

**Summary Minutes of the US Environmental Protection Agency
Science Advisory Board
Review of the Draft SAB Panel Report:
*SAB Review of EPA's Draft Risk Assessment of Potential Human
Health Effects Associated with PFOA and Its Salts*
Public Teleconference Meeting
February 15, 2006
1:45 pm – 4:00 pm (Eastern Time)
Meeting Location: Via Telephone Only**

Purpose of the Meeting: The Meeting was held to allow for the Chartered SAB to review and approve the subject draft report. The meeting agenda is in Attachment A.

Members Participating in the Meeting:

Dr. M. Granger Morgan, Chair	Dr. James Bus
Dr. Trudy Ann Cameron	Dr. Deborah Cory-Slechta
Dr. A. Myrick Freeman	Dr. James Galloway
Dr. Rogene Henderson	Dr. Phil Hopke
Dr. George Lambert	Dr. Genevieve Matanoski
Dr. Michael McFarland	Dr. Jana Milford
Dr. Rebecca Parkin	Dr. Kathleen Segerson
Dr. Deborah Swackhamer	Dr. Thomas L. Theis
Dr. Robert Twiss	Dr. Terry Young
Dr. Lauren Zeise	

Others Participating in the Meeting:

SAB Staff: Dr. Suhair Shallal, DFO; Tom Miller, DFO, Dr. Vanessa Vu, Director

EPA Staff and Public: See attachment B for a list of those who contacted the DFO noting their interest. A survey of actual participants was not taken during the call in the interest of time conservation.

Public Commenters: Dr. Robert W. Rickard, DuPont, Inc.; Dr. John L. Butenhoff, 3M, Inc.; Dr. Gerald Hardesty, DuPont, Inc.; Dr. Jerry Hardisty, Experimental Pathology Laboratories.

MEETING SUMMARY

Wednesday, February 15, 2006

This meeting was announced in the *Federal Register* on January 30, 2006 (FR 71 4912-4913) (see Attachment C of the physical file and on the SAB website at <http://www.epa.gov/fedrgstr/EPA-SAB/2006/January/Day-30/sab583.htm>).

Mr. Thomas Miller, SAB Designated Federal Officer, convened the meeting and identified those on the call. He noted that: 1) the meeting was an official meeting of the Chartered Science Advisory Board, chaired by Dr. Granger Morgan; 2) the meeting complies with requirements of the FACA and EPA policy for expert advisory committees; and 3) the SAB members participating in this meeting had submitted updates to their confidential statements of financial interest and the Deputy Ethics Official for the SAB Staff Office had determined that Members do not have “conflict of interest” or “appearance of impartiality” issues within the meaning of the relevant ethics and conflict of interest requirements that apply to this advisory activity.

Mr. Miller stated that Member’s responsibilities during this meeting were to evaluate the draft SAB Panel report and decide whether the report:

- a) adequately addressed the Agency charge questions;
- b) is clear and logical; and
- c) conclusions drawn or recommendations made are supported by the body of the Panel’s report.

Mr. Miller noted that SAB proceedings provide an opportunity for public observation and participation and that participation can be through providing written comments to the SAB or by making short oral statements during the public meeting. Mr. Miller noted that for today’s meeting, two members from the interested public had asked for and been granted time on the agenda to make a brief oral statement. He noted that one additional commenter might also ask for time to comment. Two of these persons provided written comments to explain their views.

Mr. Miller then turned the meeting over to the SAB Chair, Dr. Granger Morgan to carry out the agenda.

Dr. Morgan summarized the intent of the meeting and the agenda (see Attachment C) and identified the report to be reviewed as *SAB Review of EPA’s Draft Risk Assessment of Potential Human Health Effects Associated with PFOA and Its Salts*, and that the Board’s task was to decide if it is ready for approval.

Dr. Morgan then introduced Dr. Jennifer Seed from EPA who introduced Dr. Oscar Hernandez of EPA’s Office of Prevention Pesticides and Toxic Substances. Dr. Hernandez thanked the SAB for its work via the PFOA Review Panel. He appreciates the broad acceptance of the approaches EPA proposed in the assessment (e.g., use of pharmacokinetic information, internal dose metrics, and the use of multiple endpoints over several life stages). The Panel identified several areas of uncertainty (e.g., PPARa mode of action analysis, immunotoxicology and developmental neurotoxicology, and human biomonitoring for blood levels) and the Agency has paid serious attention to these comments. He also acknowledged the work ongoing in the EPA ORD on some of the uncertainties (e.g., developmental toxicity studies in mice and pharmacokinetic modeling). He acknowledged the growing database on PFOA and indicated that much more is expected to be available for consideration in the final risk assessment.

Dr. Morgan then introduced Dr. John Butenhoff, 3M Medical Department who had registered to make a brief oral statement to the SAB (see his written comments in Attachment D of the physical file and on the SAB website at http://www.epa.gov/sab/pdf/3m_ltr_re_draft_pfoa_panel_report.pdf). Issues highlighted by Dr. Butenhoff included: 1) 3M is encouraged by EPA’s overall approach to the

assessment; 2) reservations about the extent to which data relied on by EPA and/or the Panel had been published or not; 3) an assertion that selective use of the data has led to an unwarranted conclusion; 4) the existence of a review of the “Sibinski” study that does not confirm PFOA as a multi-site carcinogen; and 5) the absence of discussions of this review (this is a report from a group referred to as the Pathology Working Group – PWG) of the Sibinski study in the report.

Dr. Morgan introduced Dr. Robert Rickard, DuPont, Inc. (see his written comments on the SAB website at http://www.epa.gov/sab/pdf/rickard_dupont_comments_re_draft_pfoa.pdf and in Attachment E to the physical file). Dr. Rickard noted his support for the Agency’s overall approach to the assessment and noted his firm’s disappointment that the Panel had not incorporated information provided by DuPont into their report. He also noted concern about whether the Panel had relied only on peer reviewed published literature in its work. He urged the SAB to clarify the issue of what new data might have been considered in its report. He also believes that portions of the Panel report do not reflect the weight of evidence in the literature. He noted that the Panel’s cancer classification was inconsistent with the conclusions from an external panel, the PWG, that had reviewed the literature in question (i.e., the Sibinsky study) and asked that the SAB be allowed to hear from Dr. Jerry Hardesty who chaired that group in a brief oral statement that would summarize that review.

Dr. Morgan agreed to hear from Dr. Hardesty. Dr. Hardesty noted that the external workgroup, the PWG, had reviewed the neoplastic mammary lesions in the questioned study using the same approach that is employed by EPA in carrying out its pesticides regulations. The approach is widely used outside of EPA as well. The review concluded that the mammary lesions were not significantly increased above the historical controls for the species and strain tested.

Dr. Morgan asked Dr. Hardesty if the PWG’s review of the study had been published, or if there were any intentions to publish the analysis and Dr. Hardesty stated that it had not been.

Dr. Morgan then asked Dr. Cory-Slechta, Chair of the SAB PFOA Panel to summarize the Panel’s work (see Attachment F in the physical file and on the SAB website for the draft Panel report); and to respond to any of the statements to that point. Dr. Cory-Slechta briefly discussed the review and noted some of the primary conclusions: 1) The Panel thought mechanisms of action other than PPAR alpha agonism for liver tumor induction (MOAs) were possible; 2) the predominant view was that the evidence supported multisite and multigender carcinogenicity for PFOA; 3) that the concurrent control data were most relevant in the interpretation of mammary tumors; 4) the predominance of opinion of Panel members was that the evidence for a carcinogenicity descriptor supported “likely” but a few Panel Members did not agree and thought it was only “suggestive”; 5) the pancreatic acinar and Leydig cell tumors could not be dismissed; 6) EPA’s strategy of inclusion was the best approach for now; 7) the consideration of biomonitoring studies was encouraged; and 8) non-occupational monitoring data be used in the analysis if possible.

Dr. Morgan then asked the SAB Lead Reviewers to comment on the draft report. Attachment G provides a compilation of the written comments of Board members on the draft report. Members generally deferred to those comments and during the meeting only mentioned specific comments that they believed to be in need of highlighting.

Dr. Zeise noted that the draft was well written, clear and logical and that the conclusions were supported. She suggested that the Panel add more information on the mammary tumor issue and that the letter to the Administrator be written in a manner that targeted an educated, non-expert reader.

Dr. Matanoski stated that the report was well written, clear and put forth the varied opinions within the Panel on certain issues, and that the conclusions were clear. She asked if in regard to children's health issues whether the Panel discussions had focused on the fetus in addition to the neonate and young children.

Dr. Bus noted that the report was clear that the Panel members had disagreements on some issues that are discussed in the report. He noted that in most cases in the report, the majority opinion was well-documented and that the minority view was not so well documented. He urged that the dissenting opinions be characterized in more detail. He noted that there is a need for more detail on the mammary tumor issue because it is key to the multi-gender/multi-site issue. Given that the Panel's suggestion would elevate the classification to "likely" the issue needs thorough discussion. He applauded the Panels recommendation on internal dose and suggested the Panel add more on how adjustments of existing defaults could be considered by EPA in deciding on whether they should be changed. He noted that the cover letter statement on use of peer-reviewed literature only needed to be clarified. The issue of highly exposed populations outside of the labor force needs clarification.

Dr. Morgan asked Dr. Cory-Slechta to respond to these points. Dr. Cory-Slechta noted:

- a) The report's Executive Summary inadvertently included the term "published" literature -- the Panel only used "peer-reviewed" literature but that some of that was not published -- the Panel had to consider all the information in the Draft document.
- b) The Panel did consider the Pathology Working Group's unpublished analysis and recommended that EPA conduct an NTP-style pathology working group to verify the PWG results.
- c) The Panel's report does not discuss the minority view in detail because it often coincided with statements already in the EPA draft risk assessment document, and it would, therefore, be duplicative to restate it. Thus the Panel report emphasized the reasons for the majority views as they differed from the EPA draft document. Further, all Panel members approved the language in the draft and had an opportunity to make their views known.

Dr. Morgan then called on other SAB Members to ask questions or make comments. Comments included:

- a) The PFOA risk assessment brings forward the same problem to those doing benefits analysis that all EPA assessments inject and that is presenting results at the extreme of the distribution. Economists deal with the central tendency and thus such results are less useful in the policy analysis steps that follow risk assessment.
- b) Adding more information to give a sense of the breakout in majority vs. minority number would help.
- c) The letter to the Administrator needs to be shortened and to be made less technical.
- d) There is a need to clarify how the PWG analysis was considered by the Panel and also more on why the Sibinski study was included.

Dr. Cory-Slechta noted that the draft Panel report does point out that the EPA draft risk assessment needs to be revised and updated. The report does not close the door on this or other issues being included in EPA's future risk assessments for PFOA. The Panel identified a set of issues that need addressing and one of those can be whether or not the PWG analysis does follow an approach that is identical to that used by the NTP.

The Board offered and seconded a motion for approval of the draft report contingent upon certain clarifications being made. Revisions to be considered include:

- a) shortening the letter to the Administrator;
- b) clarifying what literature was included in the Panel's consideration and also being more specific in recommending that EPA be clear about what it includes and what it does not include in its revised risk assessment;
- c) be more specific regarding the number of Panel members in the majority vs minority positions (breakdown regarding views); and
- d) clarification of how the issues relate to the Cancer Guidelines specifically the descriptors "likely" and "suggestive"

The edited draft report should be provided to several members who will serve as vettors of the revisions and their addressing the SAB's discussions today. Vettors will include: Drs. Genevieve Matanoski, Lauren Zeise, James Bus, and Granger Morgan. The report will return to the SAB for further consideration only if there are issues that can't be resolved between the Panel and the Vettors.

Dr. Morgan called the motion to a vote asking if there was dissent from the motion. None was given and thus the motion passed unanimously.

The meeting was adjourned by the Designated Federal Officer.

Respectfully Submitted:

/ Signed /

Thomas O. Miller
Designated Federal Officer
US EPA Science Advisory Board

Certified as True:

/ Signed /

Dr. M. Granger Morgan
Chair, EPA Science Advisory Board

Attachments:

- A Meeting Agenda
- B Table of Interested Public (including EPA)
- C FR Announcement (in physical file only)
- D Comments from 3M, Inc.
- E Comments from DuPont, Inc.
- F Draft report from the SAB PFOA Panel
- G Compilation of SAB Member Written Comments on the Draft

ATTACHMENT A

US Environmental Protection Agency
Science Advisory Board
Review of the Draft SAB Panel Report:
*SAB Review of EPA's Draft Risk Assessment of Potential Human
Health Effects Associated with PFOA and Its Salts*
Agenda
Public Teleconference Meeting
February 15, 2006
1:45 pm – 4:00 pm (Eastern Time)

Meeting Location: Via Telephone Only
Members of the public may obtain the call in number at 202-343-9999

Wednesday, February 15, 2006

1:45 pm	<u>Convene the Teleconference Call</u> Announcements, Summarize Agenda, Attendance	Mr. Thomas Miller, Designated Federal Officer
1:50 pm	<u>Welcome, Introduction and Comments</u>	Dr. Granger Morgan, SAB Chair
	a. Comments by EPA	Dr. Jennifer Seed, US EPA
	b. Public Comments	
2:10 pm	<u>Review of Draft Report</u>	
	<u>Review Panel</u> – PFOA Risk Assessment Review Panel <u>Chair</u> - Dr. Deborah Cory-Slechta <u>Lead Reviewers</u> are:	
	1) Dr. James Bus 2) Dr. Gene Matanoski 3) Dr. Lauren Zeise	
3:30 pm	<u>Disposition of the Draft Report by the Board</u>	Chair and Members
4:00 pm	<u>Adjourn</u> (time approximate)	

**Registered Public Commenters for SAB PFOA Meeting
February 15, 2006**

<u>NAME</u>	<u>TITLE & ORGANIZATION</u>	<u>REPRESENTING</u>
1. Dr. John L. Butenhoff	3M Medical Department	3M
2. Dr. Robert W. Rickard	Director, Haskell Laboratory	E.I. DuPont de Nemours and Co.

ATTACHMENT B

Public Requests for PFOA Contact Info and/or Oral Statements

No.	Name	Organization	Date
1	John Heinz,	Env health Research Fndn	1-30-2006
2	Rob Bilott	Attorney, Ohio	1-30
3	Treavor Noblic	Inside EPA	1-30
4	Mailyn Kurray	US EPA OGC	1-30
5	B. Sachau	?	1-30
6	Samantha Flores	Heard, Robins, ...attorney	1-30
7	Steve Via	AWWA	1-30
8	Dave Menotti	Pillsbury, Winthrop...attorney	1-30
9	Randall Chase	Associated Press	1-30
10	Helen Goeden	MN Dept of Health	1-30
11	Nancy Beck	OMB	1-30
12	Jon Webster	WM	1-30
13	Linda Aller	Bennet & Williams, attorney	1-30
14	Jean Rhodes	Promerus	1-30
15	Connie Brower	NC	1-30
16	April Dreeke	United Steelworkers of Amer	1-30
17	Jane Houlihan	Environmental Working Group	1-30
18	Ken Kulig	Physician	1-30
19	Emma Morris	Nature	1-31
20	Jennifer O'Donnel	DD Altman Co.	1-31
21	Jonathan Freedman	Group SJR	1-31
22	Ari Lewis	Gradient	1-31
23	Anthrny Scialli	Science International	1-31
24	Todd Kelleher	OH EPA	1-31
25	Susan Goldhaber	NC DEH	1-31
26	Robert Patterson	Temple Univ	1-31
27	Cheryl Hogue	ACS	1-31
28	Erin Russell	Clariant	1-31
29	Jamie Benedict	EPA	1-31
30	Paul Kearns	Exopack	1-31
31	Bill Lowe	LEXIS NEXIS	1-31
32	Barbara Beck	Gradient	2-1
33	Todd Stedeford	EPA	2-1
34	Jessy Kurias	Envir Canada	2-1
35	Blake Biles	Arnold & Porter	2-1
36	Gloria Post	NJ DEP	2-1
37	Carolyn Frantz	Univ of Chicago	2-2
38	Daria Church	Clariant	2-2
39	Ilene Merdinger	Patronus	2-1
40	Arthur Helmus	Hartford Insurance Co.	2-2
41	Bruce Berger	?	2-2
42	Perry McDaniel	WV DEP	2-2
43	Jennifer Seed	US EPA – Request to Comment	2-2
44	Willett Monk	?	2-4
45	Mike Santora	3-M	2-5

No.	Name	Organization	Date
46	Jackie McQueen	EPA/ORD	2-6
47	Ross Highsmith	EPA/NERL	2-6
48	Dennis Utterback	EPA/ORD/OSP	2-6
47	Pam Schnepfer	NH EHP	2-6
48	Rick Sugatt	EPA	2-6
49	Paul South	US FDA	2-6
50	Brian Mayes	GE	2-6
51	Jack Fowle	ORD	2-7
52	Beth Havlik	Barr	2-7
53	Susan Hunter-Youngren	Lawfirm	2-7
54	Kathy Rhyne	KSLaw	2-10
55	Mary Dominiak	OPPTS	2-10
56	Barbara Smith	WV DHHR	2-10
57	Robert Trout	Whitford Corep	2-14
58	Carla Hutton	Bergeson & Campbell	2-14
59	Edison Lee	Levick Communications	2-13
60	Bob Sussman	Latham Watkins	2-13
61	Patt Phibbs	BNA	2-13
62	Max Swetman		2-14
63	Nancy Rachman	Food Products Association	2-14
64	Helen McMenamin	PTCN	2-14
65	Bill Cross	Felters	2-14
66	Barbara Walton	EPA	2-14
67	David Kestenbaum	NPR	2-14
68	Dale Haroski	EPA/OPA	2-14
69	Brooke Moore		2-14
70	Jason Stoogenke	WRAL TV	2-14
71	Sara Schaffer-Munoz	Wall Street Journal	2-15
72	Tom McKinney	NCDAQ	2-15
73	David Gray	Tetrattech	2-15
74	Jared Pederson		2-15
75	Elisabeth Moore	Step toe and Johnson	2-15
76	John Katchko	Wausau Paper	2-15
77	Amy Perbeck	MI Dept He	2-15
78	Amy Hensley	SWAPE	2-15
79	Enesta Jones	EPA Press Office	2-13
80	John Butenhoff	3-M	
81	Robert Rickard	DuPont	2-15

ATTACHMENT C

See the SAB Website at:

<http://www.epa.gov/fedrgstr/EPA-SAB/2006/January/Day-30/sab583.htm>

ATTACHMENT D

The 3M written comments are on the SAB Website at:

http://www.epa.gov/sab/pdf/3m_ltr_re_draft_pfoa_panel_report.pdf

ATTACHMENT E

The DuPont written comments are on the SAB Website at:

http://www.epa.gov/sab/pdf/rickard_dupont_comments_re_draft_pfoa.pdf

ATTACHMENT F

See the Draft Panel Report on the SAB Website at:

http://www.epa.gov/sab/pdf/2006_0120_final_draft_pfoa_report.pdf

ATTACHMENT G

Compilation of Board Comments on Draft PFOA Panel Report

[2-15-2006]

A. Lead Reviewers:

1. Dr. James Bus

SAB review of EPA's Draft Risk Assessment of the Potential Human Health Effects Associated With PFOA and Its Salts

Are the original charge questions presented to the SAB adequately addressed?

The report clearly indicates that the SAB panel did not reach agreement to the answers of several of the important charge questions (e.g., MOA; cancer descriptor; toxicity endpoints selected for risk assessment; adequacy of human exposure data for MOE calculations). Although the positions of the panel members apparently supporting the majority position were described in some detail, corresponding commentary describing the positions of the minority were generally not as detailed. Thus it is difficult for the reader and ultimately the EPA to judge the merits and weight of the balancing positions. The Panel should consider expanding the text describing the dissenting opinions in order to more clearly delineate the strengths and weaknesses of the Panel answers to the charge questions.

The Panel comment on the proposed descriptor for carcinogenic potential of PFOA does not appear to have fully considered the breadth of the available data. The Panel concluded that the cancer descriptor proposed by the EPA draft ("suggestive evidence") should be replaced with the stronger descriptor of "likely to be carcinogenic". This conclusion was based on the Panel evaluation that PFOA represents a "multi-site and multi-gender" carcinogen. The public record of external comment provided to the Panel indicates that it was provided with a detailed analysis of the significance of the rat mammary tumors reported in the 1987 Sibinski study. This analysis included a report of an expert Pathology Working Group that concluded that PFOA did not produce any excess of benign or malignant mammary tumors, in agreement with the conclusions of the original study authors. Importantly, the value of a Pathology Working Group evaluation of the mammary tumor question in facilitating the cancer evaluation appears to have emerged from early Panel discussions. However, both the Letter to the Administrator and draft Panel report itself make no specific mention of the strong conclusions of this report. If the report is to retain the statement that PFOA represents a multi-gender and multi-site carcinogen, and since this conclusion appears to be a primary rationale for elevation of the cancer descriptor, the reasons for dismissing the conclusions of both the Sibinski report itself and the subsequent PWG must be transparently delineated. In addition, the draft Panel report does not make it clear that the two primary cancer bioassays for PFOA replicated cancer at only a single site – testicular Leydig cell tumors. Both the hepatocellular and pancreatic acinar cell tumor responses observed in the Biegel study were not observed in Sibinski, despite similarities in dose, route of administration, and test species. Thus, more discussion is merited as to why these data, taken in their whole, should be taken as evidence of multi-site carcinogenicity of sufficient weight to justify elevation of the cancer descriptor from that proposed in the EPA draft risk assessment (or expansion of dissenting opinion?).

Is the SAB Panel draft report clear and logical?

Given the observations raised above, the Panel position of PFOA as a "likely" human carcinogen is not clearly and logically supported and should either be more fully justified or reconsidered.

The Panel specifically comments that application of internal dose metrics for use in MOE calculations constituted a "significant step toward reducing uncertainty related to cross-species extrapolation", particularly as it relates to the approximate 3X uncertainty factor accounting for toxicokinetic differences. Despite this important conclusion, and the Panel's observation that the toxicokinetic factor for PFOA "would fall within the range of one to three", it was recommended that the full inter-species default factor of three be retained. Thus, it is not clear how Panel believes the internal dose metric approach would indeed contribute to a reduction in uncertainty if it is unwilling to suggest that such dose metrics should be used. Is the Panel endorsing the fundamental approach suggested by the draft assessment, but is recommending either further PFOA-specific or generic research to justify actual use of this

approach? The Panel should consider that the US FDA routinely constructs pharmaceutical risk evaluations based on internal dose comparisons between human clinical drug/metabolite concentrations and equivalent animal AUC/Cmax data. The Panel should further consider recommending that the future use of these types of data comparisons would benefit from a multi-agency discussion and agreement on acceptable approaches to this important concept.

The report specifically comments (p.27) on the implications of an association between PFOA worker exposures, altered lipid levels and a potential for increased cerebrovascular disease mortality. However, given that this review was not specifically charged to review human data in detail, and consequently did not examine the full range of epidemiological and medical monitoring studies available for PFOA, this suggestion is clearly not warranted and likely extends a conclusion well beyond existing data. The Panel should also consider the contradicting observation that a study examining the relationship of potential PFOA exposure to death from cerebrovascular disease found no evidence of a causal association (DuPont comments submitted to EPA, Feb. 7, 2006).

Are the conclusions drawn and/or recommendations made supported by information in the body of the draft report?

See comments above.

The Panel review concludes that the weight of evidence is sufficient to support a PPAR α MOA for liver tumor induction in rats. Although the review expresses concerns that potential alternative mechanisms might also contribute to PFOA tumorigenicity, these suggested alternative MOAs would also be expected to operate by nonlinear dose-responses. Thus, the Panel should affirm that regardless of the debate surrounding potential MOA within the Panel members, the proposed EPA MOE risk assessment approach represents the most appropriate methodology for the assessment.

Other comments

Letter to the Administrator:

p.1, l. 30-31: It is clear the Panel considered data beyond the “peer-reviewed published” literature. Although this practice is acceptable, the report should specifically note when such data were considered, and more importantly, describe under what conditions the data were generated (e.g., GLP), if the actual study data have been made available to the EPA, the Panel and the public for peer review by these mechanisms.

p.2, l. 39-41: The Panel refers here and in the report to the existence of a “highly exposed” population apart from the occupational environment, and this population provides the rationale for conducting MOE assessments to apparently equivalently exposed occupational cohorts. However, the Panel should note the specific evidence it reviewed to justify the existence of such a “highly exposed” subset of the general population.

Report:

p.8, l.3-5: The statement “no information currently exists with respect to critical periods” is not fully correct. A 2-generation reproduction study contained several perinatal endpoints and observations that were judged by the Panel as useful for evaluating some aspects of developmental susceptibility.

p.9, l. 23-24: It is not clear why the assumption of steady state may not be valid for blood samples collected from children 2-12 years of age. Does the Panel have any data to suggest that serum levels in these children would be expected to higher than those contained in adults? Given the relatively long half-life projected for PFOA in humans (approximately 4 years), environmental exposures to such an agent would not be expected to produce peak serum concentrations rapidly during the early life years, but rather would slowly reach steady state in early adulthood.

p.20, l. 28-30: It is not clear from the statement “Issues on which the Panel members opinions diverged...liver tumor induction might occur in humans” if such “divergence” represented a majority opinion.

p.20, l. 35-36: The lack of data on hepatocyte proliferation and suppression of apoptosis is cited as a “critical deficiency” in the perspectives of “many” Panel members. However, since PFOA also did not produce any PPAR α

associated response in receptor knockout animals, did the Panel discuss if such a research tool, that was not available when original cell proliferation and apoptosis criteria were established as PPAR α MOA criteria, is now adequate to supplant the specific absence of these specific data?

p.23, l. 43-45: The statement that “organ and body weights are among the least sensitive endpoints...” should be referenced. This statement is likely not correct.

p.27, l. 33-36: The statement about “zero distance” and “cause” of health effects represents an oversimplification of often very complex evaluations and should be deleted. Thus, just because a serum concentration might be associated within a human health effect does not infer causation.

2. Dr. Genevieve Matanoski

Comments on Panel Report on PFOA

The panel report is very well written and the issues are clearly explained and answered. The document has addressed each of the points on which the EPA has requested advice. The review has shown only two areas that might require some attention by the panel.

1. Page 17 lines 38-41. The sentence has two negative statements, which makes it somewhat difficult to read. Could it be re-worded?
2. Page 29 final paragraph. The discussion refers to findings from studies of siloxanes. Is this discussion included because siloxane should act like PFOA or is this just a general characteristic of chemicals to which the panel wishes to call attention? It might be helpful to clarify this point so the reader can evaluate the strength and relevance of the observation in regard to PFOA.

The only other point that may be worth a comment is in regard to fetal exposures to PFOA. The panel may have had extensive discussion about this and it is not worth a change. I am not asking for any change directly. However, although there is discussion about the problems with extrapolation to children little is said about fetuses except in the early part of the document under tissue differences. However, perhaps there are major differences in the specific tissue dose to fetuses. Proportions of tissue are not the same in the earliest period of development. The toxicokinetic mechanisms may not even be developed at certain embryonic stages. I have no direct data on how these apply but I wondered if the panel had discussed these potential differences and whether there should be some mention of the fetus, not just the neonate and the child. Since the exposure is ubiquitous, the fetus should have exposure from the maternal blood in early development. This was just a thought as I read the document.

3. Dr. Lauren Zeise

Review of Draft SAB Review of EPA's Draft PFOA Risk Assessment

The SAB draft report is well written and adequately addresses the charge questions. It is clear and logical. The conclusions drawn and recommendations are sufficiently supported by information in the body of the SAB draft.

The cover letter to the Administrator captures the key conclusions of the SAB review. However, it is written more for the technical expert and could be improved by simplifying the language - to the extent possible - so that it would be more understandable to the non-expert educated reader.

Minor editorial comments

P 4, lines 19-20. It is unclear what is intended by the recommendation that "biomonitoring data be included for identifying potential human health effects."

P 16, line 30. Missing word "is" after "thus"

P 19, line 9. Language a little awkward: "the current evidence fails to exceed the descriptor "suggestive" of carcinogenicity."

P 19, paragraph on mammary tumors. Naming the labs for the Sibinski study and the historical Chandra data base would add context to the discussion of the historical control comparisons.

P 24, line 20. Unclear what is meant by "data will need to be derived in rats"

B. Other Board Members:

1. Dr. A. Myrick Freeman

I have read the Jan. 20, 2006 Draft SAB Review of the EPA Draft PFOA risk assessment. In my judgment, the answers to the 3 reviewers' charge questions are "yes," "yes," and "yes."

2. Dr. Rogene Henderson

I reviewed the letter and the executive summary. I found the report was responsive to the charge. The letter was clear and logical. There was a great deal of "some thought this" and "some thought the other" in the advice. I know of no way to get around that and I suppose it does let the agency know that the issues are controversial. I saw in the news that industry was voluntarily withdrawing this product for many uses. I note one typo. On the third line of the letter, "Perfluorooctonoic" should be Perfluorooctanoic."

3. Dr. Meryl Karol

I think that the draft report is excellent. The charge questions were adequately addressed and the conclusions are supported by information in the draft report. For added clarification, I suggest the following:

- > in describing viewpoints of the expert panel members, where there was dissent among the panel, instead of saying "many" or "a few" or "some", it would be helpful to indicate if the viewpoints represented the majority, a minority, or were isolated viewpoints.
- >The section PPAR-alpha-independent liver effects (p. 21, lines 19-34) should be rewritten for clarification. I had to read it several times before I fully understood it.

4. Dr. Jill Lipoti

I read the report and have no comments.

5. Dr. Michael McFarland

In general, the SAB PFOA Panel provided an excellent review of the Agency's Draft Risk Assessment of Potential Human Health Effects Associated with Perfluorooctanoic Acid (PFOA) and Its Salts. Although the topic under discussion is outside my immediate area of technical expertise, the Panel's responses to Agency charge questions appear to be comprehensive and sufficiently detailed.

The overarching concern that I had from reading the document was the extensive degree of non-consensus that characterized PFOA panel member positions. The document is replete with examples of where the majority of panel members are of one view with respect to a particular technical issue while a minority of panel members supports an opposing view. In attempting to understand the SAB's responses to the Agency, it seemed that, on the whole, the Panel believes that much of the data (human biomonitoring as well as animal laboratory studies) being adduced to support the Agency's position relative to PFOA's potential human carcinogenicity is inconclusive or, at any rate, open to various interpretations. Moreover, it seems that there is Panel consensus supporting the need for more comprehensive, longer-term studies.

In any event, while it is important to describe where there is significant divergence in scientific opinion, the report, in my view, would be more compelling and strengthened if positions of unanimity were more fully developed (if possible), particularly in the letter to the administrator and in the Executive Summary. To its credit, the Panel's report provides an excellent description of the uncertainty associated with the interpretation of laboratory and field study results as well as output from toxicokinetic and pharmacokinetic models. On the other hand, it is not entirely clear what specific advice or recommendations are being strongly supported by the SAB.

In reading the report, I surmised that, in many instances, Panel members were at variance with one another on many key scientific issues. Arguably, the inability to achieve panel consensus on these issues is reflective of the broad range of uncertainty associated with this particular topic. Although I have no doubt that the divergent panelist

opinions have scientific merit, providing the Agency with clear and unambiguous guidance as to how they should proceed to resolve uncertainties would enhance the strength of the report.

Minor Edit:

Page 9 Line 17 – I think the word “uncertainly” should be changed to “uncertainty”.

6. Dr. Jana Milford

I have a few minor comments/questions regarding the draft review of the PFOA Risk Assessment. I thought the SAB panel did a good job of addressing the charge questions and found the report well written and well organized. My minor comments are as follows:

1) I don't know if there is a style convention that argues against this, but I felt the executive summary would have benefited from a few citations in places where the panel was referring to one or a few studies that were critical to their points. For example, on p. 5, lines 2-14, the clarity of the presentation would have been helped by citing the Yang et al. (2002) study.

2) On p. 14, lines 28-35, it's not clear whether the statement that compartmental modeling "provides a sound approach" is an assertion by EPA or a conclusion of the panel. I believe this section is meant to be laying out the issues the panel is reviewing, so it should be the former, but that could be clarified.

3) On p. 31, lines 36-40, the panel says that EPA used LOAEL-driven MOE calculations instead of "more appropriate Bench Mark Dose methodologies." This statement seems like it warrants some explanation -- if Bench Mark Dose methods are more appropriate, why didn't EPA use them, and why isn't the panel suggesting they use them? Maybe I missed that explanation somewhere?

7. Dr. Granger Morgan

I've read the PFOA document. Looks to me to be in good shape (except that as usual it is full of duplication).

8. Dr. Rebecca Parkin

I am fine with this report. I found it to be well-written, clear, logical and the conclusions appropriately supported. I have no edits or comments for improvements

9. Dr. Kristin Shrader-Frechette

Sorry not to be able to join you for the PFOA discussion. The report is very good, and I agree with it. I have minor points that would help clarify its message, but substantively, it is superb.

10. Dr. Valerie Thomas

She concurs with the report.