

**MINUTES FROM THE EPA SCIENCE ADVISORY BOARD**  
**Perfluorooctanoic Acid (PFOA) Draft Risk Assessment Review Panel**  
**Face-to-Face Meeting Conference Meeting**  
**February 22-23, 2005**

**PURPOSE:** The Perfluorooctanoic Acid (PFOA) Draft Risk Assessment Review Panel of the EPA Science Advisory Board (SAB) met on February 22-23, 2005 to review the Agency's Draft Risk Assessment of Potential Human Health Effects Associated with PFOA and Its Salts. The purpose of the teleconference meeting was for the SAB PFOA Review Panel to consider available advisory and background materials, to hear oral presentations by members of the public and other interested parties, and to discuss and deliberate on the draft charge questions to the SAB. Attachment A is the Federal Register notice announcing the teleconference (70 FR 8, January 12, 2005). A meeting agenda is included as Attachment B.

**LOCATION:** SAB Conference Center, Woodies Building, 3<sup>rd</sup> floor, 1025 F St., NW, Washington, DC

**DATE AND TIME:** February 22-23, 2005, 8:30 - 5:00 pm Eastern Time.

**PARTICIPANTS:** The following individuals participated in this meeting: PFOA Review Panel Members - Drs. Deborah Cory-Slechta (Chair), James Kehrer, Norman Drinkwater, James Klaunig, Ron Melnick, Ernest Abel, Thomas Zoeller, Steve Roberts, Mathew Longnecker, Michael Kamrin, Melvin Andersen, William Hayton, Frank Mink, George Corcoran, David Ozonoff, and Anne Sweeney. Dr. Buck-Louis was unable to participate in this panel. The PFOA Review Panel roster is included as Attachment C and a set of biographical sketches is included in Attachment D. SAB Staff - Dr. Vanessa Vu, SAB Staff Office Director, Mr. Tom Miller and Dr. Sue Shallal, Designated Federal Officers (DFO); EPA Staff Presenters - Dr. Jennifer Seed of the EPA Office of Pollution Prevention and Toxics and Dr. Hugh Barton of the EPA Office of Research and Development (ORD); Other Participants - Approximately 30 other EPA Staff and members of the public listened in (Attachment E)

**MEETING SUMMARY:** The meeting followed the agenda (Attachment B). A summary of the meeting follows.

Convene the Meeting and Introductory Remarks – Dr. Suhair Shallal, Designated Federal Officer (DFO), opened the meeting at 8:30 pm and gave an overview of SAB procedures for panel formation and then outlined the purpose of this meeting, namely to review the draft PFOA RA document and respond to the charge questions. Dr. Shallal also explained the next steps regarding the development and approval of the SAB Panel's report. Dr. Shallal then introduced Dr. Cory-Slechta, Chair of the PFOA Review Panel, to proceed with the agenda.

Dr. Cory-Slechta gave Dr. Vu of the SAB Staff Office an opportunity to speak. Dr. Vu thanked Dr. Cory-Slechta for her willingness to serve as Chair of PFOA Review Panel and thanked the other Panel Members for taking time from their busy schedules to participate in this review. Dr. Vu reiterated that the report would take several weeks to complete and must be

approved by the Members of the Board before it is transmitted to the Administrator.

Dr. Cory-Slechta then reviewed the agenda and asked panel members to introduce themselves. She then introduced the first speaker Mr. Jim Willis.

#### Overview of the draft PFOA Risk Assessment

Mr. Willis referred participants to the powerpoint presentation that he was using as a guide for his talk (Attachment F). He explained that the presentation was written to highlight the background and the Agency's ongoing activities to develop a risk assessment for PFOA and its salts.

He noted that interest in perfluorinated compounds began in the late 1990's. PFOA has unique chemical properties that make it a commercially valuable chemical with numerous uses (elastomers, flame retardants, lubricants, architectural coatings, etc.). He informed the panel members of ongoing activities to gather more data on PFOA that include: biomonitoring by CDC, toxicology data being generated by EPA ORD and NTP, as well as, activities to try to understand the pathways of exposure to PFOA.

He reminded panel members that the current draft RA considers information available as of June 2004 and that it is not intended to provide final risk estimates. He stated that OPPTS is seeking advice on their conclusions with regards to the carcinogenic potential of PFOA, the appropriateness of the toxicological endpoints that were selected, the pharmacokinetic modeling and internal dose metrics approaches that were used, cross-species extrapolation and robustness of the biomonitoring database.

Dr. Cory-Slechta thanked Mr. Willis for his presentation and allowed panel members to ask questions.

Dr. Ozonoff inquired as to what is meant by "robust" database. Dr. Seed responded that it meant how reliable it is. She also noted that more data will be generated through the CDC NHANES study that Mr. Willis spoke of during his presentation.

There were no further questions and Dr. Cory Slechta proceeded to calling the public commenters to make their presentations.

#### Presentation by Public Commenters

There were 8 individuals registered to speak (Attachment G). Ms. Deborah Cochran was absent and therefore the next commenter was called, Dr. John Moore.

Dr. Moore focused his presentation (Attachment H) on the endpoints used in the draft PFOA RA, suggested other data sets that should have been used, and advocated the use of a Benchmark Dose approach. He agreed that the male rat body weight is an important endpoint, but added that EPA's prenatal endpoint for male body weight gain between weaning and sexual maturity reflects effects from direct dosing, **not** from prenatal exposure as evidenced by the York (2002) study. Additionally, he contended that the Sibinski (1987) data on adult female body weight effects was not suitable for establishing a NOAEL.

Dr. Joseph Rodrick was the next presenter (Attachment I). He discussed the Agency's MOE approach, internal dose comparisons, Benchmark Dose and uncertainty factors for interspecies comparisons. He agreed with the use of the MOE approach comparing animal and human serum levels. Furthermore, he stated that the data are adequate for internal dose (AUC) comparisons for all endpoints. He also recommended the use of Benchmark Dose approach instead of a NOAEL since it normalizes the data across the varying dose rates. He also believed that the uncertainty factor for interspecies extrapolation can be reduced by using the data for internal dose (serum levels).

Dr. Abel questioned why liver weight to brain weight ratio was used? Dr. Rodrick explained that the brain weight is not as readily affected by insults and remains relatively stable.

Dr. Melnick asked about the BMD analysis and wondered if it would be useful to characterize the lower dose range since 10 is within the range of experimental data. Dr. Roderick stated that this was a rare database which has information about this many different populations, and is thought to be reliable.

Dr. Geary Olsen

Dr. Olsen showed (Attachment J) that human PFOA Biomonitoring Data is available (e.g., Children study, American Red Cross adult study, Elderly study). He asserted that a re-analysis of data from Kannan et al (YEAR?) showed a lower serum level than previously reported. He also presented data from a half-life of serum elimination study using retired 3M workers that showed a half-life of 3.8 years for PFOA. He concluded that PFOA biomonitoring data was consistent in the general population, PFOA serum levels are at near steady state condition, and that these were adequate for use in calculating a MOE.

Dr. Cory Slechta enquired about the stability of PFOA. Dr. Olsen stated that it was stable through several freeze-thaw cycles and when kept at -20°C. When Dr. Olsen was asked about the rationale for using retirees, he stated that "new" (non-occupational exposures) were minimal, in the range of 0.07 -5.0 ug/ml. Dr. Melnick questioned the accuracy of the conclusion that the retirees had reached a steady state condition since children have the same blood levels. Dr. Melnick also wondered if children could be at steady state when the half-life was up to 4.5 years.

Dr. James Popp

Dr. James Popp was the next presenter (Attachment K) and began by stating that the PFOA RA was a well written document covering a vast amount of data. He devoted his comments to the Agency's final characterization of the carcinogenic potential of PFOA: "...suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential". He felt that it overstates the level of concern. He argued that PFOA probably does not cause a human carcinogenic response due to its mode of action and internal exposure differential between humans and rodents. Further, he explained that this conclusion was consistent with other reviews (i.e., Hepatic tumors PPAR alpha agonists "...Not likely to occur

in humans..” ILSI review and Non hepatic tumors “...probably do not represent a significant cancer hazard for humans...” EPA draft pages 8 and 84).

Dr. Popp explained that in the case of mammary tumors, there was no evidence of tumor progression since the high dose showed a lower tumor incidence than the lower doses. The incidence of tumors falls within historical control data. He stated that rat liver tumors are known to occur via a PPAR alpha MOA which is not relevant to humans.

Dr. Ozonoff asked if there was any information regarding PPAR gamma agonist activity or immunotoxicity issues with regards to PFOA. Dr. Popp responded that PPAR alpha receptor binding occurs with PFOA. Cell proliferation occurs and is then followed by peroxisome proliferation.

Dr. Corcoran added that the timing of the necrosis analysis is important. In the original study, necrosis was described but no liver tumors were found. In the second study, tumors were found but necrosis was not evaluated in addition no cell proliferation was found.

Dr. Cory Slechta indicated that PPARalpha receptors are found in the brain. What are the effects of PFOA on the brain? There is no information on brain effects.

Dr. Drinkwater noted that the mutant mouse data show an increase liver weight through a receptor-independent MOA. There is no histopathology associated with the increase in weight and appears to be a degenerative response. There appears to be another pathway other than PPAR alpha at work in mice.

Dr. Jane Houlihan and Dr. Timothy Kropp

Dr. Houlihan began the presentation (Attachment L) by stating that there are eight health effects from PFOA that have failed to identify a NOAEL, including ovary, pituitary, kidney, hormonal systems, immune system, spleen, male reproductive system (seminal vesicles, Leydig cell morphology), and developmental effects (growth). She further stated that PFOA causes adverse health effects through five basic mechanisms (modes of action), *At least four of these are relevant to humans*, mitochondrial toxicity, inhibition of gap junction , intercellular communication, thyroid hormone, serum estradiol changes (via liver aromatase), and peroxisome proliferation

Dr. Kropp suggested that the Science Advisory Board’s PFOA Panel urge EPA to the relevance to humans of mammary, testicular and pancreatic cancer findings, to consider the relevance of tumors to infants and children, to adopt the standard risk assessment methodology we have presented here, and to err on the side of human health protection when technical choices arise.

Dr. Kropp continued to suggest that PFOA be classified as a likely human carcinogen since tumors are seen in more than one species and in more than one sex. For non-cancer risk, he stated that EWG recommended a BMDL approach.

Mr. Robert Griffin (Attachment M)

Mr. Griffin identified himself as a civil engineer and is the general manager of a non-profit rural water system located in Southeast Ohio, The Little Hocking Water Association, which serves approximately 12,000 people. Mr Griffin stated that their water wells are located along the Ohio River directly across from Dupont's Washington works plant in Wood County, West Virginia where C8 is used in the fluoropolymer manufacturing process and where telomers are also produced.

Mr. Griffin reminded the panel that PFOA is an industrial chemical for which there is very limited scientific data to determine the acceptable level of that chemical in drinking water. As a consequence, he urged that the panel to put public health first by applying the precautionary principle.

Another public commenter, Ms. Debra Cochran, had not yet arrived.

Mr. Robert Billot of Taft, Stettinius & Hollister LLP who had been inadvertently left off the public commenter list was given 2 minutes to address the panel. He reminded the panel members of the blood data that was included in public comments (Attachment N) provided to the panel prior to the face-to-face meeting. These data included non-occupational blood levels for individuals living near manufacturing facilities and on landfills. The duration of the exposures were unknown, however the water testing occurred in 1984. There is a cancer survey being conducted which is in press.

The panel reconvened at 1:15 PM after a one hour break.

The panel began discussing their assigned charge questions. Dr. Cory-Slechta asked Dr. Drinkwater to summarize the findings for the Issue 1 group.

#### Issue 1

Dr. Drinkwater was the lead discussant for the Issue 1 group; its members include Dr. Drinkwater, Dr. Kehrer, and Dr. Klaunig. Their charge question was: *Please comment on the weight of evidence and adequacy of the data available to identify the key events for the PPAR alpha agonist induced rodent liver toxicity and hepatocarcinogenesis for PFOA. Discuss whether the uncertainties and limitations of these data have been adequately characterized.*

Dr. Drinkwater summarized the group's comments as follows:  
The sequence of four key events that defines the mode of action by which PPAR-alpha agonists induce liver tumors includes (1) activation of PPAR-alpha (2) increased cell proliferation and/or decreased cell death. (3) clonal expansion of the preneoplastic lesions, (4) development of hepatocellular neoplasms.

The issue 1 group agreed that the weight of evidence strongly supports the conclusion that hepatotoxicity and liver tumor induction in rats by PFOA results from a mode of action

involving PPAR-alpha agonism. However, studies of PPAR-alpha mutant mice by Yang *et al.* (2002), which are cited in the report in the context of the receptor dependence of PFOA immunotoxicity, did indicate an increased liver weight in PFOA treated mutant mice. A more critical issue is whether arguments related to the relevance to humans of this mode of action for induction of liver tumors in adults may be extended to exposed infants and children.

Additionally, there are no data available on the effects of peroxisome proliferators in human Kupffer cells. The role of Kupffer cell activation in the induction of DNA synthesis and subsequent neoplastic development by PPAR $\alpha$  agonists has not been characterized and thus results from the PPAR $\alpha$  null mouse are not directly applicable to the human situation in which PPAR $\alpha$  is present and can be activated.

Much of the discussion that ensued focused on the Yang et al study using the PPAR alpha null mouse and the role of Kupffer cells.

## **Issue 2: Descriptor for Carcinogenic Potential**

Dr. Melnick was the lead discussant for the Issue 2 group; the members included Dr. Melnick, Dr. Klaunig and Dr. Drinkwater. Their charge question was as follows: *OPPT has proposed that the PFOA cancer data may be best described as providing “suggestive evidence of carcinogenicity, but not sufficient to assess human carcinogenic potential” under the interim 1999 EPA Guidelines for Carcinogen Risk Assessment, as well as the 2003 draft EPA Guidelines for Carcinogen Risk Assessment. The determination of an appropriate descriptor for carcinogenic potential requires an examination of the available carcinogenicity data, an evaluation of mechanistic or mode-of-action (MOA) data, and guidance on how EPA applies various descriptors for summarizing weight of evidence.*

Dr. Melnick suggested that in order to respond to the charge question he would first discuss the cancer studies for PFOA, the Mode of action for PFOA and the application of cancer descriptors by the Agency.

Dr. Melnick concluded that the selection of “likely to be carcinogenic to humans” as presented in the 2003 EPA cancer guidelines appears to be the best descriptor of carcinogenicity. This was based on the fact that PFOA tested positive at multiple sites in Sprague-Dawley rats (males: liver, testis, pancreas; females: mammary gland), some of the tumor responses were highly significant and included relatively uncommon sites, and mechanistic data do not justify the exclusion of these responses as irrelevant to humans.

A review of the cancer descriptors that are found in both the 1999 and 2003 draft cancer guidelines ensued. Some panel members expressed some uneasiness in labeling PFOA a “likely human carcinogen” when there is uncertainty that exists. They were not able to assign a probability associated with the likelihood of being carcinogenic to humans.

## **Issue 3- Question 3**

Dr. Roberts was the lead discussant for the Issue 3 group; the members included Dr.

Roberts, Dr. Abel, Dr. Zoeller and Dr. Longnecker. Their charge question was as follows:  
*Please comment on the selection of these toxicity endpoints for the risk assessment.*

Dr. Roberts stated that the toxicity endpoints chosen are reasonable and that the presentation of results from multiple endpoints is valuable. He continued that organ and body weights are likely to be among the least sensitive endpoints for toxicants that exert specific effects on physiological or developmental systems. Nevertheless, in the absence of information leading one to propose that PFOA exerts a specific effect on non-cancer endpoints, the proposed endpoints are likely to be the most revealing.

Additional endpoints that were suggested by the issue 3 group members included:

- 1) neoplastic responses observed in rats (liver, testis, pancreas, and mammary gland)
- 2) ataxia in the female rat 2-year feed study (4% controls, 18% at 30 ppm, and 30% at 300 ppm)
- 3) reductions in thyroxine and triiodothyronine in the 6-month oral study in monkeys
- 4) increased severity and incidence of ovarian stromal hyperplasia in the 2-year feed study in female rats
- 5) decreased pituitary weights in F1 female rats

The discussion that followed Dr. Roberts' summary further elaborated on the issue of the lack of sensitivity of body weight and organ weight as an indicator of toxicity. Other confounding factors that need to be taken into account include maternal toxicity (e.g., malaise) which may affect offspring development.

#### **Issue 3- Question 4**

*Given the available data to date, please comment on the most appropriate lifestage/gender/species for assessing human risk.*

Dr. Roberts continued to explain the viewpoints of issue 3 group members regarding this question. There are those who prefer a more "conservative" approach since there is already substantial, widespread environmental contamination with this persistent, bioaccumulative compound and the prospect of increasing levels of contamination in the future are possible. Others prefer to use the adult non-human primate data as the most appropriate model for assessing human risk. These test animals are most similar biologically to humans.

Panel members discussed the appropriateness of rat vs monkey data. Panel members noted that the half-life of PFOA in rats appeared to reach a steady state, i.e., as the dose increased, serum levels remained the same. The half-life of PFOA in monkey was very short. There were additional limitations with the monkey data since it did not present any life-stage data for comparison of effects in adults vs. infants and children.

#### **Issue 3- Question 5**

*Please comment on the appropriateness of the available animal models. Please comment on whether additional animal models should be investigated, and if so, what information would better enable us to ascertain potential human risks.*

Dr. Roberts indicated that group members thought the available animal models are appropriate. Wildlife may serve as sentinels. He added that for DDT it was effects in wildlife that drove the policy to reduce use. He explained that continued monitoring of human populations, especially exposed workers was important, with an obvious need for more information about how humans are being exposed to this compound.

After Dr. Roberts completed his summary, panel members reiterated the need for further studies with PPAR-alpha knockout mice and rats. Some panel members suggested that the animal model to be used is dependent upon which endpoint was being evaluated.

#### **Issue 4a**

Dr. Mel Andersen was lead discussant for the Issue 4a group. The members of this group included Dr. Andersen, Dr. Hayton, and Dr. Kamrin. Dr. Andersen began by stating he wished to address question 7 before addressing question 6. Dr. Andersen provided a summary of his group's response, as follows:

**Issue 4a Question 7:** *Please comment on the use of the AUC as a measure of internal dose for rats and humans for calculation of the MOE.*

Dr. Andersen continued to respond to charge question 7. He stated that all three reviewers provided a guarded endorsement of the use of AUC as a better measure of dose than provided by a daily intake. Each of the three also discussed other measures of dose related to pharmacodynamics that might also be considered superior to an average AUC (or average daily concentration). There may not be sufficient information to discern the appropriate dose measure; however, some discussion of the intentions in using the AUC and in potential alternative dose measures appears essential. In addition, it would be extremely useful to attempt in the document to compare, to the extent possible, the MOEs derived from alternate dose measures with the currently estimated MOEs. For instance, if maximum daily concentrations were used, how would the MOE compare to the ones in the present document in at least a qualitative manner.

**Issue 4a Question 6:** *Please comment on the use of the one compartment pharmacokinetic model.*

The one compartment model used to calculate AUC for rats based on daily intake of PFOA in rats provided an adequate **approximation** for the purposes of the calculations of AUC in the rat. The Palazzo 13-week study could be used directly to estimate the rat steady-state AUC. The underlying assumptions in using this PK modeling approach should be clarified in an appendix to the document. All three reviewers noted areas where multi-compartment PK models with more mechanistic detail might be developed to provide an improved analysis of the rat and the monkey pharmacokinetic data and a better understanding of the biological processes that control the kinetics of PFOA in test animals and humans.

Other panel members appeared to agree with the Issue 4a group and no further discussion took place.

#### **Issue 4b**

Question 8 - *Please comment on the need to use or modify the default value of 10 for cross species extrapolation given the pharmacokinetic analysis.*

Dr. Mink was the lead discussant for the Issue 4b group. The group members included Drs. Mink, Corcoran, and Roberts (Drs Melnick and Kamrin had also provided some input to this group's response. Dr. Mink summarized the group's response, as follows:

He stated that the use of an uncertainty/safety factor to account for pharmacodynamic equivalence was generally accepted (with a caveat by Dr. Kamrin based on his assessment of the data's statistical robustness). He continued that a modification could be made given the complexity of the data sets- with an uncertainty factor ranging of 3 to 200 proposed. Some questioned the use of LOAEL/NOAEL methodology for systemic effects versus using a Bench Mark Dose approach. Issues of newer data, steady state serum equilibrium assumptions, life stage, and cumulative effects of the C-8 class were also mentioned in regard to the overall complexity of the dynamics analysis.

The subsequent discussions focused on the complexity of the PFOA pharmacokinetic data and the uncertainty that exists. Dr. Andersen explained that a 10X factor is usually added to account for interspecies (3X) and intra-species (3X) difference. Although the use of internal dose metrics may eliminate the need for the interspecies uncertainty factor of 3X, panelists were generally not willing to remove or reduce it due to the obvious gender differences seen in the rat studies.

#### **Issue 4c**

Question 9 *Please comment on the adequacy of the human exposure data for use in calculating a MOE.*

Dr. Anne Sweeney was the lead discussant for the issue 4c group. The members of this group were Dr. Sweeney and Dr. Ozonoff; both had submitted preliminary comments and Dr. Sweeney had submitted integrated comments prior to the meeting date. Dr. Sweeney was, however, unable to attend this meeting and Dr. Cory-Slechta asked Dr Ozonoff to summarize the group's response. Dr. Cory Slechta also asked Dr. Longnecker to provide assistance during the meeting to Dr. Ozonoff as he revised the group's response.

In his summary, Dr. Ozonoff questioned the appropriateness of using a MOE approach. He also questioned the exclusion of some epidemiological data, including the worker biomonitoring data. He continued to explain that the utilization of the correct summary measures for biomonitoring data is important, i.e., using the 90<sup>th</sup>, 95<sup>th</sup> percentile or maximum

figures for any MOE calculation is the preferred method. He also stated that the data were poorly depicted.

Dr. Cory Slechta reviewed the next steps. She told panel members that they will be revising their responses to the charge questions during the subsequent day's meeting. She explained that panel members will be asked to be present at 8:30 AM when we will reconvene the meeting and discuss the format of the meeting.

The meeting adjourned at 5:45PM.

### **Wednesday February 23, 2005**

Dr Shallal opened the meeting at 8:40 AM when all panel members were present. She made some brief opening remarks and then turned the agenda over to Dr. Cory Slechta.

Dr. Cory-Slechta informed the panel members to get into their issue groups and attempt to find consensus. She said they should also determine the most important issues which they would like to include in the executive summary and letter to the Administrator.

Dr. Shallal directed the panelists to their meeting locations. The panel separated into their writing groups according to their assigned issue group at 8:50 AM.

The meeting reconvened at 10:00 AM

#### **Issue 1**

Dr. Drinkwater presented the findings for the Issue 1 group (Attachment O). The group suggested that a closer look at the relevance to infants and children should be addressed. They also suggested a closer look at the immunotoxic effects seen in the Yang et al study.

#### **Issue 2**

Dr. Melnick presented the response for the Issue 2 group (Attachment P). He discussed the carcinogenicity evidence that is available. He also summarized the difference between the cancer descriptors, suggestive vs. likely, as presented in the 1999 and 2003 cancer guidelines.

A discussion regarding the cancer classification continued and an alternative response was crafted by Dr Mink which tried to capture the variety of points of view (Attachment Q). It was agreed that this new language would be incorporated into the Issue 2 response.

#### **Issue 3**

Dr. Roberts presented the revised response for the Issue 3 group (Attachment R). Further discussion focused on the immunotoxicology and pituitary endpoints. There was also a

suggestion that the limitations of using a particular endpoint for calculating an MOE be clearly articulated. It was agreed that additional information regarding the epidemiology data will be provided by the Issue 4c group.

#### **Issue 4a**

Dr. Andersen presented the revised integrated comments for the issue 4a group (Attachment Y). A discussion on using the average serum concentration for calculating AUC concluded with an agreement that a statement regarding its appropriateness or that of another measure would be added to the final response.

#### **Issue 4b**

Dr. Mink discussed the revised response for the Issue 4b group (Attachment S). He stated that there needs to be a discussion of what is currently done and how uncertainty is dealt with. There continued to discussion regarding the use of uncertainty factor when a pharmacokinetic model is being used. Some questioned the utility of developing such models if they will not impact the use of uncertainty factors. All panel members agreed that there was not enough data available to be able to modify the default value of 10 for cross species extrapolation given the pharmacokinetic analysis.

#### **Issue 4c**

Dr. Ozonoff presented the revised response (Attachment T) for the Issue 4c group with input from Dr. Longnecker. He stated that this data set is as good as others. Depiction of biomonitoring data needs to be enhanced. More information regarding children's exposure should also be included.

After a short lunch break, the Panel next began discussing the major points that they wanted to include in the Executive Summary and letter to the Administrator.

The following points were discussed:

- Carcinogenic potential
- Handling uncertainty factors
- Additional evaluation of non-cancer endpoints
- Improve understanding of sources of exposure
- Improve understanding of kinetics
- Endorse use of internal dose metrics
- Overall assessment is reasonably comprehensive and well-written

The Panel agreed that these are the important issues that should be included in the executive summary.

The panel took a short break and returned to continue their discussion. They now focused on the key data gaps.

- PFOA distribution

- PFOA speciation in blood and how this is related to the effects seen
- Hepatocyte proliferation in the monkey-role of PPAR alpha
- Kinetics
- Cumulative risk

Since more refinement of the executive summary was needed, it was decided that Dr. Cory-Slechta would draft the executive summary and panelists would be given an opportunity to provide comments.

Dr. Cory-Slechta then asked the panel members to revised their comments and submit them to Dr. Shallal by March 4, 2005. She will then provide them to Dr. Cory-Slechta so that she made draft the review report. The panel will likely meet via teleconference in order to finalize their draft review report. The exact time will be determined at a later date.

Finally, as a reminder, Dr. Shallal instructed all panel members to conduct all their discussion and deliberations regarding the PFOA risk assessment in the public domain. All correspondence between panel members in reference to this review should also include Dr. Shallal as a recipient.

Meeting Adjournment – Dr. Shallal stated that she would send an e-mail to all panel members reminding them of the various deliverables and their due dates as agreed. The meeting was adjourned at 2:25 pm.

Respectfully Submitted:

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Dr. Suhair Shallal  
Designated Federal Officer,  
EPA SAB PFOA Review Panel

I certify that these minutes are accurate to the best of my knowledge:

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Dr. Deborah Cory Slechta  
Chair,  
EPA SAB PFOA Review Panel