

**Compilation of Member Comments on the Radiation Advisory Committee's  
Draft Report on Radiation Cancer Risk  
SAB Teleconference of September 24, 2009**

**A. Lead Reviewers:**

**1. Dr. Jill Lipoti:**

Letter, page 1, line 32

It is unclear who is to be encouraged to publish in the peer-reviewed journal – is EPA to encourage researchers to publish? Is EPA to publish their proposed RBE for others to comment on? What is EPA to do about an RBE until the research is published? Is there an existing acceptable RBE? Is one publication enough or when is there enough data? Does the question about the RBE need to come back to the RAC?

Letter page 3, line 8

It is unclear what is meant by “reporting risk estimates associated cohorts”. Do you mean “associated *with* cohorts exposed to protracted low doses of ionizing radiation”? Is this where you want EPA to consider epidemiological evidence from cohorts of radiologists and nuclear workers? This should be clarified.

p.1. lines 23-24. Same problem as above – how can EPA encourage researchers to publish their RBEs? Should EPA fund this research? Can EPA publish something themselves? What is EPA to do in the meantime? Should they use an RBE of 1 knowing that the real RBE is in excess of 1? Is there an upper bound for the RBE so that EPA could say that the RBE is somewhere between 1 and xx, thereby including the RBE choice as part of uncertainty?

p.2. lines 6-8. Is this a continuing recommendation, that EPA should develop improved models to derive risk estimates for other cancers as survival rates improve? Is there a tipping point? When survival rates exceed a particular percentage? The current survival rate of breast cancer is about 81-85%. The rate for colon cancer is about 63%. Prostate cancer is 99%, uterine cancer is 84%. So is RAC recommending a policy to develop improved models when the survival rates exceed 60%?

p.2. lines 10-14. This recommendation is to separate the risks for nonfatal skin cancer from the overall risk estimates altogether. Two reasons are given – the rates of nonradiogenic nonmelanoma skin cancers are high, and they generally respond to treatment and are not fatal. What about breast cancer and colon cancer? These have a pretty high nonradiogenic rate and a high (relatively) survival rate. Should they be included in the overall risk estimates? Why or why not? What makes nonmelanoma skin cancer “special”? And how will fatal radiogenic nonmelanoma skin cancer be treated? Will it be included in the overall risk estimate?

p.2. lines 16-18. Awkward sentence. Is this a better way to say it? “The RAC also agrees with EPA using the same model for estimating radiogenic cancer risk for exposure to radiation which occurs *in utero*, in childhood, or in adulthood.”

p.11. line 7. Change “and” to “an”.

p.15, line 40. Suggestion is to use a similar approach for other types of cancer, such as prostate and uterus. On page 2. lines 6-8, the suggestion was “e.g. colon cancer.” So is the suggestion to look for cancers with high survival rates and consider them? This should be consistent between page 15 and page 2, and should be picked up in the letter to the administrator.

p. 16, line 2. Heading of nonfatal skin cancer hints that fatal skin cancer is dealt with somewhere else. Where?

p.16, line 7. The term basal cell carcinoma is introduced, but the relationship to NMSC is not described. Is it synonymous?

p. 16, line 11 – The rationale given here for not including NMSC in the risk estimate is that it is “in keeping with the usual practice”. That is different from the discussion on p.2. lines 10-14. This needs to be consistent and clear.

p. 16, lines 31-35, This description does not seem to say the same thing as p.2, lines 16-18. And I had trouble understanding what was meant on page 2. Can this be clarified?

## **2. Dr. Rogene Henderson:**

I have reviewed the SAB Review of "EPA Radiogenic Cancer Risk Models and Projections for the US Population.: I found the review by RAC to be clear and well-organized. Each charge question was thoroughly addressed.

My answers to the three standard questions are:

- a) the original charge questions to the SAB Standing or Ad Hoc Committee/ Panel were adequately addressed in the draft report: Definitely.
- b) the draft report is clear and logical; Quite clear and logical.
- c) the conclusions drawn, and/or recommendations made, are supported by information in the body of the draft SAB report. -- To the extent of my knowledge in this area, the conclusions were supported by the text.

## **3. Dr. Lauren Zeise**

The report is very well done. I just found a few minor points to raise. Please see responses to charge questions below.

**The charge questions were adequately addressed in the draft report.**

These recommendations lay out a way for the agency to proceed in light of the committee's concern - but of course will take a good deal of time.

Up front, a clear summary statement is needed – e.g., that the RB Exchange at this time does not appear to be scientifically justified. The sentence in the letter to the Administrator on this issue could be clearer.

**A couple additional very minor points:**

Page 24, line 16-17. I found the following somewhat unclear - “anticipate the contents of the subsequent documents based on the Blue Book.”

Page 25, line 27, word “problematical” is somewhat vague in this context.

**The conclusions drawn and recommendations made are supported by information in the body of the draft SAB report.**

**A few editorial catches:**

Page 7, line 9. The abbreviation “LSS” is used before the acronym is defined – further down the page at line 20.

Page 12, line 4 “comput0e”

Page 15, lines 31-32. The sentence has to be read a couple of times to catch the meaning.

Page 17, lines 15-16. Points “c” and “d” should be “a” and “b”

Page 24, line 15. The upper case “T” in the middle of the sentence should be lower case.

In the Administrator's letter, page 3, line 7, missing word (“with”)

**A. Other Members**

**1. Dr. Steve Heeringa:**

My overall assessment of this review is that it is thorough, responsive to the charge questions and is clearly written. The report is particularly effective at identifying issues that require clarification and then proposing an explicit approach to addressing the need for additional supporting text or the introduction of new and important topics.

Dr. Kahn circulated a list of typographical errors and minor edits that he had detected. These captured most of my editorial notes. The following is a list of additional minor edits and comments that I noted in my review of the report.

P 11 L7 “and” to “an”

P 11 L 33 “ 18.6 to 0 keV (is a leading digit missing from the upper bound?)

P 13 (comment) good argument for arithmetic mean including consistency with central tendency from the posterior generated under the Bayesian uncertainty analysis.

P13 L13 (also p25 L3) the report uses the terms “stationary” and “stable” . In the demographic literature, a stable population is a population that has a fixed age and demographic structure but is permitted to grow overall at some rate  $\lambda$ . A stationary population retains the same proportions for the age/gender distributions over time but does not grow (i.e.  $\lambda=1.0$ ). The report should standardize the use of these terms. I believe stable is the implied meaning since hazards are the focus and not total mortality.

P15 L6 Minor statistical terminology issue. For estimation of parameters I would suggest use of the term “precision” (variance) or accuracy (total error) in place of power. Power suggests a hypothesis test (maybe parameter is null or comparisons of groups). That said, this is a common use of the term “power” and should not mislead on intent.

P18 L12-L20 The report does an excellent job of presenting an issue and then following up with a recommendation. Do we wish to suggest a simplification of the “complicated” uncertainty analysis here or just note that uncertainty is dominated by the subjective priors for the type II parameters? (which is stated ). See next comment.

P19 The perturbation recommendation on Page 19 is an excellent suggestion for verifying that the multi-dimensional Bayesian simulation of uncertainty is producing a result that remains within the space of realistic uncertainty associated with individual parameters.

P24 L4-L12 (comment) excellent suggestion.

P24 L23-L25 This recommendations refers back to oral presentations made at the March 23-25, 2009 meetings. To be sure that this recommendation is understood it would be helpful to provide a description of the specific points, explanations or examples that should be brought forward. (Maybe this is clear to everyone who participated, if so, please ignore).

P 25 L3 See comment for P13 L13 above on the use of stable and stationary.

**2. Dr. Taylor Eighmy:**

Here are my comments on the review charges. The RAC has done a good job here with their review of the draft "Blue Book."

A) the original charge questions to the SAB Standing or Ad Hoc Committee/Panel were adequately addressed in the draft report;

The three charge questions are addressed.

B) the draft report is clear and logical

The report is well done.

C) the conclusions drawn, and/or recommendations made, are supported by information in the body of the draft SAB report.

The conclusions and recommendations are supported.

**3. Dr. Judy Meyer**

This is far outside my area of expertise, so my comments reflect the limited understanding of a literate non-specialist.

Quality review questions:

1) Are the charge questions addressed? Yes

2) Is the draft report clear and logical? Yes, although it is so technical, that it is opaque to the non-specialist (but that is not the audience for this report).

3) Are the conclusions supported by the body of the report? Yes.

I do have a couple specific comments:

1) The Letter strikes me as too detailed. It is a repeat of all the findings and recommendations rather than a condensation of what are the most important presented in a manner that is understandable to a high level administrator.

2) A detail, but the beginning of the Letter says this was done by the RAC, but at the end it states that it was done by the augmented RAC. It should be consistent.

3) 3b: Why is it important to be able to evaluate the contribution of the Blue Book vs. other influences on the FGR?

- 4) 2.2 I don't think all the details about the SAB review are necessary.
- 5) The charge questions are stated on pp. 6-7 and then restated when the response is written. They should be stated only once.
- 6) p. 20, line 27: This idea caught my eye because I have been thinking about multiple stressors lately. It wasn't clear if the Blue Book adequately addressed the interaction between radiation exposure and other exposures (e.g., to toxins, endocrine disruptors, etc.). Did it? Should it? Did the committee discuss this?
- 7) p. 24, line 23: I obviously wasn't there for the oral presentation, but this strikes me as a fairly vague recommendation unless just a few topics were discussed. It seems more reasonable to state the topics for which the oral explanations and examples should be included.

#### **4. Dr. Steve Roberts:**

By and large, the body of the report is well written and provides clear responses to the charge questions. The Executive Summary, however, is a liability in its current form. In a number of places, the Executive Summary does not match well with the content of the report. Some of the differences are curious but not particularly significant. For example, the response to Question 1d in the Executive Summary uses colon cancer as an example of a cancer with high survival rate, while the body of the report uses cancer of the prostate and uterus instead. In other situations, the Executive Summary does not convey well the recommendation in the report, in my opinion. Here are a couple of examples:

- The response to Question 1c with respect to leukemia states in the report, "The RAC considers the RBE of 2 may be reasonable, but recommends that the Blue Book discuss the uncertainties in this value that derive from estimating doses from alpha-particle emitters and from different temporal patterns between the LSS and the <sup>224</sup>Ra group for the appearance of leukemia." In the Executive Summary, that recommendation becomes, "For leukemia, the RAC notes the uncertainty related to the EPA changing the RBE for alpha-particle radiation from 1 to 2 and suggests that the EPA reevaluate the data and logic on which this RBE increase is based before committing to the change." Discussing the uncertainties and reevaluating the decision are not the same thing.
- The response to Question 3a regarding radiogenic brain cancer states in the report, "The RAC recommends that noncancer mortality be mentioned as a possible effect of radiation exposure even at low doses, and that the reasons be stated for not providing risk estimates for this endpoint at the present time." In the Executive Summary, this recommendation is stated as, "... the RAC recommends that the EPA enhance Blue Book contents by reporting further information from (1) studies of noncancer mortality

...” The Executive Summary version is vague and uses not too many fewer words to convey almost no sense of the actual recommendation.

- Also from the response to Question 3a, “The RAC recommends that the EPA either include the radiogenic risk to the brain in the context of the other discussed cancer sites, or discuss the rationale for excluding the radiogenic risks to the brain in the Blue Book.” In the Executive Summary, this recommendation becomes, “... the RAC recommends that the EPA enhance Blue Book contents by reporting further information from ... brain cancer studies ...” These are not the same recommendation.

Other sections of the Executive Summary are difficult to decipher, for example part of the response to Question 1e: “The RAC also agrees with the use by the EPA for estimating the adult radiogenic cancer risk of the same model for exposure to radiation in utero or in childhood. Differences in risk estimates between the two groups were not statistically significant.” I have read the report and these sentences a number of times and can’t figure out what they mean. I found the recommendation by the RAC in response to Question 1a puzzling. The report states, “The RAC considers reasonable and generally acceptable the approach proposed by the EPA for obtaining cancer risk estimates for alpha particle emitters with the RBE values that the EPA proposes.” What follows is a series of questions regarding the proposed changes by EPA to the RBE for low-energy electron and photon radiation that indicates the basis for the changes by EPA are not well explained or justified. This seems contradictory to the endorsement of the approach by the RAC. On this point, the Executive Summary is actually more lucid, explaining that the EPA review of information sufficient to conclude that the RBE exceeds one, but is insufficient for selecting an appropriate value. The solution to this proposed by the RAC seems out of character with an SAB review – the EPA should encourage publication of the justification in a peer-reviewed paper and see what the reaction is from the scientific community. Presumably the Agency is seeking more timely and formal feedback on this so that they can complete their updated Blue Book.

There are different philosophies on the letter to the Administrator. Mine is that the letter should provide general comments on the report and perhaps highlight a few issues that might merit the Administrator’s attention rather than providing a list of recommendations, as is the case here. There should be a basic message to the Administrator regarding the SAB review, and I think that it gets lost if the letter is too detailed.

##### **5. Dr. Valerie Thomas:**

Comments on Review of EPA Radiogenic Cancer Risk Models

- a) Are the original charge questions to the SAB Panel adequately addressed in the draft report?

Yes.

b) Is the draft report is clear and logical?

The discussion of the recommendations concerning the low-energy betas, gammas and x-rays is not clear. RAC recommends that a paper on low-energy RBEs be submitted to a peer-reviewed journal. But the main point seems to be that these values should not be used now; that needs to be said. Also, it is not clear if the work has already been done, or if research is needed first, and it is not clear who it is that EPA should encourage to submit the journal article. Is RAC recommending that EPA scientists submit the work they have done on the RBE for publication? Or is it outside scientists who have done the work and should submit it for publication? Has the work been done already? If the research has not been done yet, does EPA need to support research to develop the RBEs? Generally, if work has not yet been submitted to a peer-reviewed journal, more research will be needed before the work is ready for submission to a peer-reviewed journal. A clearer recommendation might be that (1) further research is needed on RBEs for low energy betas, gammas, and x-rays, (2) this work should be submitted for publication to an appropriate peer-reviewed journal, and (3) until there has been sufficient research and review, EPA's proposed RBE's for low energy betas, gammas and x-rays should not be used. For example, in the letter to the administrator, page 1 lines 30-34, and also in the Executive Summary, page 1 lines 23-25, could be replaced with:

The RAC recommends that the proposed relative biological effectiveness (RBE) values for low-energy beta particles, gamma rays, and x rays not be used at this time. Sufficient information to support these RBE values has not been presented. RAC recommends that the EPA staff encourage the scientists who have developed the proposed RBE values publish the supporting research and findings in an appropriate peer-reviewed journal. After this review and vetting, EPA would have a clearer basis for choice of RBE values.

c) are the conclusions drawn, and/or recommendations made, supported by information in the body of the draft SAB report?

Yes.

Other comment:

p. 11 line 25 – I suggest changing “Will this change be restricted only to radionuclides with energies similar to 3H?” to “Will this change be restricted only to betas with energies similar to that from 3H?” (I think the beta energy, not the energy of 3H, is what is referred to here.)

**6. Dr. James Sanders:**

a) the original charge questions to the SAB Standing or Ad Hoc Committee/Panel were adequately addressed in the draft report:

Yes, the committee has clearly addressed each question.

b) the draft report is clear and logical:

Yes. The report is brief but very clear. Each charge question was directly considered. The language is clear and concise.

c) the conclusions drawn, and/or recommendations made, are supported by information in the body of the draft SAB report:

Yes.

I have only two brief comments to make.

1. p.1, l. 16. Exec. Summary. As the authors do on the first page of the letter to the Administrator, BEIR VII should be identified as the recent NRC report.

2. p. 5, l. 41- p. 6, l. 25. This entire section repeats material found on pp. 4 and 5. I recommend deleting the entire section 2.3.1.