them. And I don't know that we're
17 adequately capturing that. And I think that's
18 something that we -- you know, I don't have an
19 answer for it, but I think it's something that
20 we're going to need to grapple with as go forward
21 here.

22 **DR. KENNETH PORTIER:** Dr. Kissel.

1 **DR. JOHN KISSEL:** Yeah, so I wanted
2 to echo somewhat what Holly said, although, maybe
3 extend a little bit, so what we have for release
4 data is mostly from TRI. And there are, at least
5 in some quarters, widespread suspicion that the
6 TRI numbers are underreported. That is to a large
7 extent a voluntary system, and industry has
8 incentives to not be too careful about how they do
9 those calculations. And if we had a more complete
10 accounting, we might be able to put two and two
11 together and try to figure out whether those TRI
12 numbers are realistic or not.

13 If you do a mass balance, if you've
14 got a certain amount being dumped in the general
15 environment, we also have ambient monitoring for
16 some of these compounds, and those things have to
17 match up somehow. There has to be some
18 consistency.

19 If 85 percent is being consumed
20 internally and only 15 percent is subject to
21 release, well great, then we can start working
22 from that 15 percent. But if we look at the 15

1 percent and then we say that only 4 percent of
2 that is ever discharged to the environment and yet
3 the environmental levels are much, much higher
4 than could be accounted for by that 4 percent,
5 then we have a problem.

6 And ultimately, Waltenberger
7 (phonetic) is trying to get at management of
8 chemicals in the environment, and historically
9 there has been massive externalization of cost,
10 which is what pollution is. And we need to do a
11 better job and a more consistent job of how we
12 assess that, and that means that we need to be
13 able to look at data for a whole slew of compounds
14 and see if there are outliers, see if there are
15 compounds for which the numbers add up well and
16 compounds for which the numbers don't add up at
17 all. And then we could focus on the ones where we
18 seem to have the biggest problem.

19 But somehow despite the prohibition
20 on spills -- and I'm not sure -- I've never
21 bothered to go look and see what that language
22 actually says. It's certainly in society's

1 interest to understand what routine fugitive
2 emissions are, which may or may not qualify as
3 spill.

4 I understand that it's hard to
5 predict truck accidents when a tanker overturns
6 somewhere, which can be locally an important
7 event. But there is a certain amount of leakage
8 out of the system, and that has to be considered
9 in the overall cost to society of dealing in
10 whatever that chemical is.

11 And then, also, the "spill" is kind
12 of benign word. We have a history with a whole
13 lot of compounds, especially with chlorinated
14 solvents, that the spillage wasn't accidental.
15 The spillage was deliberate. And that's probably
16 not covered by TSCA either, but it is a huge
17 societal problem, and it has imposed huge costs on
18 society that industry has not paid. And we just
19 need to be able to do better accounting to manage
20 that problem.

1 **DR. KENNETH PORTIER:** Thank you, Dr.
2 Kissel. Dr. Cobb, I see your hand's still up.
3 And then Dr. Davies, your hand's still up.

4 **DR. GEORGE COBB:** Ken, this is
5 George, and I wanted to follow up a little bit on
6 what John just said and also on the table in some
7 of the conversation around that table. It's we
8 don't have data in the problem formulation from
9 2014 for production-related releases, but we do
10 for 2015. And there are 2 million pounds of
11 purported to be lost in 2015, and so that's over 2
12 -- well it's actually 1.97 to be exact. That's
13 over 2 percent of the total production volume, and
14 that's 10 percent of the solvents in degreasing if
15 you're saying that the functional fluids are
16 closed system.

17 So regardless of how you can't slice
18 and dice what we're using and where it may or may
19 not be released, the problem formulation has 2
20 million pounds, almost all of it, 90-something
21 percent of it going to fugitive releases to the
22 atmosphere.

1 DR. KENNETH PORTIER: Thank you.

2 Dr. Blystone.

3 DR. SHERI BLYSTONE: I would agree
4 with Dr. Kissel that TRI is not necessarily very
5 good data. I would disagree with his
6 characterization of it being underrepresented. I
7 believe it's actually overrepresented. It is
8 definitely not a voluntary program. But exactly
9 what Dr. Cobb was just talking about but for some
10 of the other commenters, when you don't
11 necessarily have monitoring information, you're
12 doing an estimate and it's relieving -- it has to
13 be released somewhere, so you report it as a
14 fugitive air release. And that's where that 2
15 million pounds is coming from. It is an estimate.
16 It's not measured.

17 People are doing their best to
18 figure out I'm using this. This is what I got.
19 This is how much I consumed, and this is the
20 number of pounds or whatever the estimation -- I'm
21 not the TRI guy, so I'm probably misspeaking, but
22 whatever their approved methods of estimated are,

1 but that's most likely actually an overestimate
2 not an underestimate.

3 **DR. KENNETH PORTIER:** I think we
4 understand what you're saying, Dr. Blystone, in
5 that because they're what's left over. You know
6 what you used in processing. You know what you
7 bought. What's left is released and if you
8 understand your process, you have a pretty good
9 idea of where it went. But you may be erring on
10 the high side when you report it. Dr. Kissel,
11 your hand's still up. Did you have further
12 comments? And Dr. Cobb, your hand. John?

13 **DR. JOHN KISSEL:** Go ahead. This is
14 Dr. Kissel. I've been teaching hazardous waste
15 management for 35 years or so. And the standard
16 response from industry, especially from people
17 that are high up in the food chain, is that we're
18 trying to do the best we can and it's all
19 honorable and -- but that doesn't necessarily
20 translate down to the shop floor. And there are
21 plenty of cases out there.

1 I mentioned the Woburn,
2 Massachusetts case a few days ago. There was a
3 guy at the shop floor level who decided that it
4 would be a good idea for the company, and this
5 wasn't company policy, but this guy decided he
6 could save the company about \$1,000 if he buried
7 barrels of solvent in the back yard instead of
8 handing them over to a hazardous waste manager.
9 And to save that \$1,000, he basically cost the
10 company involved about \$20 million. So a nice
11 talk from people at the top of the food chain is
12 great, and we kind of expect it, but it isn't
13 necessarily the way the world is really working.

14 **DR. KENNETH PORTIER:** Thanks, John.
15 Dr. Barone has been waiting patiently with his
16 hand up. Dr. Barone.

17 **DR. STANLEY BARONE:** I'm glad you're
18 having this discussion. I do want to point out,
19 yes, we do a life-cycle analysis. Yes, we have
20 included production volumes. We do have some
21 constraints because of CBI declarations and ranges
22 that are reported. When we're dealing with ranges

1 if you take those ranges, it doesn't always add up
2 in a mass balance per se because of the ranges.

3 I do also want to -- I think the
4 point was made about TRI. It's not voluntary. It
5 is if you're listed on TRI, you're required to
6 report every year. There was discussion about the
7 underreporting and overreporting. There's
8 probably some of both and for different reasons
9 but, again, that's something that we address when
10 we see discrepancies. EPA does. Our program
11 does.

12 One of the other asks that I have is
13 I think the graphics that you provided, Dr.
14 Davies, are helpful and would help us in our
15 follow-up discussions so if we could receive those
16 from the DFO, that would help us in our post hoc
17 analysis of the meeting.

18 **DR. KENNETH PORTIER:** I don't think
19 the committee see any problem with handing those
20 graphs over.

21 I would like to host and shift back
22 to the Figure 1 on the Physical and Chemical

1 Properties table. I think we had made -- do we
2 have that graph somewhere?

3 I wanted to make sure that we did
4 discuss all of the properties. I thought a couple
5 of people had pointed to one or two other
6 properties that they'd like to see on that table.
7 And I guess I'm thinking of Dr. Kissel and maybe
8 Dr. Doucette or Dr. Cobb had mentioned something.
9 Even, possibly, Dr. Bruckner had mentioned
10 something. You guys want to chime in and talk
11 about that just any physical chemical properties?
12 Dr. Kissel, I wanted to make sure that the ones
13 that you had mentioned get re-mentioned here.

14 **DR. GEORGE COBB:** Hey, Ken, this is
15 George. I think the comments that I heard were
16 from about these properties were primarily from
17 Bill. And he was mentioning that there are newer
18 values for some of the partition coefficients,
19 KOC, KOW, if I'm not mistaken. And that all of
20 the physical chemical parameters if there are
21 newer data or better estimates, they might be able
22 to inform the aggregate number that could be

1 listed in the EPI Suite. That's what I remember
2 from it, but I don't really want to speak for
3 Bill, but that's my remembrance of it.

4 **DR. WILLIAM DOUCETTE:** This is Bill,
5 and I'll speak for myself. And I think that was
6 certainly an issue, but I think what Ken asking
7 about was some of the additional physical chemical
8 properties that should be added to that table. I
9 know quite a long time ago I mentioned that
10 octanol/air should be added. And Dr. Kissel sent
11 me a list of, oh, maybe a dozen different
12 properties related to skin permeation that we made
13 a list in the carbon tetrachloride report, which
14 is not finalized, but that's where it was
15 presented. And I think we should maybe, Dr.
16 Kissel, if you agree, we should relist that here
17 for this report.

18 **DR. JOHN KISSEL:** This is John
19 Kissel. Yes, that is a generic recommendation
20 that a more extensive list of parameters that are
21 useful for characterizing dermal absorption be
22 just routinely presented. And for some compounds,

1 they will tell us that dermal isn't very important
2 and for some compounds, they'll tell us that
3 dermal likely is very important.

4 And they also, then, provide a check
5 against the numbers that are actually used. In
6 every percent absorbed calculation there is an
7 implied flux. And if that flux is much bigger, as
8 was the case here for the consumer exposure case,
9 if that's much bigger than a plausible flux, then
10 that would give you an automatic flag. Or
11 similarly, it might be much smaller.

12 **DR. KENNETH PORTIER:** Thank you.
13 Bill, I would like to have those kind of added in.
14 We'll assume they're spoken at this point and
15 refer -- even though they're referred to, I had
16 forgotten that we were going to add that in the
17 carbon tet report, because I wanted to see it
18 here. Dr. Morandi.

19 **DR. MARIA MORANDI:** A couple of
20 comments; one of them in terms of the properties
21 that should be listed and in the past was not only

1 the typical physical chemical properties but also
2 the ones that Dr. Kissel had recommended.

3 But maybe the protocol for this
4 should be to request that EPA report all the
5 physical chemical properties and others that are
6 used throughout the report either implicitly or
7 explicitly. And by implicitly, I mean in models
8 and so forth. And I know that whenever, let's
9 say, a model is discussed, parameters are referred
10 to and so forth, but it might be useful to have
11 all of this in a single list.

12 The other issue with this that I
13 wanted to mention is I wonder if in terms of
14 getting there to say "best estimate" for these
15 properties would be for EPA to contact the N-I-S-
16 T-, NIST, because they probably have a fairly, at
17 least for many properties, a fairly good list with
18 reliable numbers for many of these. That was all.

19 **DR. KENNETH PORTIER:** Yeah, your
20 suggestion of a list is good except when it comes
21 to the PBPK modeling. And I started thinking
22 about all the parameters that's in that model.

1 It's huge. But it does bring up a point that in
2 this particular report, the appendix where the
3 PBPK model is discussed -- and I'm trying to
4 figure out which one it is -- it really doesn't
5 even provide a list of that.

6 You have to go to the supplemental
7 files and dig through -- and that was one of the
8 things that I thought might be nice to have a
9 spreadsheet for PBPK modeling at least the
10 spreadsheet that shows all of the physiological
11 and rate parameters and everything else in one
12 place so that an expert could scan through that.
13 Because, otherwise, you're having to almost read
14 code to see what the settings are. And I may have
15 missed that file -- may be in that large PBPK
16 folder, and I may have missed it, so I'll double
17 check again. Dr. Davies.

18 **DR. HOLLY DAVIES:** This is a
19 slightly different topic. I just wanted to
20 comment Dr. Barone mentioned a lifecycle
21 assessment that had been done, or a lifecycle

1 analysis. And that would be really interesting to
2 see the details of if EPA had done that.

3 **DR. KENNETH PORTIER:** And if I
4 remember, we did talk a little bit about that
5 among ourselves and wondered whether amounts could
6 be put onto that cycle so you could see how much
7 mass of material or percent of manufacturing moved
8 along what pathways, but that's essentially this
9 Table 1-2 all over again. Dr. Barone, I see your
10 hand's still up. I'm thinking you have more
11 comments?

12 **DR. STANLEY BARONE:** I do. Thank
13 you, Dr. Portier. To answer the question that Dr.
14 Davies just asked, yes, the lifecycle analysis, I
15 believe, was in the problem formulation and gave
16 the high-level overview. And it's something that
17 will be in the scopes for the next 20, so
18 definitely a part of the background materials.

19 One of the points that was made
20 earlier was about different properties, p-chem
21 properties. And it would really help us to know
22 what specific properties that the committee is

1 suggesting. And if those were added in or listed
2 out in these graphics or tables that you're
3 preparing, that would help us.

4 I would also like to underscore a
5 point that you made, Dr. Portier about
6 stakeholders looking at what the committee
7 recommends. And I will tell you that your
8 recommendations are being looked at broadly and
9 come up often. The recommendations for exposure
10 and exposure analysis in different factors come up
11 often in our discussions as we view outreach with
12 our different stakeholders. So this is a very,
13 very relevant conversation. And the more we can
14 put this into concrete terms -- tables, graphics -
15 - I think it helps move this conversation forward
16 for our evaluation program.

17 **DR. KENNETH PORTIER:** And, Dr.
18 Barone, part of my objective in this conversation
19 is to try to in a sense standardize the formats
20 for as many of these tables as we can so that, 1,
21 you're not inventing it, reinventing it chemical
22 by chemical but, also, because then your

1 stakeholders see a pattern here. They see, oh,
2 this table shows up each time. If we can help
3 fill it out, that's one less thing that we have to
4 worry about "EPA getting wrong." Or us being asked
5 to rush to completion and not being able to do a
6 good job of coming up with physical chemical
7 properties and, as it was related to marketing,
8 appropriately deidentified and aggregated
9 marketing information so the public will
10 understand sources and sinks in this process. Dr.
11 Bruckner, your hand's up. You're still muted, Dr.
12 Bruckner.

13 **DR. JAMES BRUCKNER:** How am I now?

14 **DR. KENNETH PORTIER:** Now you're
15 fine.

16 **DR. JAMES BRUCKNER:** Okay, good.
17 I'd mentioned previously expanding our description
18 of the PBPK model, actually having the structure -
19 - and I think your idea of having a table with the
20 parameters there with that description that were
21 actually used. A lot of times when we look at our
22 simple things it's like oil/water partition

1 coefficients or volatility. Those descriptions
2 are -- you can't check them, they're years old.

3 It would be really nice to have
4 those parameters up front and what their
5 derivation was so we can understand what was done.
6 And perhaps those are some of the most important
7 properties to determine the kinetics of chemicals,
8 so that would be an excellent thing. And I'll
9 make that as one of my recommendations.

10 **DR. KENNETH PORTIER:** Yeah, and
11 especially that the physical chemical properties
12 seem to weigh heavily in fate and transport, and
13 in environmental exposure. So getting them right
14 and understanding variability and uncertainty in
15 those parameters helps me be more comfortable,
16 especially on the environmental exposures part of
17 the report. Dr. Jimenez-Gonzalez?

18 **DR. CONCEPCION JIMENEZ-GONZALEZ:**
19 Yes, thank you. And I lift up my hand when the
20 conversation on the life-cycle analysis was
21 happening and just one point of reminder that I'm
22 sure the EPA is fully aware of that's an integral

1 part of a life-cycle assessment, includes the
2 uncertainty and sensitivity analysis. Mostly
3 because by doing those type of analysis, we expect
4 to have less than perfect data in terms of getting
5 the best estimate. So that's probably part of the
6 reason that I tend to bring that up.

7 **DR. KENNETH PORTIER:** Excellent
8 point. Anyone else want to comment on Question
9 7.1?

10 **DR. HOLLY DAVIES:** Yes, this is Dr.
11 Davies. I wanted to get people's feedback more on
12 Table 5-1, because it looks like we've talked
13 about this table a lot, the Summary of
14 Unreasonable Risk Determinations by Condition of
15 Use. And it looks like EPA made a fairly large
16 change by making a simpler table and having more
17 details below, instead of having all of the
18 details in the table. And I just wanted to get
19 more committee members' opinion on that.

20 **DR. KENNETH PORTIER:** Any comments?
21 I did look at that table, and I do find it easier
22 to read. I guess the only thing we talked about

1 earlier this morning was some measure of
2 confidence or lack of confidence in that
3 determination or what might be the caveat in that
4 determination. So for example, what is it, on
5 environmental risks, I guess that's manufacturing,
6 processing -- these are uses, so anyone else?

7 **DR. HOLLY DAVIES:** Okay. Well,
8 thanks, everyone.

9 **DR. KENNETH PORTIER:** That may be a
10 question that comes up on the next chemical again,
11 and maybe we'll have a better answer at that
12 point, Dr. Davies. I think at this point let's go
13 ahead and move onto Question 7.2, see if we have a
14 final comments on -- I mean questions -- comments
15 on the final question?

16 **DR. HEIDI BETHEL:** Okay, I'm just
17 getting to that, moving back to that document that
18 I have. So I got, again, a lot of good comments
19 from the associates and other members of the
20 committee. Committee members commented that the
21 species sensitivity distribution's a good
22 visualization tool to determine the potential

1 relative impact to different species. And it may
2 be useful to inform actions depending on the
3 ecology of the aquatic environment. It was also
4 very positive that the sensitivity assessment was
5 included to the consumer exposure model.

6 In general, EPA does a good job of
7 explaining how the TSCA assessment differs in
8 scope and focus from the IRIS assessment.
9 Moreover, it's mentioned in multiple places that
10 the hazard and risk assessments done previously
11 are used as a starting point and then updated for
12 the present assessment. However, a more
13 informative summary could be provided, for
14 example, that lists the critical endpoints for
15 acute and chronic non-cancer effects in cancer.
16 The critical studies identified for each endpoint
17 and those that were used to determine the POD
18 values.

19 There's an impression of bias in the
20 descriptions of the fetal cardiac malformations in
21 relation to the literature, especially Johnson et
22 al., (2003) and the Charles River, (2019) study.

1 Suggestion is that the EPA consider a full,
2 complete description of the issue -- and we've
3 talked about this several times already this week.
4 Why is this endpoint so controversial, for
5 instance, and provide a more complete discussion
6 of other relevant studies to help explain results
7 relevant to the data coherence between studies
8 conducted by the same route of administration.

9 Another, this was brought up earlier
10 with another question. Committee members brought
11 up a concern related to the questions arising
12 publicly regarding the alleged changes to the EPA
13 risk evaluation, and the claim the draft provided
14 for interagency review identified the fetal
15 cardiac malformations as the most sensitive
16 endpoint, using it to derive the points of
17 departure for making determinations of risk
18 consistent with prior reviews.

19 This public allegation makes a full
20 discussion more important for the rationale of
21 checking -- rationale of excluding the fetal heart
22 malformations as endpoints. And the allegation

1 should be investigated as a mere suggestion that
2 EPA changed the earlier scientific evaluation,
3 based on pressures from non-scientific sources,
4 cast significant doubt to the scientific integrity
5 that EPA has worked so hard to maintain.

6 Moving onto something else, overall
7 it seems that EPA judges said equality, but it's
8 difficult to understand how study relevance
9 factors into any conclusions in choosing a
10 particular study from which to develop a POD and
11 resulting value to carry through for the risk
12 assessment. So examine the breadth of data for
13 coherence, skeptically evaluate apparent outliers
14 in the dataset for plausible explanations and
15 choose studies based on the overall weight of
16 evidence, not just the lowest exposure from which
17 adverse effects were observed.

18 Another topic, the development of
19 cancer risk was difficult to ascertain. In the
20 section on page 250 the EPA states that the IUR
21 was adjusted by a factor of four to account for
22 estimating risk from all three cancer types yet

1 later suggests lifetime cancer risks were first
2 calculated and then summed across all three types,
3 so which was that -- to provide more clarity on
4 how cancer risks were estimated by showing the
5 math that was done.

6 In the executive summary on page 30
7 it says a linear non-threshold assumption was
8 applied to the TCE cancer dose-response analyses,
9 because there's sufficient evidence that TCE-
10 induced kidney cancer operates primarily through
11 mutagenic mode of action while it cannot be ruled
12 out for the other two cancer types. And the
13 comment on this is that not sure this is a correct
14 statement and not being aware that there's a
15 consensus so would like you to provide more
16 support for that or modify the statement to
17 reflect the lack of consensus.

18 And then throughout the document the
19 need to be consistent about the cutoff for adults.
20 It should follow the DHHS guidelines of adults
21 being over age 18. And in some places EPA uses a
22 16 or 21 as a cutoff, and it's unclear about this

1 lack of consistency. And there's one example on
2 page 186 about the adults being above 11. And
3 then in that last comment about the term "overt
4 toxicity" on page 225 that needs a clearer
5 definition. So that's the comments I've gotten
6 before, and people can comment on them or add more
7 or expand them.

8 **DR. KENNETH PORTIER:** Any additional
9 comments or expansion discussions on these
10 comments from the panel? Dr. Morandi.

11 **DR. MARIA MORANDI:** I was focused
12 more on the sensitivity of the Agency's
13 conclusions to analytical decisions made. From
14 the point of view of exposure, I think that there
15 is an inherent -- I hate to call it bias -- but
16 the preference for using monitoring data over
17 modeling approaches. And I think this is
18 connected to an issue that has come up in prior
19 reviews too, which is the adherence to the
20 preferred approaches in terms of data sources for
21 estimating exposures. And so I keep on finding it
22 problematic when I see an estimate based on

1 measurements that only had two data points. And
2 so there is this inherent issue that may be
3 introducing biases in many cases because of the
4 preference for monitoring data in all cases -- or
5 in most cases, I should correct that. That's all
6 the comment that I have.

7 **DR. KENNETH PORTIER:** Yeah, Dr.
8 Morandi, I'm reminded of conversations we've had
9 before the committee in the past about how EPA
10 uses the hierarchy of preferences. And with
11 monitoring data above modelled data above -- and I
12 guess at the lowest level would be professional
13 guesstimates, but you're right. If the real
14 monitoring data is two real data points and
15 everything is below quantification limits, then is
16 that actually better information than a good
17 validated model? And I think, again, professional
18 judgement needs to come in there. And that's
19 where this thinking about uncertainties factors
20 into it as well. Dr. Morandi?

21 **DR. MARIA MORANDI:** Yes. Well,
22 sometimes there's just two datapoints and both of

1 them detectable and no other measurement, which is
2 -- so it's not that the two -- I agree with you
3 that that's also a concern, the fact that you may
4 have these measurements above a detection level
5 and most of them under. But in some cases, there
6 is only two datapoints, both of them are above
7 detection, there is only two, and there are no
8 other values. So it's a problem.

9 **DR. KENNETH PORTIER:** Yeah. Dr.
10 Anderson?

11 **DR. HENRY ANDERSON:** Okay. Yeah, I
12 just got a suggestion again to go back to the risk
13 determination summaries and in the use of PPE.
14 I'm just wondering -- if you go on page 377, under
15 Workers, it says, EPA expects there may be
16 compliance with worker standards unless case-
17 specific facts indicate otherwise. And
18 apparently, then, there's not a determination that
19 there are no case-specific facts indicating
20 otherwise.

21 It would seem to me that the
22 assumption ought to be that workers are not being

1 adequately protected unless there's evidence to
2 show that they are. And that would then put the
3 onus on getting the data together on PPE use in
4 the various ONUs.

5 So I would just raise that I think
6 we need to take a look at some of these
7 definitions and assumptions that you assume
8 everything is fine unless you have sufficient data
9 or evidence to show that they are not. And then
10 if there isn't such information, we just go
11 forward with well, everything must be working
12 appropriately. And I think there was quite a bit
13 of public presentation on the fact that PPE is not
14 universally utilized or even in a high proportion
15 of the workforce for this chemical. Yet that
16 continues to be used in this documentation.

17 So again, it's kind of what is
18 necessary? I don't see a definition on what
19 constitutes case-specific facts indicating
20 otherwise. What information is necessary to show
21 that? Again, I would say the there's concern
22 about using the OSHA inspection data, but that

1 certainly would be one data source that could show
2 about the appropriateness of respirator use. And
3 there are a couple of the relatively old
4 evaluations that were done that show respirators
5 are not widely used in all the sectors.

6 So I think that's just -- I really
7 don't know how we define that what constitutes or
8 why we require there be evidence showing that
9 they're not being used rather than evidence that
10 they are being widely used.

11 **DR. KENNETH PORTIER:** Dr. Anderson,
12 you remind me of the previous meeting where the
13 industry had done a really good study of PPE use
14 and were able to come back with a report that said
15 it is being used, at least in the major
16 manufacturers, in an appropriate way. So you're
17 kind of saying guilty until you prove innocence,
18 right?

19 **DR. HENRY ANDERSON:** Well, I
20 wouldn't go quite that far. What I would say is I
21 would halfway turn it around a little bit. That
22 would then encourage the industry to provide the

1 data or do studies rather than the current way is
2 for EPA to do a literature search. There's
3 nothing there, or it's so old that you could say,
4 well, it's no longer relevant anymore and
5 therefore just continue with the assumption that
6 it is being used.

7 So I don't know how we encourage --
8 either encourage EPA to do such surveys or to work
9 with NIOSH or OSHA to do it or to encourage
10 industry. I mean, as I said earlier, if you could
11 proactively, knowing the next chemical's coming,
12 could do a very small survey a few questions
13 asking the industry to send in some data that
14 could be used to give you a good summary. And if
15 they don't send it in, then there are consequences
16 to that.

17 **DR. KENNETH PORTIER:** Dr. Morandi,
18 your hand's still up. Dr. Blystone?

19 **DR. SHERI BLYSTONE:** Yeah, I
20 struggle with this concept of assuming
21 noncompliance with regulations, assuming guilty
22 before -- and proving that you are in compliance,

1 whether or it's for PPE or disposal of waste or
2 any of that stuff. I'm not quite sure I know how
3 -- I mean I understand the concern of when things
4 are not done properly. But to assume that they
5 are not done properly, then one would argue why we
6 are doing regulations at all. So I just wanted to
7 get that on the record that I am certainly not in
8 favor of assuming noncompliance.

9 **DR. HENRY ANDERSON:** I guess what
10 I'm saying is why do you have a regulatory
11 inspection program if you're not using that to
12 document compliance? And that's basically what
13 I'm saying instead of it's voluntary to all you
14 got to do is say I'm complying. That's my problem
15 with this.

16 And again, I would say the
17 inspection programs that are out there for OSHA
18 over the studies that are done by NIOSH all
19 provide the kind of information that could help
20 inform that to say when somebody goes out and
21 evaluates situations, what do they find? And
22 rather than assuming that all of those companies

1 are compliant, I would assume most of them are,
2 but we don't know that.

3 **DR. SHERI BLYSTONE:** This is Dr
4 Blystone again, just there's a lot of problems
5 with asking a company if they comply.

6 **DR. HENRY ANDERSON:** Well, you can
7 ask them what they do.

8 **DR. SHERI BLYSTONE:** I comply.

9 **DR. HENRY ANDERSON:** I would say the
10 whole voluntary compliance programs that are in
11 place, that's what they do.

12 **DR. KENNETH PORTIER:** And I would
13 argue that the public health thinking here would
14 be to assume that they're not necessarily
15 compliant. I understand what you're coming from,
16 Dr. Blystone, in the sense that you have no data
17 either way, so where do you go? And we've asked
18 EPA, essentially, to provide both cases, the no
19 PPE use case and the best guess, best PPE use
20 case. And so it brackets it, and in a risk
21 assessment I think that's appropriate.

1 We're kind of pushing into risk
2 mitigation, risk management, and I don't think
3 that's part of this document. But I'm glad that
4 Henry pointed out this statement on page 377,
5 because I think that's not quite what they're
6 wanting to do in this document. So that may be a
7 mistake question.

8 Dr. Kissel and then Dr. Morandi. I
9 wanted to get another voice in here. John? John,
10 your phone may still be muted. We don't hear you.

11 **DR. JOHN KISSEL:** That's the second
12 time it's done that. I don't know -- I wanted to
13 talk about, again, voluntary, but my focus is on
14 waste rather than on PPE.

15 But I would disagree with the notion
16 that if you don't expect compliance, that you
17 shouldn't regulate at all. I think anybody who
18 does regulation expects that you'll get a large
19 degree of compliance but not complete compliance.
20 And then so the people that are not complying are
21 going to be leakage from the system in the case of
22 waste. And that's why I wanted to get the mass

1 balances, because I assume that there still are
2 people that are, for instance, midnight dumping.
3 And I think there's good evidence for that.

4 We don't have any way of surveying
5 completely, but we've been through this circle in
6 RCRA world and much notoriety given to people that
7 were doing egregious dumping. And there have been
8 criminal penalties and all manner of things that
9 have happened.

10 And yet an example I use in my
11 classes is a guy from the mid-2010s who was
12 collecting fracking waste in Ohio. And because
13 there was a boom, there was a lot of pressure on
14 the disposal wells, and they were jacking up their
15 prices. And so the guy decided, well, the easy
16 thing to do would be just to drain my tank into
17 the Mahoning River at night.

18 And he did that. And he did that --
19 that's about a five-year-old story now. So the
20 notion that everybody is now complying because the
21 law is there is a fairytale.

1 I did want to say that I did
2 misspeak when I said that TRI was voluntary. It's
3 not voluntary in the sense that you have to
4 report. But it is -- the rationale behind TRI was
5 that it provide incentives. The notion was that
6 if companies were self-outing and reporting that
7 they were dumping large amounts of chemical mass
8 into the general environment that the public would
9 take notice and disapprove. And so they would
10 have a public relations incentive to do something
11 about those releases.

12 And that's the part that's
13 voluntary, because TRI doesn't have any caps on
14 releases. It just says you have to report what
15 you're doing -- and to set up incentives that
16 people might then want to voluntarily reduce their
17 emissions. And that's the extent that it's
18 voluntary. And, of course, there are two ways to
19 reduce your emission numbers, one of which is to
20 actually reduce them, and the other one is just
21 report lower numbers.

22 **DR. KENNETH PORTIER:** Dr. Morandi?

1 **DR. MARIA MORANDI:** Yes, I do agree
2 with many of the comments that Dr. Kissel has
3 made. And we have to go to the issue is that we
4 cannot assume that every company is not in
5 compliance. There are many companies they have
6 health and safety departments, and those
7 organizations probably have good programs that
8 sometimes go beyond what the guidelines require.
9 But it's also true that many others don't.

10 And as the available data in terms
11 of survey data or adherence to PPE, it shows that
12 there are a lot of problems, and so it is
13 problematic. And I can see the use of reporting
14 the risk with and without PPE, even though we
15 don't know if the whole chain of control measures,
16 the hierarchy of control measures, past being the
17 previous that have been actually implemented or
18 not, and PPE is the last resort. But I think it's
19 useful to some extent, because it calls to
20 attention the fact that in many cases for many
21 uses even if you assume that PPE is used and it's
22 used correctly, the risks are excessive.

1 So there is some use to this. I
2 just think that it has to be presented in a manner
3 that reflects clearly all the uncertainties
4 including that assumption of use of PPE and not
5 put it at the same level of confidence, in many
6 cases, as the estimates without PPE.

7 **DR. KENNETH PORTIER:** Dr. Anderson,
8 I think I'm going to give you the last word on
9 this.

10 **DR. HENRY ANDERSON:** Well, I've been
11 a broken record, I think everybody knows it. I
12 mean, what I am looking for is how do we go about
13 gathering information or using information without
14 -- in part I would say the concern; and it isn't
15 so much with this chemical because other than
16 comparative exceedances you have, even if you're
17 wearing the best respiratory protection and you're
18 in a well-organized medical monitoring program
19 that's part of your respiratory protection
20 program, all of those are the very expensive
21 imposition on industry. And so their incentive is

1 to layer up on the list of a replacement of the
2 compound or do other kind of controls on it.

3 So I'm just concerned that when we
4 get to other chemicals, that when you get away
5 from the science folks looking at it, when
6 somebody's making an administrative decision, they
7 look at this report and they say, oh, there's no
8 problem. And they gloss over the issue of
9 respiratory protection issues. I think it's
10 important information to get out there to say that
11 one solution to the exposures in the meantime, is
12 we're getting to the point of other upstream
13 controls, is to use PPE.

14 But I'm just concerned that what
15 happens as you look at it and, well, because
16 there's no unreasonable risk if everybody were to
17 be wearing PPE, not really -- isn't a realistic
18 assumption.

19 It's a bit like saying, well, we
20 have a requirement for wearing seatbelts, so we
21 assume everybody wears seatbelts or drinking and
22 driving, things like that. There's all sorts of

1 things that are out there that just are not fully
2 adhered to. And that's true for the use of PPE,
3 which is why there's a hierarchy.

4 I would agree on the earlier
5 comments in the week, and we could still remember
6 what they were, saying that there ought to be some
7 attention to what the other parts of hierarchy of
8 broad controls can contribute here so that you're
9 not jumping right to the use of PPE. I think
10 that's partially what this currently does.

11 **DR. KENNETH PORTIER:** And Dr.
12 Kissel, I see your hand's still up. Okay. I
13 don't see any additional hands up on this comment.
14 Before we leave Question 7, I wanted to go to back
15 to 7.1 and make one point that I made on the
16 carbon tetrachloride report, and I'd like to see
17 it also in this one.

18 And that is under Section 1.3 on
19 Regulatory and Assessment History. This
20 subsection has basically come down to about two
21 pages with one page just being EPA assessments and
22 other U.S.-based organization's assessment and

1 links to those documents. And one of the comments
2 we made is because the cost of assessment is a
3 fraction of total exposures, which means it only
4 addresses a certain subsection of risk that this
5 section on assessment history should also include
6 a little bit more about the status of where
7 assessment of risk for the water under the Clean
8 Water Act and the status of where we are with the
9 assessment of TCE risk under the Clean Air Act.

10 There is a link to an Office of
11 Water report 2015, and that may be the water
12 status report. But I don't see anything under
13 air. And I think that to kind of round out and
14 prepare the reader for getting a slightly bigger,
15 complete picture of risk, you should at least
16 mention something in there of where we are in the
17 regulatory and assessment status under the Clean
18 Air and Clean Water Acts. So I will send that
19 along to Dr. Davies for inclusion.

20 Do we have any final comments on
21 Question 7.1 and 7.2? Dr. Davies.

1 **DR. HOLLY DAVIES:** I just wanted to
2 agree with what you just said about the more on
3 the status of where it is under other statutes.
4 And it ties into this question we have of how much
5 to link to other documents and how much to keep in
6 the report. And in a lot of places it's helpful
7 to have a couple of sentences not the whole thing,
8 so you can still link to it but just what does
9 this mean where we can see it in one place.

10 **DR. KENNETH PORTIER:** And I'm
11 thinking of two sentences that says TCE was last
12 evaluated under the Clean Air Act in 2014, and
13 it's not scheduled for review until 2025. Okay,
14 that at least tells where we are with respect to
15 this chemical under these two other major
16 regulatory statutes. Your hand's still up, Dr.
17 Davies, yeah.

18 **DR. HOLLY DAVIES:** Yeah.

19 **DR. KENNETH PORTIER:** Did you want
20 to add anything else?

21 **DR. HOLLY DAVIES:** Oh no, I should
22 be saying I should put my hand down.

1 **DR. KENNETH PORTIER:** Okay and I was
2 going to turn to you anyway and say did you get
3 the -- you got most of the conversation down
4 already, so I actually don't have any concerns
5 that you don't have it.

6 **DR. HOLLY DAVIES:** But I see Dr.
7 Doucette has his hand up.

8 **DR. KENNETH PORTIER:** Who?

9 **DR. HOLLY DAVIES:** Bill.

10 **DR. KENNETH PORTIER:** Oh yeah, Dr.
11 Doucette.

12 **DR. WILLIAM DOUCETTE:** Yeah, just
13 really to follow up on that in addition to just
14 where we are from a regulatory point of view it
15 would seem like there's some really simple
16 information that could be obtained from what's
17 been learned. For example, TCE contamination in
18 ground water associated with Superfund sites would
19 certainly -- there's tons of evidence to show that
20 there is sorption and that TCE doesn't immediately
21 disappear into the air.

1 So I think there's things that not
2 only from a regulatory point of view but just a
3 factual point of view that could be brought over
4 from all the experience the EPA has dealing with
5 it in non-TSCA-related activities.

6 **DR. KENNETH PORTIER:** Well, the
7 Superfund regulation would be another one that at
8 least the status report on that or link to a
9 webpage. EPA has a lot of this already summarized
10 in their web universe. Even linking to the
11 appropriate webpages would be useful. Dr.
12 Morandi, your hand is still up.

13 **DR. MARIA MORANDI:** Yes, I wanted to
14 add something that I should have mentioned earlier
15 with respect to legislation. And this is
16 particularly relevant for consumer exposures,
17 where the exposures are mostly in their homes.
18 And if they said that EPA actually doesn't have
19 regulatory authority for indoor air, it has
20 regulatory authority for ambient air. Now
21 concentrations indoors can be otherwise addressed

1 by looking at initials from products, so using
2 materials and so forth.

3 So to say, in the case of exposures
4 that occur mainly indoors in residences, there is
5 really no specific authority that supervises that
6 as far as I know. So I just wanted to make that
7 point.

8 **DR. KENNETH PORTIER:** Not much we
9 can do about that. Dr. Anderson.

10 **DR. HENRY ANDERSON:** No, I don't
11 want to be totally negative all the time, so I'm
12 going to say I really appreciate it, the links
13 that are now in the document most of them were
14 functional.

15 The one thing that would be helpful
16 to have is, at least in the one that I had,
17 others, while there may be mention in the text
18 about information that's in the docket, it'd be
19 nice to have links to the docket. I mean the
20 docket, there's a lot of things there. And just
21 from the title, it's often hard to tell when
22 you're trying to validate that what's in the

1 report is, in fact, in one of those support
2 documents.

3 But a lot of the literature I think
4 that were within the document was helpful to be
5 able to link to some of those. I know I had --
6 you got the abstract. And if you wanted to open
7 the article, you were expected to pay. And being
8 a university person, I simply just went to our
9 library online and was able to avoid a payment,
10 which kind of stiffes the publishers. But for
11 those of you who don't have the access somewhere,
12 EPA needs to look at being sure that, in fact,
13 when you click on it, the article's actually
14 securely attached to the document.

15 But, in general, it was much easier
16 to find things when you're looking to verify that
17 something that may not look quite right, it could
18 be a typo, you don't want to say, oh, there's a
19 typo here unless you can actually verify that. So
20 moving forward, I think having those kind of
21 links, unfortunately, it makes it so a lot of
22 people can only work on these documents online.

1 But given the size of these, that's the really
2 only practical thing. To try to print out a 700-
3 page document is pretty excessive use of paper.
4 But this has worked very well.

5 And when you're all done, I have one
6 last comment I'd like to make, but I won't do it
7 yet till we're finished discussing.

8 **DR. KENNETH PORTIER:** Well, I think
9 we're almost done. Dr. Doucette, your hand is
10 still up.

11 **DR. WILLIAM DOUCETTE:** Sorry, I
12 meant to take that off.

13 **DR. KENNETH PORTIER:** Okay. Dr.
14 Anderson, I think we're at the last comment here.

15 **DR. HENRY ANDERSON:** Okay, what I
16 just wanted to raise I got an email notice that
17 the April meeting is now one month away. We
18 haven't gotten any documents for that. It's
19 intended to be online -- this review as well.

20 And I just want to say it might be
21 worth, before we get as we did this time right on
22 the eve of this -- or this next chemical meeting,

1 do we really want to move forward to have to --
2 for those who are in the leads on this document,
3 they're going to have to rush to get their
4 comments all summarized together, route it to
5 everybody to review. At the same time we're
6 reading and preparing for the next document and
7 then dedicating a full week towards the end of
8 April for review.

9 I would wonder if it wouldn't be
10 best to try to postpone this one till the May
11 dates that are arranged. For those of you who are
12 in the modeling business, at least today, this
13 morning I missed a call because our modeling group
14 was meeting in order to look over what we're
15 projecting for Wisconsin and if we're able to
16 maintain our activities.

17 So far, we're looking at about the
18 27th of April as being the peak of our cases in
19 Wisconsin. So between now and then most states
20 will increase in demands on everybody to
21 participate in that. So for those of us who are
22 in the public health field, we're in for at least

1 next month to really be ramping things up. So I
2 would just ask EPA to look at whether it's really
3 critically important to have the next meeting in
4 April.

5 From my perspective, I'd rather have
6 their staff work on finalizing some of the
7 documents that we've already reviewed and sent
8 into our comments, so we haven't got a final
9 product yet to look at it and all. So that's just
10 something I would raise that it's best to begin
11 thinking about.

12 I won't ask now for EPA to do that,
13 but I do think we need to really look at what are
14 we want to do in the next month and how much of
15 that time should be spent on looking at another
16 compound and trying to do a comprehensive job for
17 the public to review that completely that it
18 certainly was problematic for me.

19 And my participation in this meeting
20 was seeing that my computer is outside where I can
21 see and supervising folks inside. I couldn't
22 bring the computer in there, because you're not

1 allowed to do personal work while we're in a
2 secure environment, so had a student monitoring it
3 for me and trying to go in and out as I could. So
4 it's been problematic. That's just me --

5 **DR. KENNETH PORTIER:** So Henry, I'm
6 going to talk with Dr. Steven Knott. And sometime
7 next week we'll do another censusing of the
8 committee on their availability for the end of
9 April. I hear what you're saying, and I've heard
10 those comments from a number of members. I want
11 to express my appreciation for everyone being here
12 for four days to participate in this one. But
13 we're going to go back and review successes and
14 failures out of this particular experience and
15 reassess.

16 These meetings involve a lot of
17 informing the public, and it involves a lot of
18 negotiating with different parts of EPA and
19 others. So it's kind of hard for me to figure out
20 when this is going to show up and not. And I
21 don't think I want to get into the conversation

1 right now. But I'll talk to Dr. Knott, and we'll
2 get back to the committee on that. Okay?

3 **DR. HENRY ANDERSON:** That's fine.
4 That's why I say it's better to start thinking
5 about it and talking about it now and rather than
6 have to make all changes potentially at the end.
7 I'm just saying that --

8 **DR. KENNETH PORTIER:** Yeah, well, I
9 understand what you're saying.

10 **DR. HENRY ANDERSON:** -- things are
11 not going to continue to -- we're not solving the
12 outbreak issue. And I would, when you query
13 members I would -- it's one thing to say could you
14 be available --

15 **DR. TODD PETERSON:** Dr. Anderson,
16 Dr. Anderson, this is the DFO. I'd like to have
17 you defer this topic. It's not a part of the
18 meeting deliberations, and I think Dr. Portier is
19 correct, we can continue this offline.

20 **DR. KENNETH PORTIER:** And we'll
21 query. At this point I want to turn to EPA and

1 say do you have any final and closing comments on
2 the Question 7?

3 **DR. STANLEY BARONE:** No, Dr.
4 Portier. And again, we want to thank the
5 committee for their deliberations, their
6 thoughtful comments, the contribution for making
7 our program better and this particular risk
8 evaluation better. This robust dialog is part and
9 parcel of the transparency and peer review
10 process, and it's critical for us to move forward.
11 Thank you very much for all the committee's work
12 and all the help that you've put together. We
13 recognize this has not been an easy task,
14 particularly under the circumstance. Thank you.

15 **DR. KENNETH PORTIER:** At this point
16 I think we've completed our task list before the
17 committee. And I want to add my appreciation to
18 the committee for all the hard work you've done
19 and the work we have yet to do to produce a
20 written report to accompany this meeting. At this
21 point I'm going to turn the timing back over to

1 Todd, the DFO, for some final comments and close
2 out. Todd?

3 **DR. TODD PETERSON:** Yeah, this is
4 Todd Peterson. And as DFO I too want to thank the
5 SACC peer reviewers and the public for listening
6 online. Truly this week's TSCA SACC meeting is a
7 first online meeting for the SACC, and I believe
8 it may be a first for our peer review team in the
9 EPA Office of Science Coordination and Policy. So
10 let me add a special emphasize note at this point.
11 From what I'm hearing, we had many members of the
12 public listening, and I thank you all for your
13 virtual attendance online.

14 I want to make a special recognition
15 of the OPP team for being online in an efficient
16 and responsive way for providing your interactions
17 with the SACC peer reviewers. Things went quite
18 smoothly in that regard.

19 Finally, I say over and over again,
20 but the peer reviewers deserve our continued thank
21 yous for your work and robust deliberations and
22 contributions that will certainly lead to the

1 recommendations and advice to the Agency as to how
2 the evaluation for TCE can be refined.

3 So this concludes the peer review
4 activities for today, and this concludes the SACC
5 meeting for the peer review of EPA's Draft Risk
6 Evaluation for Trichloroethylene. This day's
7 session is now adjourned.

8
9 **[MEETING ADJOURNED]**