UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAR 3 2010

THE ADMINISTRATOR

EPA-SAB-10-001

Deborah L. Swackhamer, Ph.D.
Chair, Science Advisory Board
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

Dear Dr. Swackhamer:

Thank you for sending your report on the U.S. Environmental Protection Agency draft document *EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population* (December 2008). The Agency appreciates the Radiation Advisory Committee's efforts in conducting a comprehensive technical peer review of this draft, which lays out EPA's proposed updated methodology for quantitatively estimating radiogenic cancer risks.

We are pleased that the Science Advisory Board Committee found "...the EPA's draft revised Blue Book [to be] impressively researched, based on carefully considered concepts and well written." We also appreciate the finding that "...the draft revised Blue Book has commendable accuracy and balance."

The SAB Committee's recommendations to the Agency's three specific charge questions are extremely useful in advancing the state of the science. In particular, we will add material related to the appropriateness of models not taken directly from the 2006 National Research Council Biological Effects of Ionizing Radiation Report, will include additional analyses related to the adequacy and reasonableness of our uncertainty analysis and will expand the text regarding the presentation of overall information and the application of BEIR VII. Enclosed is a detailed response to your principal recommendations.

Thank you again for the thoughtful comments and recommendations that the SAB has provided.

Sincerely,

Lisa P. Jackson

Enclosure

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This document provides responses to recommendations contained in the Executive Summary of the Radiation Advisory Committee (RAC) of the Science Advisory Board (SAB) review of the draft "EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population" (December 2008). The SAB Committee recommendations are highlighted in italics; page numbers are indicated when additional comments or recommendations from the report itself have been cited.

1a. *For low-energy beta particles (notably tritium) and low-energy photons, on the other hand, the RAC finds that while the EPA review of information is sufficient to conclude that the RBE exceeds 1, it is insufficient for selecting appropriate RBE values.* ***The RAC recommends that EPA staff publish, for review by the scientific community, a compilation and evaluation of pertinent studies in a peer-reviewed journal and then select an RBE value based on this document and professional responses to it.*** *This effort should not delay publication of the Blue Book, but its results should be available before the EPA issues the revised FGR 13.*

EPA has reviewed the literature on RBE for low energy photons and electrons, including several reports by expert panels. Based on that review, it appears that the relative biological effectiveness (RBE) of tritium beta particles is 2-3, relative to ^{60}Co gamma rays, and that the biological effectiveness of 100-250 kV_p X-rays are also significantly higher than that of ^{60}Co gamma rays but lower than that for tritium beta particles. It is understood that the higher RBEs stem from the higher density of ionizations produced, especially at the ends of electron tracks.

The draft Blue Book outlined an approach for assigning RBEs for low energy photons and electrons based on the calculated fraction (F) of the total energy deposited at the ends of electron tracks (i.e., by electrons below some cut-off energy between 1 and 5 keV). For illustrative purposes, RBEs were estimated for tritium beta particles and 200 kV_p X-rays using approximate curves generated by Nikjoo and Goodhead. EPA is working to obtain estimates of F, as a function of photon or electron energy, using more accurate Monte Carlo methods. These results can then be translated into estimated values of RBE for all beta particles and photons of interest. It is anticipated that a paper based on this work will be submitted to a peer-reviewed journal this year, which will describe the methodology and results and include a discussion of references pertinent to determination of these RBEs. An outline of the approach will also be contained in the revised Blue Book with at least some preliminary results. Based on the outcome of this effort, EPA intends to incorporate energy-dependent RBEs for low energy beta/photon emitters into the calculation of risk coefficients for the revised FGR-13 Report.

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We accept the RAC recommendation to use weighted arithmetic means for each pair of EAR and ERR values. As the RAC pointed out in its report (page 10), there is no theoretical

basis for using either the arithmetic or geometric mean. However, the arithmetic mean will yield larger values than the geometric mean, and when weights are equal, the arithmetic mean has the desirable property of "equally balanc[ing] the low and high risk estimates." In a related matter, we intend to use the same weights (for EAR and ERR) as in BEIR VII for almost all cancer sites. This is consistent with the RAC recommendation that "weighting should emphasize ERR models more than EAR models except for outcomes with enough relevant data outside the LSS population (e.g., breast cancer) to indicate that EAR models transfer risk more accurately" (page 10). Further, we also plan to include a brief discussion "concerning the greater weight given to ERR-based" projections as the RAC recommended (page 10).

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To do this, we will consider distributions for which the expected value for the weight assigned to the ERR model is approximately equal to the nominal weight value used for the point estimate, i.e. 0.7 for most cancer sites. Examples of distributions which have this property are mixtures of the triangular distribution T(0,1,1), and the Binomial distribution with n = 1 and p = 0.7. The expected value of such distributions would be between 2/3 and 0.7.

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We agree and greatly appreciate these RAC recommendations and comments. We will expand the discussion of the rationale for use of the stationary population. It will include the presentation of population pyramids.

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The RAC suggests that radium dial painter data would serve as a better basis for estimating risk from internally deposited Ra-226 than data obtained from studies of patients injected with Ra-224. EPA proposed to employ a linear, no-threshold model derived from the Ra-224 patients as a basis for estimating the risk of bone cancer, as outlined in the draft Blue Book.

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cell-killing term were included. However, although the preferred model of Hoel and Carnes fits the data relatively well and is mathematically simple, it is lacking a plausible biological basis. It is a particular example of a 2-component linear spline function, one in which the slope is zero over the dose interval 0 to 9 Gy. Alternative 2-component linear splines would also be consistent with the data, including one with a low-dose slope similar to that derived from a linear, non-threshold fit to the Ra-224 patient data. Further, the lack of observed cases among the dial painters for doses below 10 Gy is not inconsistent with EPA's risk coefficient for alpha-particle induced bone cancer.

The final version of the Blue Book will elaborate on these points, including additional references associated with the biological mechanism for bone cancer. In addition, the radium dial painter data and other evidence for a threshold or nonlinear dose-response will be considered in setting an uncertainty distribution for radiation-induced bone cancer risk.

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EPA appreciates and concurs with this finding.

1e. ***The RAC agrees with the EPA approach for separating from its overall risk estimates the nonfatal skin cancer risk estimates because of the dominance of spontaneous (nonradiogenic) nonmelanoma skin cancers and the associated experience that most respond to treatment and are not fatal. Their inclusion with cancers that result in a much higher mortality rate would greatly distort the overall cancer morbidity and mortality risk estimates.***

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of each major contributor to uncertainty over a reasonable range to recalculate the corresponding range of the point estimate and demonstrate the validity of the recommended uncertainty.

We will use the perturbation approach suggested in the RAC review. The perturbation approach should provide a "reality check" on uncertainty intervals derived from the more complicated Markov Chain Monte Carlo (MCMC) approach.

2b. ***The RAC recommends that the EPA expand the text to clarify the reasoning behind the selection of distributions chosen for the various sources of uncertainty.*** *The discussion of subjective priors listed partially in Table 4-1 of the draft Blue Book should justify the assigned distributions so that the reader can trace the basis of each decision concerning central value, uncertainty, and distribution, and have confidence in these characteristics.*

We will follow the RAC advice, and expand the text to further clarify the reasoning behind the selection of distributions chosen for sources of uncertainty. In doing so, we will incorporate material presented to the RAC in March, 2009. The discussion will include, for each source of uncertainty, salient characteristics of the assigned distribution(s) such as central value, range (when appropriate), and standard deviation.

Among its specific comments, the RAC correctly pointed out that the use of lognormal multiplicative factors (with mean values other than 1) in the derivation of uncertainty intervals for the LAR might introduce bias. It is also true that the use of multiplicative factors with mean values equal to 1 for some sources of uncertainty would also introduce bias. For example, for selection bias in the LSS, the distribution should ***not*** have a mean value equal to 1. The final version of the Blue Book will discuss the issue of bias in more detail. We will distinguish between the features of distributions for sources of uncertainty whose effect would be to shift the distribution for LAR (relates to both central value and bias) versus those that widen the LAR distributions.

3a. *The RAC recognizes the scientific defensibility and appropriateness of the Blue Book.* ***However, the RAC recommends that EPA enhance Blue Book contents by reporting further information on radiogenic cancer [and noncancer health effects] at low radiation doses from (1) studies of noncancer mortality; (2) brain cancer studies; (3) recent ICRP and UNSCEAR reviews; and (4) NCRP Report #159 on the risk of radiation-induced thyroid cancer (NCRP 2009).***

(1) EPA will add a section discussing potential noncancer effects from low dose ionizing radiation, including hereditary effects and cardiovascular disease.

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response for central nervous system tumors of various histological types ..." EPA will investigate the feasibility and practicality of deriving a separate risk model for the brain and other central nervous system (CNS) tumors. In particular, EPA would need to consider whether there is an appropriate method for combining results from the several studies on radiogenic brain tumor risks.

(3) EPA's risk projections on BEIR VII will be compared against those most recently published by the ICRP and UNSCEAR.

(4) As suggested in the main body of the RAC report (page 22), EPA intends to base its final risk model for thyroid on the NCRP Report #159, which was not publicly available at the time the draft Blue Book was prepared. In particular, the EPA model will reflect a declining radiogenic risk with time since exposure.

3b. ***The RAC recommends that the EPA clarify the purpose and application of the Blue Book by presenting in detail, in its first Section, the contributions by Blue Book contents in preparing Federal Guidance Report (FGR) 13 and, in its last Section, FGR 13 values of radionuclide risk coefficients.*** *This information should be sufficient to permit the reader to attribute any significant changes in FGR 13 values to changes proposed in this Blue Book, or to changes in the physiological models with which they will be combined...*

The RAC recommends that the EPA include...specific information concerning the anticipated radionuclide risk coefficient values in the revised FGR 13, based on currently available dosimetric models. Tables A4a and A4b in the 1994 Blue Book can be taken as models.

EPA will include a discussion of how the Blue Book contents will be applied to develop radionuclide risk coefficients in FGR 13. EPA also will discuss how changes in the risk models will impact the numerical risk coefficients in FGR 13, but we have not yet decided whether to include detailed tabulations. As no FGR 13 Report was available or even anticipated when the original Blue Book was published, the 1994 tables served an important purpose in providing EPA recommended radionuclide-specific risk coefficients. Publishing risk coefficients based on updated risk models but soon-to-be-superseded dose and usage factors in the revised Blue Book would, in our view, be less useful and potentially confusing.

3c. ***The RAC recommends that the EPA enhance the level of detail by expanding its discussion of the following risk estimates: (1) those based on studies of cohorts exposed to low-dose protracted radiation, and (2) those distinguishable types of cancer within a given organ.***

The revised Blue Book will contain more detailed information and discussion on these points. In particular, as suggested in the body of the report (page 24), the Agency will comment on risk estimates for specific leukemia subtypes.

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EPA-SAB-10-001

Bernd Kahn, Ph.D.
Chair, Radiation Advisory Committee
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

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(4) As suggested in the main body of the RAC report (page 22), EPA intends to base its final risk model for thyroid on the NCRP Report #159, which was not publicly available at the time the draft Blue Book was prepared. In particular, the EPA model will reflect a declining radiogenic risk with time since exposure.

3b. ***The RAC recommends that the EPA clarify the purpose and application of the Blue Book by presenting in detail, in its first Section, the contributions by Blue Book contents in preparing Federal Guidance Report (FGR) 13 and, in its last Section, FGR 13 values of radionuclide risk coefficients.*** *This information should be sufficient to permit the reader to attribute any significant changes in FGR 13 values to changes proposed in this Blue Book, or to changes in the physiological models with which they will be combined...*

The RAC recommends that the EPA include...specific information concerning the anticipated radionuclide risk coefficient values in the revised FGR 13, based on currently available dosimetric models. Tables A4a and A4b in the 1994 Blue Book can be taken as models.

EPA will include a discussion of how the Blue Book contents will be applied to develop radionuclide risk coefficients in FGR 13. EPA also will discuss how changes in the risk models will impact the numerical risk coefficients in FGR 13, but we have not yet decided whether to include detailed tabulations. As no FGR 13 Report was available or even anticipated when the original Blue Book was published, the 1994 tables served an important purpose in providing EPA recommended radionuclide-specific risk coefficients. Publishing risk coefficients based on updated risk models but soon-to-be-superseded dose and usage factors in the revised Blue Book would, in our view, be less useful and potentially confusing.

3c. ***The RAC recommends that the EPA enhance the level of detail by expanding its discussion of the following risk estimates: (1) those based on studies of cohorts exposed to low-dose protracted radiation, and (2) those distinguishable types of cancer within a given organ.***

The revised Blue Book will contain more detailed information and discussion on these points. In particular, as suggested in the body of the report (page 24), the Agency will comment on risk estimates for specific leukemia subtypes.