UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

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Working Draft of July15, 2009

EPA-SAB-09-xxx

The Honorable Lisa Jackson
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Subject: SAB Review of "EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population," Draft December 2008

Dear Administrator Jackson:

The Radiation Advisory Committee (RAC) of the Science Advisory Board has reviewed the draft document *"EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population*, December 2008." In this draft "Blue Book," the Agency's Office of Radiation and Indoor Air (ORIA) presents new EPA estimates of cancer incidence and mortality risks associated with exposure to low doses of ionizing radiation for the U.S. population, with the scientific bases for these decisions. Most estimates are calculated with models recommended in the National Research Council's BEIR VII Report (U.S. NAS/NRC 2006), sponsored by EPA and other federal agencies.

The draft "Blue Book" is impressively researched and well written. The RAC responses to the request for comment on the three topics that EPA staff itemized are listed below.

1) Appropriateness of approaches used by EPA that were not specified in BEIR VII or modified relative to BEIR VII.

The RAC recommends that for low-energy beta particles, gamma rays, and x rays, because insufficient information for selecting RBE values has been presented, EPA staff encourage publication in a peer-reviewed journal of such information for review by the scientific community and then propose RBE values based on this survey.

The RAC recommends—in contrast to BEIR VII -- use of a weighted arithmetic mean for each set of excess absolute risk (EAR) and excess relative risk (ERR) values in transferring lifetime attributable risk (LAR) to the U.S. population from the Japanese life-span study (LSS) population. Use of neither the arithmetic nor geometric mean has a theoretical basis. The most important reasons for using the arithmetic mean are that the choice of weights

explicitly captures judgments about the relative importance of the ERR-and EAR-based risk estimates, and that risk estimates can be added.

The RAC agrees with the approaches proposed by EPA to derive risk estimates for solid cancers not specified in BEIR VII (kidney, skin) or that differed from those used by BEIR VII (lung, liver, leukemia), and also agrees with the EPA approach for skin cancer and prenatal exposure. ***The RAC recommends that, for bone, the EPA utilize the radium data for the dial painter cohort (as asserted in the"Blue Book", but not done), especially applying recent analyses of the data.***

The RAC compliments EPA on developing an improved model that considers the survival rate of breast cancer patients. It suggests applying this model to other cancers with high rates of survival.

2) Adequacy and reasonableness of the uncertainty analysis by the EPA, which is somewhat altered and expanded relative to BEIR VII.

The approach to uncertainty analysis in the draft "Blue Book" is reasonable and comprehensive for deriving overall risk estimate uncertainty from sampling variation, model parameters, and data transfer to the U.S. population***. The RAC recommends greater clarity and transparency in quantifying each source of uncertainty.***

The RAC recommends detailed explanations of Bayesian analysis strengths and weaknesses. The two distinct approaches to obtain best estimates and confidence intervals should be justified, and why Bayesian analysis is used for the latter.

The RAC recommends verifying the uncertainty analysis by determining uncertainty intervals by a perturbation approach. The value of each major contributor to uncertainty should be varied over a reasonable range to calculate the corresponding range of point estimates.

The RAC recommends that EPA clarify the reasoning behind the selection of distributions chosen for the sources of uncertainty. The discussion should justify the assigned distributions and trace each decision concerning central value, uncertainty, and distribution.

3) Validity of EPA approach in terms of scientific defensibility, appropriateness, presentation of calculations and results, and accuracy, balance, and level of detail.

The "Blue Book" is scientifically defensible and appropriate. ***The RAC recommends that EPA enhance content by reporting further information from (1) studies of noncancer mortality; (2) recent*** **International Commission on Radiological Protection** ***(ICRP) and*** **United Nations Scientific Committee on the Effects of Atomic Radiation (***UNSCEAR) ***reviews; and (3*****) National Council on Radiation Protection and Measurements** ***(NCRP) Report #159 on the risks of radiation-induced thyroid cancer.***

The calculations and results presented in the draft "Blue Book" are understandable. ***The RAC recommends for improved understanding that (1) the first chapter include a thorough***

discussion of EPA plans to use "Blue Book" contents in preparing Federal Guidance Report (FGR) 13, and (2) the seventh chapter present sufficient FRG values of radionuclide risk coefficients to permit evaluating the impact of the presented models and values.

The draft "Blue Book" with the suggested improvements will have the accuracy, balance and level of detail appropriate to its intended purpose. ***The RAC recommends that improvements include: (1) reporting available studies of cohorts exposed to protracted low doses of ionizing radiation; (2) focusing on the major sources of error in uncertainty analysis; and (3) considering distinguishable types of cancer within a given organ.***

The augmented RAC appreciates the opportunity to review this draft document and hopes that its recommendations will enable EPA to implement modifications in the current methods for estimating radiogenic cancer risks and update the "Blue Book" accordingly. We look forward to your response to the recommendations contained in this review.

Sincerely,

Dr. Deborah L. Swackhammer
Chair, Science Advisory Board

Dr. Bernd Kahn
Chair, Radiation Advisory Committee Augmented for Review of the Agency's Radiogenic Cancer Risk Assessment
Science Advisory Board

NOTICE

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U.S. Environmental Protection Agency
Science Advisory Board (SAB)
Radiation Advisory Committee (RAC)
Augmented for the Review of EPA's Radiogenic Cancer Risk Assessment

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1. EXECUTIVE SUMMARY

The Radiation Advisory Committee (RAC) of the Science Advisory Board (SAB) has completed its review of the Agency's draft titled *"EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population "* dated December 2008, also known as the "Blue Book." (U.S. EPA. ORIA. 2008). In the draft Blue Book, the EPA's Office of Radiation and Indoor Air (ORIA) outlined proposed changes in the Agency's methodology for estimating radiogenic cancers and estimating radiogenic cancer risk. The EPA sought the RAC's advice on its draft Blue Book to conduct the radiogenic cancer risk assessment for EPA's purposes.

The RAC responded as follows to the itemized requests by ORIA for comments:

Charge Question 1 on models not directly taken from BEIR VII

1a. The RAC agrees with the risk estimates proposed by EPA for alpha particles, which have greater linear energy transfer (LET) than beta particles, gamma rays and X rays and higher relative biological effectiveness (RBE) values. In contrast, for low-energy beta particles (notably tritium) and low-energy photons, the RAC finds that the EPA review of information is sufficient to conclude that the RBE exceeds 1, but insufficient for selecting appropriate RBE values. ***The RAC recommends that EPA staff encourage publication of information that will support proposed RBE values of low-energy beta particles and photons for review by the scientific community in a peer-reviewed journal, and then select the RBE based on these models and values.***

1b. ***The RAC recommends – in contrast to BEIR VII -- use of a weighted arithmetic mean for each set of excess absolute risk (EAR) and excess relative risk (ERR) values in transferring lifetime attributable risk (LAR) to the U.S. population from the life span study (LSS) population.*** The most important reason, in the absence of a theoretical basis for either the arithmetic or the geometric mean, is that the arithmetic mean results from a linear addition and averaging of excess risk data, with equal emphasis on higher and lower values. The choice of weighting factor then explicitly captures judgments about the relative importance of the ERR- and EAR-based risk estimates. This approach has other benefits as well, such as consistency with uncertainty estimates. Neither the EPA approach nor the BEIR VII approach to calculating the geometric mean (although the former was supported in the RAC review of the EPA White Paper because of its calculational consistency) provides any calculational advantages relative to the arithmetic mean.

1c. The RAC agrees with the approaches proposed by EPA to derive risk estimates not specified in BEIR VII for solid cancers (kidney, skin), or that differed from those used by BEIR VII (liver, lung, leukemia). ***The RAC recommends that, for bone, the EPA utilize the radium data for the dial painter cohort (as asserted in the Blue Book, p.64, but not done), especially applying recent analyses of the data***. With regard to the liver, the RAC cautions that the organ is subject to tumors with diverse histopathologies and possibly different outcomes. For leukemia, the RAC notes the considerable uncertainty related to EPA changing the RBE for alpha-particle radiation from 1 to 2.

1d. The RAC compliments EPA on developing an improved model that considers the survival rate of breast cancer patients. It suggests applying this model to derive risk estimates for other cancers (e.g., colon cancer) for which the survival rates are now relatively higher than previously.

1e. The RAC agrees with the EPA approach for separating from its overall risk estimates the specific risks for nonfatal skin cancer. Because of the high rate of spontaneous (nonradiogenic) nonmelanoma skin cancers and the experience that most nonmelanoma skin cancers are responsive to treatment, their inclusion with cancers that result in a much higher mortality rate would greatly distort the overall cancer morbidity and morbidity risk estimates.

The RAC also agrees with use by EPA of the same model for fetal and childhood exposure in calculating adult cancer risk. Differences between the two groups were not statistically significant.

Charge Question 2 on uncertainty analysis

2a. The RAC considers the approach to uncertainty analysis in the draft Blue Book to be reasonable and comprehensive in deriving overall risk estimate uncertainty from sampling variation, the various model parameters, and transfer of data to the U.S. population. ***The RAC recommends greater specificity, clarity and transparency in identifying and quantifying each source of uncertainty.*** One effective technique is to discuss each contributing uncertainty to the LAR in the text and summarizing it in a table (in greater detail than is now in the Blue Book), with emphasis on the major sources of uncertainty and how they are quantified.

The RAC recommends that the Blue Book make the Bayesian uncertainty analysis as consistent as possible with the point estimates of risk. Use of two separate approaches to obtain best estimate values and confidence intervals should be justified..

The RAC recommends verifying the uncertainty analysis by obtaining uncertainty intervals with a perturbation approach. The value of each major contributor to uncertainty should be varied over a reasonable range to recalculate the corresponding range of the point estimate to demonstrate whether the recommended uncertainty is valid.

2b. ***The RAC recommends that 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 is able to trace the basis of each decision concerning central value, uncertainty, and distribution, and have confidence in these characteristics.

Charge Question 3 on scientific defensibility, presentation, and completeness

3a. The RAC recognizes the scientific defensibility and appropriateness of the Blue Book***. The RAC recommends that EPA enhance Blue Book contents by reporting further information***

from (1) studies of non-cancer mortality; (2) recent ICRP and UNSCEAR reviews; (3) NCRP Report #159 on the risk of radiation-induced thyroid cancer, and (4) brain cancer studies.

3b. The RAC found that most of the calculations and results presented in the draft Blue Book were readily understandable. ***The RAC recommends an initial overview of the applications of models and values presented in the Blue Book; and a clearer and more transparent discussion of sources of uncertainty, their distribution, and of the Bayesian approach*** (see also 2a and 2b, above).

3c. The RAC considers the draft Blue Book to have the accuracy, balance and level of detail appropriate to its intended purpose, once the recommended revisions noted in this review are implemented. ***The RAC recommends enhancing the Blue Book by giving additional attention to the following specific items: (1) available studies of cohorts exposed to low-dose protracted exposure; (2) the major sources or error in uncertainty analysis (3) distinguishable types of cancer within a given organ; and (4) a list of at least some values of radionuclide risk coefficients to indicate the ultimate products toward which the draft "Blue Book" is directed.***

2. INTRODUCTION

2.1 Background

In 1994, the U.S. Environmental Protection Agency (EPA) published the report, titled *"Estimating Radiogenic Cancer Risks,"* often referred to as the "Blue Book", derived from the blue cover on the document (http://epa.gov/radiation/docs/assessment/402-r-93-076.pdf). This EPA estimation of cancer risks due to low-Linear Energy Transfer (LET) radiation exposures is based on information, mainly about the Japanese atomic bomb survivors, that had become available since the publication of BEIR III Report (U.S. NAS/NRC, 1980) and the Blue Book (EPA 1984) that followed it. The incidence of fatal cancer in specified organs and tissues per unit dose was estimated for a stationary U.S. population based on 1980 vital statistics. The effect of high-LET alpha particles also was considered in terms of their relative biological effectiveness (RBE). The 1994 report replaced the 1984 EPA report.

In 1999, an addendum to the 1994 report made minor adjustments to the previous values in terms of more recent vital statistics. The addendum also presented a partial analysis of the uncertainties in the values (http://epa.gov/radiation/docs/assessment/402-r-99-003.pdf) to provide a confidence interval for the cancer risk per unit radiation dose.

Also in 1999, the Agency applied the 1994 Blue Book contents, metabolic models, and usage patterns to publish Federal Guidance Report 13, *"Health Risks from Low-level Environmental Exposure to Radionuclides"*, with cancer risk estimates for over 800 radionuclides by several exposure pathways. (http://epa.gov/radiation/docs/federal/402-r-99-001.pdf). models and U.S..usage patterns. The data were later updated at (http://www.epa.gov/radiation/federal/techdocs.html#cd_supplement). Prior to their publications, the Blue Book and the two subsequent documents were reviewed by the EPA's Science Advisory Board (SAB).

In 2006, the National Research Council of the U.S. National Academies of Sciences (NAS/NRC) released *"Health Risks from Exposure to Low Levels of Ionizing Radiation BEIR VII Phase 2"*(BEIR 2006), which primarily addresses cancer and genetic risks from low doses of low-LET radiation (available at http://newton.nap.edu/catalog/11340.html#toc). The Agency was one of the sponsors of this report.

Also in 2006, EPA prepared the draft "*White Paper: Modifying EPA Radiation Risk Models Based on BEIR VII"* (EPA/ORIA 2006), (available at http://epa.gov/radiation/docs/assessment/white-paper8106.pdf), in anticipation of issuing a revised Blue Book. In the White Paper, the Agency proposed changes to the EPA's methodology for estimating radiogenic cancers. The Agency expected to adopt the models and methodology recommended in BEIR VII, but believed that certain modifications and expansions were desirable or necessary for the EPA's purposes. EPA's Office of Radiation and Indoor Air (ORIA) requested the SAB to review the Agency's draft White Paper and provide advice

regarding the proposed approach to dose-response assessment of radionuclides. The EPA SAB/RAC prepared an advisory, EPA-SAB-08-006 (EPA/SAB 2006) (see http://yosemite.epa.gov/sab/sabproduct.nsf/FD9963E56C66E4FF852573E200493359/$File/EPA-SAB-08-006-unsigned.pdf). The SAB reviews responding to the above-cited EPA documents can be found on the EPA SAB Web site at http://www.epa.gov/sab.

The EPA's Office of Radiation and Indoor Air (ORIA) issued the draft of the revised Blue Book, entitled *"EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population"* (EPA, December 2008), and asked the SAB to review it. The draft document utilizes the advice contained in the BEIR VII, Phase 2 report, as well as the SAB's recently completed advisory for the White Paper described above; The Charge Memorandum (EPA/ORIA 2009) has the specific charge questions given in Section 2.3 below, provided to the SAB's augmented RAC with the completed draft document. The document reviewed – the draft Blue Book -- includes the uncertainty estimates (from the 1999 document review by the SAB/RAC), and contains specific methodology applications for estimating the risks of radiogenic cancers for many organs and tissues.

2.2 Review Process and Acknowledgement

The SAB RAC met in a public teleconference on February 27, 2009, and conducted a public meeting on March 23, 24, and 25, 2009, for this review (see 74 Fed. Reg., 5935, February 3, 2009). Additional public teleconference took place on June 18, 2009 (see 74 Fed. Reg., 25529, May 28, 2009) and July 22, 2009 __. These notices, the charge to the RAC and other supplemental information may be found at the SAB's Web site (http://www.sab.gov/sab). The quality review draft advisory dated August __, 2009, was forwarded to the Chartered SAB for its September 23, 2009, public teleconference meeting (see 74 Fed. Reg., _____, August __, 2009). This advisory also reflects suggested editorial changes from the Charter SAB.

The draft document *"EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population," December*, 2008 was scientifically sound and well written. Presentations by the EPA staff to the RAC, as well as the public commentary, in the course of the public meetings were helpful. The EPA staff provided useful clarifications of its approach to preparation of the draft Blue Book, and conveyed information in response to questions by the augmented RAC that was necessary to perform this review. The EPA/ORIA staff responded to all RAC requests and was forthcoming in explanations and clarifications.

2.3 EPA Charge to the Committee

2.3.1 Background

In 1994, the Environmental Protection Agency (EPA) published a report, referred to as the "Blue Book," which lays out EPA's current methodology for quantitatively estimating radiogenic cancer risks. A follow-on report made minor adjustments to the previous estimates and presented a partial analysis of the uncertainties in the numerical estimates. Finally, the Agency published Federal Guidance Report 13 (FGR-13), which utilized the previously

published cancer risk models, in conjunction with International Commission on Radiological Protection (ICRP) dosimetric models and U.S. usage patterns, to obtain cancer risk estimates for over 800 radionuclides, and for several exposure pathways. Prior to their publications, these three documents were first reviewed by the Science Advisory Board (SAB).

The National Research Council of the National Academies of Sciences released a report in 2006 on the health risks from exposure to low levels of ionizing radiation. Co-sponsored by the EPA and several other Federal agencies, *Health Risks from Exposure to Low Levels of Ionizing Radiation BEIR VII Phase 2* (BEIR VII) primarily addresses cancer and genetic risks from low doses of low-energy transfer (LET) radiation.

In a White Paper which was the subject of an SAB advisory review in 2006, the Agency outlined proposed changes to its methodology for estimating radiogenic cancers, based on the contents of BEIR VII and some ancillary information. For the most part, the Agency proposed adopting the models and methodology recommended in BEIR VII; however, in the White Paper the Agency also noted that certain modifications and expansions were desirable or necessary for their purposes.

The Agency accepted the recommendations of SAB, and is now requesting that the Agency's Science Advisory Board review the attached draft document entitled *EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population,* dated December 2008, which was developed as a result of the previous White Paper advisory review The revised Blue Book will then serve as a basis for an updated version of FGR-13.

2.3.2 Specific Request

This draft document presents the scientific basis for new EPA estimates of cancer incidence and mortality risks due to low doses of ionizing radiation (IR) for the U.S. population. These estimates are based on available information, and for the most part, are calculated using models recommended in the National Research Council's BEIR VII Report.

1. As in BEIR VII, models are provided in the draft document for estimating lifetime risk as a function of age at exposure, gender, and cancer site, but a number of extensions and modifications to the BEIR VII approach have been implemented. First, BEIR VII focused on the risk from low-LET radiation only, whereas risks from higher LET radiations are also addressed here. Second, this document presents a slightly modified approach for combining BEIR VII models for projecting risks from Japanese A-bomb survivors to the U.S. population. Third, this document goes beyond BEIR VII in providing estimates of risk for kidney, skin, and bone cancers. Fourth, a modified method is employed for estimating breast cancer mortality risk, which corrects for temporal changes in breast cancer incidence and survival. Finally, quantitative estimates of risks for skin cancers and from prenatal exposures are included. Please comment on the appropriateness of the following either not specified in BEIR VII or otherwise modified by EPA from BEIR VII:

a. Approaches described for extending risk estimates to radiations of different LETs - in particular, deriving site-specific risk estimates for alpha or low-energy electron and low-energy photon radiations based on models derived from the A-bomb survivors, who were primarily exposed to higher energy gamma rays (see Section 5) .[Note: the Sections indicated here refer to the draft EPA/ORIA Report.]
b. EPA's adaptation of the BEIR VII weighted geometric mean approach for combining the EAR and ERR models for projecting risk from the LSS to the U.S. population (see Sections 3.9).
c. Estimation of risks not specified in BEIR VII, including kidney, bone, and skin cancers, as well as for alpha particle irradiation of the liver (see Sections 3.3 and 5.1).
d. Method for calculating breast cancer mortality risk, accounting for the relatively long time from detection until death (see Section 3.10).
e. Approach for separating out nonfatal skin cancers and risks from prenatal exposures from the overall risk estimates (see Sections 3.3 and 6).

2. BEIR VII's approach to uncertainty is primarily based on data from the Life Span Study (LSS). The LSS provides a great deal of information on risks for many cancer sites; however precision is limited by errors in dosimetry and sampling errors. The sampling errors are often quite large for specific cancer types, and the uncertainties are even larger if one focuses on a specific gender, age at exposure, or time after exposure. Another important uncertainty is the transfer of site-specific cancer risk estimates to the U.S. population, based on results obtained on the LSS population, for sites with substantially different baseline incidence rate. Compared to BEIR VII, this document provides a somewhat altered and expanded analysis of the uncertainties in the cancer risk estimates.

   Regarding the uncertainty analysis contained in Section 4,

   a. Please comment on the adequacy of the approach to uncertainty analysis.
   b. Are the distributions chosen for the various sources of uncertainty reasonable?

3. Please comment on the presentation of the following overall information and application of BEIR VII contained in the draft document:

   a. Scientific defensibility and appropriateness of the models and assumptions employed for estimating risk.
   b. Presentations of the calculations and results.
   c. Regarding the document's intended purpose, the accuracy, balance, and level of detail of the scientific background material presented.

2.4 Blue Book Overview

The introductory Chapter 1 cites the earlier Blue Book (EPA 1994) and the BEIR VII Report (2006). The BEIR VII Report is the major source of information, but more recently published information has also been considered. Major sources of uncertainty are highlighted.

Chapter 2 presents the scientific basis for cancer risk. It briefly discusses biological mechanisms that lead to radiogenic carcinogenesis. It describes a modified linear no-threshold hypothesis and the extrapolation of low–LET risks from the measured results at relatively high radiation doses to exposures at low doses and low dose rates. A Dose/Dose Rate Effectiveness Factor (DDREF) is introduced for calculating the risk due to chronic low-dose and low-dose-rate radiation exposure. Several effects that have been observed or proposed at low doses are discussed, but are not invoked in subsequent calculations of risk. The authors present a survey of the epidemiologic evidence for radiogenic cancer risk, notably the Life-span Study (LSS) of atomic bomb survivors at Hiroshima and Nagasaki, but also patients exposed to medical radiation. Epidemiological studies are cited of cohorts exposed to low levels of radiation over extended periods, such as radiologists and nuclear workers.

The draft Blue Book presents revised estimates of cancer incidence and mortality risks due to low doses of ionizing radiation for the U.S. population. The risk estimates for solid cancers and leukemia, following exposure to low doses of low-LET radiations, are derived exclusively from preferred models developed by the BEIR VII committee. These models are applied to a stationary population based on survival rates in the U.S. to obtain an estimate of the lifetime attributable risk (LAR) per person-Gy for the U.S. population

The process for obtaining LAR is described in Chapter 3. It is based on a set of parameter values for the preferred Excess Relative Risk (ERR) and Excess Absolute Risk (EAR) models in BEIR VII (Table 3-3). The EPA then uses a geometric weighting scheme to combine the results from both the ERR and EAR models to obtain a point estimate of the excess absolute risk, M (d,a,e), at an attained age a, following a single exposure to dose d, at age e. This is applied to the stationary population to obtain their “best estimate” LAR.

Uncertainties in projections of LAR for low-LET radiations are described in Chapter 4. The focus of the uncertainty analysis is on the calculation of LAR per-person-Gy for the U.S. population based on the data for the LSS. It is an independent assessment of uncertainty with a methodology quite different from that used to obtain point estimates in Chapter 3.

Risk of radiogenic cancer associated with the high LET radiation of alpha particles is discussed in Chapter 5. Laboratory studies and human data are discussed. The latter include bone cancer associated with internal exposure to radium isotopes by injection (Radium-224) or ingestion (Radium-226, Radium-228); liver cancer associated with administration of diagnostic doses of Thorotrast to patients; plutonium intake by nuclear workers; and lung cancer among underground miners exposed to alpha particles from inhalation of radon gas and radon-daughter particles, and among Russian nuclear workers at risk of inhaling plutonium particles. The risk is

evaluated in terms of the RBE values based on contemporary data for alpha particles in specific organs or tissues.

Chapter 6 addresses risk from prenatal exposure to radiation. Induction of childhood cancer due to fetal radiation has been show in various case-control studies (Stewart, Webb et al. 1958; Macmahon 1962, and other references in Chapter 6, p.96). While a causal link between in utero radiation exposure and childhood cancer is generally accepted (Doll and Wakeford 1997), some have termed the evidence for childhood cancers other than leukemia equivocal (Boice and Miller 1999).

The atomic bomb survivors provide the only data on radiation effects on adult-onset cancer risks among persons exposed in utero (Preston, Cullings et al. 2008). The survivor data exhibit a statistically significant radiation dose response for adult-onset cancers with levels of risk that are considerably less than those reported for childhood cancers. There is also a weak suggestion that the radiation effect for those exposed in utero may be less than what has been seen for atomic bomb survivors exposed as children. The EPA makes the reasonable decision to base risk estimates for childhood cancers following in utero exposure on the summary risk estimates presented in (Doll and Wakeford 1997) and recommended by the ICRP (International Commission on Radiological Protection 2000), and risk estimates for adult-onset cancers on the corresponding risk estimates for childhood exposure.

In the very brief Chapter 7, application to calculating radionuclide risk coefficients is considered. The EPA will combine the revised excess cancer morbidity and mortality risk per Sv from this Blue Book with the latest available ICRP dose models to revise the risk for each radionuclide per Bq intake or per unit exposure by external radiation. This information will be reported in a revision of Federal Guidance Report 13. The authors expect some increases and some decreases, depending on the radionuclide and target organ.

3. RESPONSE TO CHARGE QUESTION 1: APPLICATION OF THE EXTENSIONS AND MODIFICATIONS TO THE BEIR VII APPROACH AS DESCRIBED IN THE DRAFT BLUE BOOK

3.1 Charge Question # 1: *As in BEIR VII, models are provided in the draft document for estimating risk as a function of age at exposure, age at risk, gender, and cancer site, but a number of extensions and modifications to the BEIR VII approach have been implemented. First, BEIR VII focused on the risk from low-LET radiation only, whereas risks from higher LET radiations are also addressed here. Second, this document presents a slightly modified approach for combining BEIR VII models for projecting risks from Japanese A-bomb survivors to the U.S. population. Third, this document goes beyond BEIR VII in providing estimates of risk for certain other cancers. Fourth, a modified method is employed for estimating breast cancer mortality risk, which corrects for temporal changes in breast cancer incidence and survival. Finally, quantitative estimates of risks for skin cancers and from prenatal exposures are included. Please comment on the appropriateness of the following either not specified in BEIR VII or else otherwise modified by EPA from BEIR VII:*

a. Approaches described for extending risk estimates to radiations of different LETs - in particular, deriving site-specific risk estimates for alpha or low energy electron and photon radiations based on models derived from the A-bomb survivors, who were primarily exposed to higher energy gamma rays (see Section 5).

b. EPA's adaptation of the BEIR VII weighted geometric mean approach for combining the EAR and ERR models for projecting risk from the LSS to the U.S. population (see Section 3.9).

c. Estimation of risks not specified in BEIR VII, including kidney, bone, and skin cancers, as well as for alpha particle irradiation of the liver (see Sections 3.3 and 5.1).

d. Method for calculating breast cancer mortality risk, accounting for the relatively long time from detection until death (see Section 3.10)

e. Approach for separating out nonfatal skin cancers and risks from prenatal exposures from the overall risk estimates (see Sections 3.3 and 6).

3.2 Response to Charge Question # 1a

3.2.1 Alpha Particle Radiation

To derive risk estimates for site-specific alpha particle-induced cancers, EPA proposes to use the BEIR VII gamma-ray risk estimates, directly or with proposed modifications as necessary, after applying an RBE of 20. Exceptions to this general approach are proposed for 1) Leukemia for which an RBE of 2 will be applied to the BEIR VII-based gamma-ray estimate; 2) Liver cancer with an RBE of 40;

3) Lung cancer, for which EPA proposes continuing its use of models derived from BEIR VI to estimate the lung cancer risk from inhaled radon progeny; and
4) Bone cancer for which the alpha particle risk per Gy is obtained by for patients exposed to ^{224}Ra by injection. This value will be divided by an RBE of 10 to obtain the low-LET risk..

The RAC considers reasonable and generally acceptable the general approach proposed by EPA for obtaining cancer risk estimates for alpha particle emitters using the RBE values that EPA proposes. Specific advice is given in response to question #1c (Section 3.4 below).

3.2.2 Low-Energy Electron and Photon Radiations

Extensive discussion by RAC members regarding proposed changes by EPA to the RBE for low-energy electron and photon radiations identified the following items that should be addressed in the Blue Book:

- Was this change recommended/suggested/implied in BEIR VII?
- Does ICRP, NCRP, UNSCEAR have similar recommendations?
- Does NIOSH (IREP) use an RBE > 1?
- Is the scientific rationale for this change suitably mature at present (Health Protection Agency report)?
- What will be the reference source (1 MeV electrons and/or ^{60}Co)?
- Will this change be restricted only to radionuclides with energies similar to ^{3}H?
- How will the “estimations” of “low energies” be determined in the case of mixed exposures (e.g., photons and beta particles)?
- What is the rationale for using cutoffs at specific energies, i.e., 1, 3 or 5 eV.
- Which radionuclides will be included and/or excluded?

In previous comments on the EPA White Paper (2006), RAC supported EPA use of an RBE of 2 – 2.5 for photons of energies less than 30 keV and for ^{3}H beta particles (18.6 – 0 keV). In light of this and the current discussion, the RAC recommends that EPA prepare a detailed argument/justification to support all proposed changes in the RBE values for specific ionizing radiations. The EPA should encourage preparation of a peer-reviewed publication that addresses these issues, and consideration of the responses by the scientific community.

In particular, more detailed justifications are recommended for proposed changes to the RBE (to ~ 1.4) for photon energies used in diagnostic medical x rays. Given that medical radiation exposures make up the majority of the average US individual’s annual radiation doses, the implications for individuals undergoing mammograms or CT scans might be significant in the long term. This justification is particularly important in light of the reference in the Blue Book to the Hunter and Muirhead (2009) study (page 95), Risk coefficients derived from studies of cohorts medically irradiated with x rays are in some cases lower than what has been observed for the A-bomb survivors.

3.3 Response to Charge Question # 1b

The site-specific risk estimates in BEIR VII were computed as a weighted geometric mean of ERR- and EAR-based LAR estimates for the current (2000) US population. The EPA has proposed a method to compute an average excess risk function as a weighted geometric mean of age- (and age-at-exposure-) specific excess rates for the ERR and EAR models and then to apply this average excess rate function to a stationary US population to compute the LAR. The EPA specifically asked the RAC about its decision to use an average excess rate function rather than averaging the ERR- and EAR-based LAR estimates. EPA staff explained during the meeting that the primary motivation for developing the average rate method was to insure additivity of age-specific risks.

The RAC recommends that the LAR computation makes use of the weighted arithmetic mean instead of the choice described by EPA. The RAC considers the arithmetic mean preferable even though this is a departure from the BEIR VII approach and even though the RAC endorsed the average rate method in its review of the White Paper (U.S.EPA/SAB 2008). The primary reason for this RAC recommendation is that the geometric mean implicitly tends toward the lower risk estimate whereas the arithmetic mean equally balances the low and high risk estimates. It is the selection of weights that explicitly captures judgments about the relative importance of the ERR-and EAR-based risk estimates for weighted arithmetic means. Furthermore, because the use of arithmetic means for risk estimates insures additivity of the age-specific risk estimates, the RAC also recommends that the Blue Book present both ERR- and EAR-based LAR estimates and then compute the suggested risk estimate as a weighted arithmetic mean of the two estimates.

The BEIR VII report does not discuss these issues; geometric means may have been used primarily because they simplified the analytical uncertainty assessment carried out for BEIR VII. Because the EPA is using Bayesian Monte-Carlo methods to assess uncertainty, the complexity of the uncertainty evaluation is not affected by how the risks are combined.

Arithmetic means have been used for the current (and earlier) ICRP recommendations. The Interactive Radio-epidemiology Program (IREP) also uses arithmetic means to combine relative-risk and excess-risk based estimates when computing probability of causation estimates. The 2000 and 2008 UNSCEAR reports (UNSCEAR 2000, 2008) present ERR- and EAR-based estimates, but do not combine them.

A key issue is the weighting of the two models. The general sense of the RAC is 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 more accurately. This emphasis appears in the point estimation process, which to the extent that it follows BEIR-VII places a weight of 0.7 on the ERR and 0.3 on the EAR results. Observations of tumor sites with different frequency of background occurrence, and sometimes also over different strains of experimental animals, show that ERR parameters tend to be more similar than EAR parameters (Preston et al. 2007).

Use of arithmetic instead of geometric means for averaging results based on ERR and EAR models should improve consistency between the recommended point estimates and central estimates from the uncertainty analysis. To resolve remaining discrepancies, the RAC suggests that EPA make the prior distributions of weight parameters for the ERR and EAR models used in the uncertainty analysis more compatible with the provided point estimates.

One question that arises if weighted arithmetic means are used in place of weighted geometric means concerns the need to change the site-specific ERR/EAR weights recommended by BEIR VII. The RAC does not believe that EPA should do so because BEIR VII members apparently were thinking in terms of linear (arithmetic) weights when they defined the weights used in their computations. The RAC does recommend that the Blue Book include a brief discussion concerning the greater weight given to the ERR-based risks than to the EAR-based risks in most cases, but not all (for example, lung and breast cancer).

The RAC agrees with the EPA decision to use a stationary population rather than a census-based population in LAR computations. The reasons for this change were cogently described in the EPA staff presentation to the RAC. The RAC recommends that this discussion (including presentation of gender-specific population pyramids (or age-adjusted rates for selected cancers) be included in the Blue Book to show the effect on risk estimates for solid cancers of the switch from a census based population to a stationary population.

3.4 Response to Charge Question # 1c

3.4.1 Kidney

In the absence of adequate epidemiological data for deriving a separate estimate for the risk of radiogenic kidney cancer following exposure to low LET, the EPA rationale for its proposed approach to kidney cancer by using the BEIR VII residual cancers ERR model and the EAR model with an adjustment factor is reasonable. The RAC recommends that EPA, in support for its rationale, look to the expected summary of cancer sites that have limited or inadequate data in the soon-to-be-published updated report by the International Agency for Research on Cancer (IARC) on the cancer risks of ionizing radiation.

3.4.2 Bone

The RAC notes that its Advisory on the Agency Draft White Paper (2008) (section 5.7, page 19) supported the use of human data to derive estimates of the bone cancer risk from ^{224}Ra. The data from the study of radium dial painters who were exposed to ^{226}Ra and ^{228}Ra were recommended to derive directly the bone cancer risk from these radionuclides. Although these approaches are outlined in the draft Blue Book (section 4.2.2, page 64), use of the radium dial painter data was proposed but apparently not pursued. The more detailed approach proposed in section 5.1.2, pages 84-85, does not reflect attention to the Advisory's recommendation. The RAC now reiterates this recommendation because the nature of the exposures (chronic, lifetime) and their biokinetics for ^{226}Ra and ^{228}Ra are different than for ^{224}Ra.

When reconsidering the use of the radium dial painter data, the RAC recommends that EPA include the more recent analyses of the data for this population (Carnes et al. Radiat.Res.1997; Hoel and Carnes, 2004).

3.4.3 Skin (Fatal and Non-Fatal Non-melanoma Cancers)

EPA proposes, in draft Blue Book pages 31-32, to deviate from its previous approach (EPA 1994) based on ICRP recommendations (ICRP 1991b) for estimating the risk of radiation-induced non-melanoma skin cancer (NMSC). This change reflects the findings of more recent epidemiological analyses, changing disease patterns, and the conclusion that essentially all NMSCs induced by low-to moderate doses of ionizing radiation are of the basal cell type and non-fatal (Shore 2001; Preston et al 2007; Karagas et al1999; Ramsey, 2006 – as in the draft Blue Book).

The RAC considers the proposed updated approach for deriving risk estimates for fatal and nonfatal NMSC to be reasonable and acceptable. This EPA approach applies its new model described in the Blue Book with age-specific baseline incidence rates to derive the ERR for nonfatal (incidence) radiation-induced NMSC. More recent estimates of mortality due to basal cell carcinoma in the general population (Lewis and Weinstock, 2004) will be used as baseline data in estimating the risk of fatal radiogenic NMSC. The NMSC risks for both incidence and mortality will be estimated for males and females separately and in combination (sex-averaged). EPA also will use the revised DDREF value of 1.5 (BEIR VII) to derive NMSC risk estimates in the low-dose range in place of the value 2 used previously.

3.4.4 Liver

The liver is recognized as a target organ for certain alpha-particle emitters. The relevance of the colloidal nature of Thorotrast should be considered and how this might impact the radiogenic risks of liver cancer. Comparison of the liver cancer risk estimate for gamma radiation derived by BEIR VII from the LSS data with that obtained from the follow-up study of Danish Thorotrast patients suggested an RBE of 20 for alpha-particle radiation (Andersson et al. 1994). While recognizing the uncertainties inherent in both studies with respect to liver cancer and the value of this RBE, EPA initially proposed the use of an RBE of 20 with the BEIR VII liver cancer risk estimate to derive an estimate for alpha particle-induced liver cancer (U.S. EPA/ORIA, 2006). The RAC supported this approach for liver and certain other cancers that have been associated with alpha particle radiation (U.S. EPA/SAB, 2008) with the recommendation that any additional epidemiological data be taken into consideration.

Based on additional data from the follow-up study of German Thorotrast patients (Van Kaick et al. 1999) and a reanalysis of the Danish patient data (Leenhouts et al. 2002) with an empirical model and a lifetime risk projection, EPA has revised its proposal to use a scaled version of the BEIR VII model. The EPA now will use BEIR VII's low-LET age and gender-specific liver cancer risk estimates and an RBE of 40 to provide risk estimates for alpha-particle induced liver cancer at environmental low doses. The RAC considers this approach reasonable, and the use of an RBE of 40 as appropriate. However, because in the context of this report, 'liver cancer' (like 'cancer' in most other organs) is an all-embracing term that includes a diverse

number of histopathologies, the RAC cautions that the uncertainties associated with grouping these different tumor histopathologies may outweigh any benefits gained by changing the RBE to 40.

3.4.5 Lung

The draft Blue Book adopts an RBE of 20 for lung cancer by alpha-particle emitters other than radon, for which BEIR VI models are used. A separate risk model for radon is the best approach as outlined in the draft Blue Book. The human epidemiological evidence for other inhaled alpha-particle emitters comes primarily from the Mayak studies, because other studies do not have significant power to estimate risks. As noted in the draft Blue Book, the Mayak studies are in an early stage, but several reports are available. The lung cancer risk estimates reported by the two most recent Mayak reports (Jacob et al. 2007; Sokolnikov et al. 2008) were consistent with an RBE of 20 for males and 10 for females (Kreisheimer et al. 2000).

Given the preliminary nature of the Mayak studies, EPA proposes to use an RBE of 20 for both males and females. The RAC considers this approach reasonable. The same value of 20 has been recommended recently by the ICRP (2003, 2005).

Animal studies show RBE values at, above, and below 20. Some animal studies of radionuclides deposited in the lung obtained an RBE value of 20 or above (Gilbert et al. 1997; Hahn et al. 1999; Lundgren et al. 1995, 1996, 1997; Muggenburg et al. 1996, 2008) by comparing the effects of radionuclides that emit alpha particles with those that emit beta particles and gamma rays. Other animal studies suggest a much lower RBE (Priest et al. 2006). The RAC suggests caution in applying these values for animals in many of these groups that were exposed to doses above 1Gy, well above the low-dose range, because results from such elevated doses have a strong influence on the shape of the dose response curve and the calculated RBE.

3.4.6 Leukemia

The draft Blue Book recommends an RBE of 2 for alpha-particle induced leukemia based on human epidemiological studies at low doses of ^{224}Ra. This is a change from the value of 1 used in past EPA reports. The RAC considers the RBE of 2 to be reasonable, and 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 ^{224}Ra group for the appearance of leukemia. Animal studies have not been helpful in understanding the RBE for alpha particles because they have not had sufficient power to estimate leukemia risks from radiation (REF.).

3.5 Response to Charge Question # 1d

BEIR VII computed breast cancer mortality risk estimates by scaling age-specific incidence risks for the ratio of the (age-specific) mortality-to-incidence rate ratios. EPA proposes replacing this simple ratio by a factor that allows for the relative survival of breast cancer patients. The data presented to the RAC by EPA staff strongly suggest that the modified method leads to more realistic breast cancer mortality risk estimates. The RAC believes that the EPA method is an improvement over that used by BEIR VII because the relative survival of

breast cancer patients is high and the excess risk estimates, including those derived by application of ERR estimates, used in the LAR computations increase with attained age. The EPA should consider using a similar approach in computing mortality risks for other types of cancer, particularly those, such as prostate and uterus, with relatively high survival rates.

3.6 Response to Charge Question # 1e

3.6.1 Nonfatal Skin Cancer

As noted in the response to Question #1c with regard to Skin (Fatal and nonfatal cancers), the RAC supports the EPA proposal to update its approach for estimating the risks of radiation-induced NMSC in the light of more recent epidemiological data. In particular, the RAC supports Shore's conclusion that essentially all NMSC induced by ionizing radiation in the low to moderate dose range are of the basal cell type (BCC) with a very low mortality rate (Shore 2001), and hence, the EPA proposal to derive risk estimates for incidence and mortality due to radiation-induced NMSC from data for BCC.

The RAC supports EPA's decision, in keeping with usual practice, not to include NMSC risk estimates in estimating the estimates of total radiogenic cancer risk (see Tables in the draft Blue Book, Sections 3 and 4).

3.6.2 Prenatal Cancer Risk

The RAC considers that estimation of cancer risks from prenatal radiation in the draft Blue Book is appropriately based on the literature. Prenatal radiation exposure has been shown in some studies to be causally associated with increases in childhood cancers and, in the LSS, with increases in adult cancers.

In the draft Blue Book, EPA accepts a childhood cancer risk value of 0.06 Gy^{-1} (absolute risk for dying of leukemia by age 16) for prenatal exposure that was suggested by Doll and Wakeford (1997), and adopted by the ICRP (2000). This value has been controversial because other studies have been equivocal (Boice and Miller 1999), but the value is reasonable based on reviews of the evidence. This evidence is from medical x-ray doses and energies (80 kVp); the risk coefficient would be adjusted to 0.04 Gy^{-1} if the RBE of 1.4 for diagnostic medical x rays is adopted.

For estimating the risks of adult cancers among populations exposed *in utero,* EPA proposes adopting the cancer risk models in draft Blue Book section 3 with age set to zero. This approach is based on an analysis of A-bomb survivors exposed *in utero* that found a lower risk than those who were irradiated as young children, but the difference is not statistically significant (Preston et al 2008). The RAC considers this a reasonable approach.

Caution must be expressed because some spontaneous abortions may have occurred in women who received the higher doses in the periods immediately after the A-bombs. These were unaccounted for in the LSS and would lower the risk estimates. This possible problem should be mentioned by EPA as an additional source of uncertainty for prenatal exposure effects.

4. RESPONSE TO CHARGE QUESTION 2: THE UNCERTAINTY ANALYSIS

4.1 Charge Question # 2: *BEIR VII's approach to uncertainty is primarily based on data from the Life Span Study (LSS). The LSS provides a great deal of information on risks for many cancer sites; however precision is limited by errors in dosimetry and sampling errors. The sampling errors are often quite large for specific cancer types, and the uncertainties are even larger if one focuses on a specific gender, age at exposure, or time after exposure. Another important uncertainty is the transfer of site-specific cancer risk estimates to the U.S. population, based on results obtained on the LSS population, for sites with substantially different baseline incidence rate. Compared to BEIR VII, this document provides a somewhat altered and expanded analysis of the uncertainties in the cancer risk estimates.*

Regarding the uncertainty analysis contained in Section 4,

c. Please comment on the adequacy of the approach to uncertainty analysis.
d. Are the distributions chosen for the various sources of uncertainty reasonable?

4.2 Response to Charge Question # 2a

The approach to obtaining quantitative estimates of uncertainty is reasonable and comprehensive. The RAC, however, has identified specific issues, described below, related to the uncertainty analysis that should be addressed in order to clarify assumptions and to provide additional information for the readers of the draft Blue Book.

4.2.1 General Comments

The methods used for the full uncertainty analysis of stomach, colon, liver, lung, and bladder cancer are based on analysis of the data for the LSS. The LAR is a complex function of parameters that can be classified into three types. Type (I) are the risk estimates obtained from models using parameters derived from the LSS data. Type (II) are other parameters, such as RBE, DDREF, and population transfer, about which little or no direct information comes from the LSS data. Type (III) is the age distribution obtained from a hypothetical (stationary) population that mimics the US population. The goal of the uncertainty analysis in the draft Blue Book is to combine sampling variation in the estimates for Type (I) parameters with uncertainties in Type (II) parameters in order to provide an overall uncertainty estimate for the LAR that is calculated either separately for individual tumor types or for groupings of tumors (e.g. all solid tumors, leukemia).

A Bayesian analysis has been adopted by the EPA. It provides a consistent framework for the treatment of unknown parameters as random variables and a formal method for updating initial prior distributions for these random parameters with the information contained in the LSS

data about the parameters of Type (I). The Bayesian nature of the uncertainty analysis rests on a somewhat different statistical basis than a "frequentist" approach that yields the "best estimates" of LAR for these cancers. It is not surprising that the LAR uncertainty bounds from the Bayesian analysis are not symmetric around the best estimate.

Beyond the mere fact that the EPA uncertainty analysis of LAR is Bayesian in nature, the Bayesian analysis for stomach, colon, etc., actually is a joint analysis of these cancers and combines information about the linear ERR parameters across these cancer types. It estimates a common mean (but separately by sex) and a common variance in the distribution of these risk parameters. Doing this should have the useful property of reducing the uncertainty in the posterior distribution of these risk estimates, especially for rarer cancers where the information in the LSS is not large.

Because all Type (I) and Type (II) parameters are regarded as random variables, the LAR itself is treated as a random variable that is a function of these random variables in the uncertainty analysis. While this general framework is sound, it is complicated, especially given the need to provide prior distributions for all Type (I) and Type (II) parameters. Because of the large amount of direct data from the LSS related to incidence and survival, the selection of prior distributions for Type (I) parameters does not have a very strong effect on the final "posterior" estimates of these parameters. However, prior distributions specified for Type (II) parameters tend to dominate their posterior distributions because little or no information about these parameters is in the LSS data.

4.2.2 Specific Comments

The draft Blue Book should clearly state and justify why one method is used to obtain a point estimate of LAR and another method based on different assumptions is used for the uncertainty analysis. The Bayesian approach provides a posterior density function for LAR that could be used to obtain a "best estimate" (i.e. mean or median) as well as confidence limits for a quantitative description of uncertainty. Thus, a Bayesian approach could provide a consistent value for both the best estimate and uncertainty interval, to replace the frequentist approach for the best estimate, accompanied by Bayesian methods to estimate the confidence interval.

Presumably, EPA used separate approaches to obtain a best estimate and confidence intervals partly because the best estimate of a LAR for a specific cancer site does not impose the constraint that the risk estimates for each cancer be similar. Thus, because such risk estimates are not known *a priori* to be similar, it may be scientifically more sensible to use completely different analyses of each cancer subtype to give the best estimate, even if an assumption of commonality is necessary and reasonable to impose when evaluating uncertainty, especially for relatively rare cancers.

An additional reason why Bayesian analysis might not be applied to generating the best point estimates is that Bayesian estimates depend greatly on the details of the priors used for Type II parameters, which are inherently subjective. One also needs to utilize inherently subjective choices to develop the point estimate. However, the technical details and software (WinBUGS) used for the Bayesian analysis are quite delicate. Although WinBUGS (Lunn et al.

2000) is preferred for many Bayesian applications, convergence issues often arise. The Markov Chain methodology can be demanding. For example, minor changes in starting values used in the simulations can have a large effect on the results. In general, the RAC is sympathetic to the process of using specific assumptions for Type (II) parameters to produce the point estimates, but then allowing these to range widely when the uncertainty intervals are computed.

In addition to concerns relating to prior distributions, the RAC notes an overall lack of clarity concerning the likelihood function for the LSS data. The likelihood function for Poisson regression analysis of grouped survival data may not be very familiar even to readers relatively knowledgeable in statistics and should be described carefully. Moreover, because for the cancers listed above (stomach, colon, etc.), a joint analysis is being performed (where tables of person years and events are given for more than one outcome), the legitimacy of multiplying the likelihoods for each outcome together should be affirmed, even though the same "denominator" values (person years) are being used in each table.

The current description of LARs and corresponding uncertainty intervals are not sufficiently detailed. No indication is given as to which parameters, either Type (I) or Type (II), are the most influential in controlling the uncertainty intervals for LAR.

The RAC suggests that EPA create a table depicting the relative contribution of each source of uncertainty to the total uncertainty for each LAR (i.e., site-specific and overall). The sources of uncertainty include (1) incidence data (where 'incidence' includes both background and radiogenic incidence), (2) DDREF, (3) risk transport model, and (4) "other" (EPA) data sources, including age and time dependence, errors in dosimetry, and diagnostic misclassification. The relative contribution could be expressed as a percent or as the squared correlation between LAR uncertainty and each source of uncertainty, i.e. the correlations, between the random parameters and the LAR, in the Monte-Carlo simulations used to evaluate the posterior distributions of these quantities.

Given the delicate nature of the Monte Carlo Markov Chain calculations, verification of the uncertainty intervals so obtained by a perturbation approach would be beneficial as a means of extending the analysis. The RAC suggests the following: Use the results of the current approach to the uncertainty analysis to identify one or two key parameters for each point estimate (where 'key' means most contributory to overall uncertainty). Then, in the model used to generate the point estimate, vary the key parameters over their range in a parametric sensitivity analysis (perturbation analysis) to generate a range of resulting risk estimates. This should indicate the operational range of the point estimate. In this way, one can verify whether the results of the current uncertainty are appropriate for a given point estimate, and observe the width of confidence intervals for that point estimate.

As a general methodological comment on the usefulness of the posterior densities resulting from a Bayesian approach, the RAC suggests considering in future risk predictions the concept of the predictive density. It is well established in other applications of survival analysis, e.g. reliability analysis, and takes all remaining parameter uncertainty into account for the calculation of predicted quantities. Increased computing power and advances in numerical

integration (e.g., Quasi Monte Carlo Methods) make this feasible if the dimensionality of the integrand is not too high (e.g. < 10). (c.f. Bolstad 2007).

When comparing the results of the draft Blue Book to previous estimates published in FGR 13, the authors stated that "The overall increase in LAR is not due to changes in the basic risk models," but that; "…the increase in results is largely attributable to the use of the more recent SEER incidence data as a primary basis for calculating incidence rates." To what extent is this reflected in the distributions for sources of uncertainty in Table 4.2?

The prior distributions for Type (I) parameters in the ERR and EAR risk models are formed with numerical distributions of the parameters themselves from Table 4.1. Uncertainty of the Type (II) parameters is based on the product of a constant (i.e. DDREF =1.5) and a random multiplicative factor [LN (GM=1,GSD=1.35)]. What is the reason for the two different approaches? It seems that a multiplicative factor that is log-normally distributed would lead to a bias unless the mean value for this multiplicative factor is equal to 1.0. This is not the case for LN(0.95, 1.1) or LN(1.1, 1.1).

4.2.3 Additional Comments on Risk Transfer

Risk due to radiation exposure may differ between populations for many reasons. Important issues such as population differences in genetic susceptibility to cancer and how such genetic differences would interact with radiation are only now beginning to be understood. Risk assessments by UNSCEAR, ICRP, BEIR VII and the draft Blue Book, make the implicit assumption that, if the background rate of a particular cancer is similar in two populations, then the excess radiogenic cancer risk also will be similar. In reality, this may be a simplification and as we learn more about genes (or environmental exposures other than radiation) that interact with radiation, we may find that many of them differ in gene or exposure frequency between Japanese and US populations. Nevertheless, a reasonable assumption, given today's lack of knowledge, is that cancers with similar baseline rates will have similar response to radiation exposure in the two populations. This forms the basis for transferring risk models and the associated LAR calculations from the Japanese to US populations.

For cancers with widely different baseline risks (e.g., stomach or prostate cancer), between the Japan and US populations, the choice of an ERR or EAR model can make a large difference in the LAR when applying the Japanese risk estimates to the US data. One key Type (II) parameter is the weighting parameter which interpolates between the EAR and ERR models. The LSS data provide no direct information about whether EAR or ERR models are more reasonable because both models provide equivalent descriptions of the LSS data.

The uncertainty analysis gives only a slight overall bias in favor of ERR compared to EAR models in the MCMC calculations. The tendency for the EAR models to be stressed more in the uncertainty analysis than in the point estimation may be the reason why in Table 3.11 the point estimates for stomach cancer (31 cases per 10,000 person Gy) are so far from the midpoint of the uncertainty interval (9-280 cases per 10,000 person Gy).

4.3 Response to Charge Question # 2b

The RAC did not identify any specific issue with the selection of distributions used to characterize uncertainty in parameters for used in the models to obtain LAR, but recommends that the EPA clarify the reasoning behind the selection of the subjective priors used in the analysis (e.g., in Table 4-1). This information would also increase transparency of the draft Blue Book and facilitate future scrutiny and verification of the assumptions used in the uncertainty analysis.

5. RESPONSE TO CHARGE QUESTION 3: COMMENTS ON PRESENTATION OF OVERALL INFORMATION AND APPLICATION OF BEIR VII IN THE DRAFT BLUE BOOK

5.1 Charge Question 3*: Please comment on the presentation of the following overall information and application of BEIR VII contained in the draft document:*

a. Scientific defensibility and appropriateness of the models and assumptions employed for estimating risk.
b. Presentations of the calculations and results.
c. Regarding the document's intended purpose, the accuracy, balance, and level of detail of the scientific background material presented.

5.2 Response to Charge Question # 3a

The RAC finds that the draft Blue Book presents models and assumptions for estimating risk that are broadly applicable and scientifically defensible. It is part of a good effort to prepare a series of steps that apply various models – especially those by BEIR VII for low-LET radiation -- as a basis for radiation protection regulations. Also commendable is the related EPA effort to improve BEIR VII models and to apply other models for cancer risks that BEIR VII does not address. The RAC suggests the following topics for consideration in improving the draft Blue Book.

5.2.1 Consideration of Non-cancer Mortality

The current report focuses on cancer mortality and incidence, and does not address the possibility of radiation-related non-cancer mortality. Non-cancer mortality, particularly mortality from cardiovascular disease, has been linked with exposure to high therapeutic radiation doses (BEIR VII), but it is not clear whether such effects are found at lower doses. Mortality from most broad non-cancer disease categories has been found to be related to radiation dose in the LSS cohort (Preston et al., 2003). However, because the identified radiation risks were small compared to baseline risks, it was not possible to evaluate age effects or the shape of the dose-response function with any precision. For example, it was not possible to distinguish a linear dose-response from a dose-response with a threshold as high as 0.5 Gy. Indications also exist of radiation-associated increases in diseases of the circulatory system among nuclear workers in the United Kingdom (McGeoghegan et al., 2008).

Lifetime risk estimates for radiation-related non-cancer mortality for the LSS cohort are uncertain and range from zero to levels that approach those for cancer mortality estimates (Preston et al. 2003). Due to the large uncertainties in the possible magnitude, or even existence, of increased non-cancer disease risk at low doses, the EPA's decision not to provide lifetime risk estimates for non-cancer mortality is reasonable. The RAC recommends that non-cancer

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.

5.2.2 Information from ICRP and UNSCEAR Reports

Since the publication of BEIR VII, both ICRP (2007) and UNSCEAR (2008) have published reports that include lifetime risk estimates for radiation-related cancers. ICRP developed estimates for a world population defined as an average of risks for hypothetical Euro-American and Asian populations, whereas UNSCEAR developed estimates for several different countries, including the United States**.** The RAC recommends that the EPA add a brief description of the methods used in the ICRP and UNSCEAR reports and a comparison with those that are being used by EPA. Tables showing comparisons of the EPA estimates with relevant estimates from ICRP and from UNSCEAR would be a desirable addition to the Blue Book.

5.2.3 Radiogenic Thyroid Cancer

The draft Blue Book provides limited information regarding the risk of radiogenic thyroid cancer as estimated by BEIR VII, although EPA discussed this issue extensively in its draft White Paper (REF 2006), where EPA noted that "we now favor adoption of the NCRP thyroid cancer model, assuming that we would have a proper reference that can be cited."

This reference is now available in National Council on Radiation Protection and Measurements (NCRP) Report #159, "Risk to the Thyroid from Ionizing Radiation" (NCRP 2009). The RAC recommends that EPA now follow the NCRP approach, but also take into consideration in its modeling the latest epidemiological data on exposures to the thyroid, published since the NCRP was written in 2006. Particularly important are the recent publications of the Chernobyl thyroid studies.

5.2.4 Radiogenic Brain Cancer

Information on an association between ionizing radiation and brain cancer has been generated from a number of radiation-exposed cohorts that provide quantitative dose data allowing for estimation of radiogenic risks. Based on data from multiple cohorts including the atomic bomb survivors, tinea capitus cohort, hemangiomas and childhood cancer survivors, the brain-tumor epidemiology literature has reached consensus that ionizing radiation is an established risk factor for brain tumor development (Ohgaki 2009, Bondy 2008, Davis 2007). While brain tumors are complex histologically, radiation risk estimates for gliomas (the most common malignant tumor) are available from several of these cohorts. The RAC recommends that EPA present in the Blue Book the radiogenic risk to the brain in the context of the other discussed cancer sites.

5.3 Response to Charge Question # 3b

The RAC found the presentation of calculations and results in the draft Blue Book to be competent and comprehensible.

5.3.1 Table 4.2 Clarification

The RAC recommends that, in Table 4-2 on sources of uncertainty, a column listing references for the source of the distribution parameters be added, and that these be discussed in the text. It also recommends eliminating reports in several tables of the same values of lifetime risk estimates of cancer incidence or mortality.

5.3.2 Enhanced Topical Organization and Content

The RAC recommends that at the beginning of the document, EPA clearly states the intended purpose and application of the document, and anticipating the contents of the subsequent documents based on the Blue Book. The organization of the Blue Book can be improved by pulling together some scattered topics. For example, in Section 3.3 (draft Blue Book pages 29 – 32), risk models for cancers not specified by BEIR VII (kidney, bone, NMSC etc.) are discussed and conclusions presented, but estimating cancer risks for these organs is discussed in detail in Section 5.(pages 84 -88). The RAC found that some of the more detailed explanations and examples provided in the materials orally presented on March 23, 2009, to clarify the Blue Book contents greatly and suggests that they be included in the Blue Book.

5.3.3 SEER Data Clarification

The RAC suggests that additional information on the updated surveillance, epidemiology and end results (SEER) would be helpful. The statement on page 55 that increased LAR estimates (compared to those of FGR 13) are “largely attributable to the use of more recent SEER incidence [rates]” is confusing. Is the main point that FGR 13 made use of poorly approximated incidence rates computed as lethality-adjusted mortality risks but that the new estimates are based on actual age-specific incidence rates? Similarly, on page 55 is a statement that “the LAR for all cancers combined is increased by about 20%” because of using new SEER incidence data, followed by a statement that the models themselves would yield lower estimates of LAR than those published in FGR13 if the new models were applied to comparable mortality and incidence rates.

These matters should be discussed in detail. We have heard from members of the public who are concerned that the EPA will distort results to present inappropriately low risk values that will eventually be implemented in the revised FGR13. This interplay between mathematic models and compiled incidence rates should be explained in the revised Blue Book. The

rationale and implications of calculating LAR based on a life table for a hypothetical stable population rather than the existing life tables for the current US population also should be further explained to eliminate this approach as a cause of suspicion for the general reader.

5.3.4 Application of DDREF

The RAC recommends that tables with LAR estimates indicate whether the estimates include a DDREF adjustment.

5.4 Response to Charge Question # 3c

The RAC finds that the draft Blue Book, on the whole, presents the scientific background material with adequate accuracy, balance, and level of detail, but suggests the following improvements in use of information from low-dose protracted exposures and consideration of error.

5.4.1 Low-Dose Protracted Exposure.

The RAC realizes that much of the draft Blue Book relies on BEIR VII risk estimates based primarily on LSS data, but better balance would be achieved by comparing and discussing differences in risk estimates between the revised EPA estimates and risk estimates from studies of persons exposed to low-level, protracted radiation exposure such as those of nuclear workers including the 15-country radiation worker study (Cardis et al. 2007) and the study of UK National Registry of Radiation Workers (Muirhead et al. 2009). The EPA's primary concern is with the health effects of low-level, protracted radiation exposure, and acknowledges that risk estimates based on an acute exposure in a Japanese population are problematical when applied to the U.S. population.

5.4.2 Balanced Consideration of Sources of Error

The RAC encourages evaluation of the relative importance of the impact of sources of the various errors, including those currently not considered in the development of the uncertainty distributions, with focus on examining the most important contributors. As one example, in the transfer of risk between the LSS cohort and the U.S., what will be the impact on the uncertainty distribution if the true transfer model falls outside the limits defined by the purely additive and purely multiplicative risk transfer?

5.4.3 Cancer Subtypes

The RAC encourages expanding the discussion of issues related to lympho-hematopoietic cancers, for example: a) comments on the recent literature suggesting that Chronic Lymphocytic Leukemia (CLL) may be a radiogenic cancer (Linet et al. 2007; Schubauer-Berigan 2007; Silver

et al 2007), and appropriate references contained within; b) the reasons for not developing risk estimates for leukemia subtypes; and c) why risk estimates have not been presented for non-Hodgkin's lymphoma or multiple myeloma.

5.4.4 Holistic View of Stepwise EPA Path to FGR 13 Revision

The RAC recommends that EPA include specific information concerning the anticipated radionuclide risk coefficient values in the revised FGR 13, based on currently available dosimetric models. The presentation in the 1994 Blue Book, Tables A4a and A4b are an example. Actual values in Section 7 of the Blue Book will assist both professionals and the public to evaluate the combined impact of revised cancer risk projections and dosimetric models.

REFERENCES CITED

(NOTE: References to be checked and re-fomatted as appropriate. References not cited will be dropped, but are included in this version for reviewers to confer for the present. Please see notes - - - KJK & B. Kahn)

Andersson, M., M. Vyberg, J. Visfeldt, B. Carstensen and H.H. Storm. 1994. Primary liver tumors among Danish patients exposed to Thorotrast. *Radiat Res* **137**: 262-273. 1994.

Boice, J.D. Jr., R.W. Miller .1999. Childhood and adult cancer after intrauterine exposure to ionizing radiation. *Teratol* **59**(4): 227-233. 1999

Bolstad, William M. Introduction to Bayesian Statistics, 2nd ed., John Wiley & Sons, Hoboken, NJ. 2007

Bondy, M.L., M.E. Scheurer, B. Malmer, et al. 2008. Brain tumor epidemiology: consensus from the Brain Tumor Epidemiology Consortiium, *Cancer* 2008; **113**: 1953-68. 2008

Cardis, E., M. Vrijheld, M. Blettner, E. Gilbert, M. Hakama, C. Hill et al. 2007. The 15-country collaborative study of cancer risk among radiation workers in the nuclear industry: Estimates of radiation related cancer risks. *Radiat Res* **167**: 396-416. 2007

Carnes BA, Groer PG, Kotek TJ. Radium dial workers: issues concerning dose response and modeling. *Radiat Res.* **147**(6):707-14. Jun 1997

Davis, F.S., Epidemiology of brain tumors. 2007. *Expert Rev Anticancer Ther* **7**:S3-6. 2007

Doll, R. and Wakeford, R. 1997 Risk of childhood cancer from fetal irradiation. *Brit J. Radiol* **70**: 130-139, 1997

FR Citations: (others to be added as appropriate by KJK)

FR Vol. 73, No. 76, Friday, April 18, 2008, pp. 21129-21130 (FRN to augment expertise of RAC for the Blue Book Review - - - KJK)
FR Vol. 74, No. 21, February 3, 2009, pp. 5935-5936

FR Vol. 74, No. 101, May 28, 2009, pp. 25529 -25530

FR Vol __, No. __, to be added for Quality Review Announcement (KJK)

Geoghegan, D., K. Binks, M.Gillies, S. Jones and S. Whaley, The non-cancer mortality experience of male workers at British Nuclear Fuels plc, 1946-2005. *Int J Epidemiol* **37:** 506-518. 2008.

Gilbert E.S., N.A. Koshurnikova, M.E. Sokolnikov, N.S. Shilnikova, D.L. Preston, E. Ron, P.V. Okatenko, V.F. Khokhryakov, E.K.Vasilenko, S. Miller, K. Eckerman, S.A. Romanov, Lung Cancer in Mayak Workers. *Radiation Res.* 2004 Nov; **162** (5):505-16. 2004 **[NOTE: Dr. Gilbert was earlier suggesting to drop this reference, but it appears that it should stay - - - - KJK]**

Gilbert, E.S., N.A. Koshurnikova, M. Sokolnikov, V.F. Khokhryakov, S. Miller, D.L. Preston, S.A. Romanov, N.S. Shilnikova, K.G. Suslova and V.V. Vostrotin, Liver Cancers in Mayak Workers. *Radiat Res* **154:** 246-252. 2000.

Gilbert, E.S., W.C. Griffith, B.B. Boecker, G.E. Dagle, R.A. Guilmette, F.F. Hahn, B.A. Muggenburg, J.F. Park, C.R. Watson. 1998. Statistical modeling of carcinogenic risks in dogs that inhaled (PuO2)-Pu-238, *Radiation Research*, **150**(1): 66-92. July 1998.

Gilbert et al 1997 **[NOTE: According to Dr. Griffith, this citation should have been Gilbert 1998 (see above), and should be dropped - -- KJK]**

Hahn, F.F., B.A. Muggenburg, R.A. Guilmette, B.B. Boecker, Comparative stochastic effects of inhaled alpha- and beta-particle-emitting radionuclides in beagle dogs, *Radiation Research*, **152**(6): S19-S22 Supplement: Suppl S. 1999.

Hoel, D.G, and Carnes, B.A. 2004. Cancer Dose-Response Analysis of the Radium Dial Painters. In: Proceedings of the 9th. International Conference on Health Effects of Incorporated Radionuclides Emphasis on Radium, Thorium, Uranium and their Daughter Products. Neuherberg, Germany. 2004.

Hunter N, Muirhead CR. 2009. Review of relative biological effectiveness dependence on linear energy transfer for low-LET radiations. *J Radiol Prot*. 2009 Mar; **29**(1):5-21. Epub Feb 18, 2009.

International Commission on Radiological Protection. 2007. ICRP Publication 103: The 2007 Recommendations of the International Commission on Radiological Protection. *Annals of the ICRP* **37**, 9-332. 2007.

International Commission on Radiological Protection. 2005. ICRP Publication 99: Low dose extrapolation of radiation-related cancer risk. *Annals of the ICRP* **35.** 2005.

International Commission on Radiological Protection. 2003. ICRP Publication 92: Relative biological effectiveness (RBE), quality factor (Q), and radiation weighting factor (W_r). *Annals of the ICRP* **33.** 2003.

International Commission on Radiological Protection. 2002. Basic Anatomical and Physiological Data for Use in Radiological Protection Reference Values, ICRP Publication 89, *Annals of the ICRP* **32:**3-4. 2002.

International Commission on Radiological Protection. 2001. Doses to the Embryo and Fetus from Intakes of Radionuclides by the Mother. ICRP Publication 88. **31**: 1-3. Elsevier Science Ltd. New York. 2001.

International Commission on Radiological Protection. 2000. "ICRP Publication 84: Pregnancy and Medical Radiation." Annals of the ICRP **30**(1), Elsevier Science Ltd. New York. 2000.

International Commission on Radiological Protection. 1991a. Recommendations of the International Commission on Radiological Protection. ICRP Publication 60. *Annals of the ICRP* **21**: 1-3. 1991a.

International Commission on Radiological Protection. 1991b. The Biological basis for Dose Limitation in the Skin. ICRP Publication 59. *Annals of the ICRP* **22:**2. 1991b.

International Commission on Radiation Units and Measurements. 1986. The Quality Factor in Radiation Protection. ICRU Report No. 40. Bethesda, MD. 1986.

Jacob, P, R. Meckbach, M. Sokolnikov, V.V. Khokhryakov and E. Vasilenko, 2007. Lung cancer risk of Mayak workers: modelling of carcinogenesis and bystander effect. *Radiat Environ Biophys*. 2007.

Karagas, M.R., E.R. Greenberg, S.K. Spencer, T.A. Stukel and L.A. Mott. 1999. Increase in incidence rates of basal cell and squamous cell skin cancer in New Hampshire, USA. New Hampshire Skin Cancer Study Group. *Int. J Cancer* **81**(4)**:** 555-559. May 17, 1999

Koshurnikova, N.A., E.S. Gilbert, M. Sokolnikov, V.F. Khokhryakov, S. Miller, D.L. Preston, S.A. Romanov, N.S. Shilnikova, K.G. Suslova, V.V. Vostrotin. 2000. Bone cancers in Mayak workers. *Radiat Res.* **154**(3): 237-45. 2000.

Kreisheimer, M., N.A. Koshurnikova, E. Nekolla, V.F. Khokhryakov, S.A. Romanov, M.E. Sokolnikov, P.A. Okatenko, A.M. Kellerer. 2000. Lung cancer among male nuclear workers of the Mayak facilities in the former Soviet Union. *Radiation Research* **154**: 3-11. 2000.

Kreisheimer, M. M.E. Sokolnikov, N.A. Koshurnikova, V.F. Khokhryakov, S.A. Romanow, N.S. Shilnikova, P.V. Okatenko, E.A. Nekolla, A.M. Kellerer. 2003. Lung cancer mortality among nuclear workers of the Mayak facilities in the former Soviet Union – An updated analysis considering smoking as the main confounding factor. 2003.

Leenhouts, H.P., M.J.P. Brugmans, M. Andersson, H.H. Storm. 2002. A Reanalysis of liver cancer in Danish patients administered Thorotrast using two-mutation carcinogenesis model. *Radiation Research* **158**:597-606. 2002.

Lewis, K.G., M.A. Weinstock. 2004. Nonmelanoma skin cancer mortality (1988-2000). The Rhode Island follow-back study. *Arch Dermatol* **140**: 837-842. 2004

Linet, M.S., M. K. Schubauer-Berigan, D. D. Weisenburger, D. B. Richardson, O. Landgren, A. Blair, S. Silver, R. W. Field, G. Caldwell, et al.. 2007. Chronic lymphocytic leukemia: an overview of etiology in light of recent developments in classification and pathogenesis. *Br J Haematol* **139**, 672-686. 2007.

Lundgren, D.L., F.F. Hahn, W.W. Carlton, W.C. Griffith, R.A. Guilmette, N.A. Gillett. 1997. Dose responses from inhaled monodisperse aerosols of (cm2O3)-Cm-244 in the lung, liver and skeleton of F344 rats and comparison with (PuO2)-Pu-239, *Radiation Research*, **147**: Issue 5, 598-612. 1997

Lundgren, D.L., F.F. Hahn, W.C. Griffith, A.F. Hubbs, K.J. Nikula, G.J. Newton, R.G. Cuddihy, B.B. Boecker. 1996. Pulmonary carcinogenicity of relatively low doses of beta-particle radiation from inhaled (CeO2)-Ce-144 in rats, *Radiation Research*, 146: Issue 5, 525-535. 1996

Lundgren, D.L., P.J. Haley, F.F. Hahn, J.H. Diel, W.C. Griffith, B.R. Scott. 1995. Pulmonary Carcinogenicity of Repeated Inhalation Exposure of Rats to Aerosols of (PuO2)-Pu-239, *Radiation Research* **142**(1): 39-53. 1995.

Lunn, D.J., Thomas, A., Best N., and Spiegelhalter, D. 2000. WinBUGS – a Bayesian modelling framework: concepts, structure, and extensibility, *Statistics and Computing* **10**: 325-337. 2000.

Macmahon, B. 1962. "Prenatal x-ray exposure and childhood cancer." *J. Natl Cancer Inst* **28**: 1173-91. 1962.

Mohan AK, M. Hauptmann, D.M. Freedman, E. Ron, G.M. Matanoski, J.H. Lubin, B.H. Alexander, J.D. Boice, Jr, M.M. Doody, and M.S. Linet. 2003. Cancer and other causes of mortality among radiologic technologists in the United States. *Int J Cancer*. Jan 10;**103**(2):259-67. 2003.

Muggenburg, B.A., R.A. Guilmette, F.E. Hahn, J.H. Diel, J.L. Mauderly, S.K. Seilkop, B.B. Boecker. 2006. Radiotoxicity of Inhaled (PuO2)-Pu-239 in Dogs. 2003. *Radiation Research*, **170**(6): 736-757. 2006 **[NOTE: Please re-check this reference 2003? 2006? - - -KJK]**

Muggenburg B.A., B.B. Boecker, A.F. Hubbs, F.F. Hahn, M.B. Snipes, J.H. Diel, G.J. Newton, W.C. Griffith. 1998. Toxicity of inhaled (YCl3)-Y-91 in dogs, *Radiation Research*, **150**(2):212-226, August 1998 **[NOTE: The Muggenberg 1998 reference is retained here for the present, but apparently has not been cited in the report - - - KJK]**

Muggenburg, B.A., R.A. Guilmette, J.A. Mewhinney, N.A. Gillett, J.L. Mauderly, W.C. Griffith, J.H. Diel, B.R. Scott, F.F. Hahn, B.B. Boecker. 1996. Toxicity of inhaled plutonium dioxide in beagle dogs, *Radiation Research*, **145**(5): 525-612. 1996

Muirhead CR, J.A. O'Hagan, R.G. Haylock, M.A. Phillipson, T. Willcock, G.L. Berridge, and W. Zhang. 2009. Mortality and cancer incidence following occupational radiation exposure: third analysis of the National Registry for Radiation Workers. *Br J Cancer*. Jan 13;**100**(1):206-12. 2009.

NCRP. 2009. "Risk to the thyroid from ionizing radiation." National Council on Radiation Protection and Measurements (NCRP); NCRP Report #159. Bethesda, MD. 2009.

Ohgaki, H. 2009. Epidemiology of brain tumors. *Methods Mol Biol* **472**: 323-42. 2009.

Preston, D.L., H. Cullings, A. Suysama, S. Funamoto, N. Nishi, M. Soda, K. Mabuchi, K. Kodama, F. Kasagi, and R.E. Shore. 2008. "Solid cancer incidence in atomic bomb survivors exposed in utero or as young children." *J. Natl Cancer Inst* **100**(6), 428-436. 2008.

Preston, D.L., E. Ron, S. Tokuoka, S. Funamoto, N. Nishi, M. Soda, K. Mabuchi and K. Kodama. 2007. Solid cancer incidence in atomic bomb survivors: 1958-1998. *Radiat Res* **168**, 1-64. 2007.

Preston, D.L., Y. Shimizu, D.A. Pierce, A. Suyama and K. Mabuchi. 2003. Studies of mortality of atomic bomb survivors. Report 13: Solid cancer and noncancer disease mortality: 1950-1997. *Radiat Res* **160**, 381-407. 2003.

Priest, N.D., D.G. Hoel, P.N. Brooks. 2006. Relative toxicity of chronic irradiation by Ca-45 beta particles and Cm-242 alpha particles with respect to the production of lung tumors in CBA/Ca mice, *Radiation Research*, **166**(5): 782-793, 2006

Ramsey, M.L. 2006 Basal Cell Carcinoma. eMedicine website, www.emedicine.com/derm/topic47.htm **[NOTE: This is an online reference at an e-medicine site, which currently has a 2008 update with a co-author, L.D. Sewell. The previous online versions may not be available since this is not designed to be an online journal. Dr. Griffith suggests that only primary references in this article need to be selected for the points that need to be referenced. In other words, he recommends that this is not really an appropriate reference since it is not designed to be permanent. - - - KJK]**

Ron, E., B. Modan, D. Preston, E. Alfandary, M. Stovall, JD Boice. 1991. Radiation-induced skin carcinomas of the head and neck. *Radiat Res* **125**; 318-325.1991.

NOTE: One of the 3 or all might be appropriate for the Schubauer-Berigan 2007 citations (Please see below - -- KJK):

Schubauer-Berigan M.K., R.D. Daniels, D.A. Fleming, A.M. Markey, J.R. Couch, S.H. Ahrenholz, J.S. Burphy, J.L. Anderson, C.Y. Tseng. 2007. Chronic lymphocytic leukaemia and radiation: findings among workers at five US nuclear facilities and a review of the recent literature, *British Journal of Haematology*, **139**(5): 799-808, Dec. 2007

Schubauer-Berigan M.K., R.D. Daniels, D.A. Fleming. 2007. Risk of leukemia at low doses: The NIOSH multi-site leukemia case-control study, *Radiation Research*, **167**(3): 344-345, Mar. 2007.

Schubauer-Berigan M.K., R.D. Daniels, D.A.Fleming DA, A.M. Markey, J.R. Couch, S.H. Ahrenholz, J.S. Burphy, J.L. Anderson, C.Y. Tseng. 2007. Risk of chronic myeloid and acute leukemia mortality after exposure to ionizing radiation among workers at four US nuclear weapons facilities and a nuclear naval shipyard, *Radiation Research*, **167**(2): 222-232 , Feb. 2007.

Shilnikova, NS, D.L. Preston, E. Ron, E.S. Gilbert, E.K. Vassilenko, S.A. Romanov, I.S. Kuznetsova, M.E. Sokolnikov, P.V. Okatenko, V.V. Kreslov, N.A. Koshurnikova. 2003. *Rad. Res.* **159**(6):787-798. June 2003.

Shore, R.E., M. Moseson, X. Xue, Y. Tse, N. Harley, B.S. Pasternack. 2002. Skin cancer after x-ray treatment for scalp ringworm. *Radiat Res* **157**: 410-418. 2002.

Shore, R.E. 2001. Radiation-induced skin cancer in humans. *Med Pediatr Oncol.* **36**(5):549-54, May. 2001.

Silver S.R., S.L. Hiratzka, M.K. Schubauer-Berigan, R.D. Daniels. 2007. Chronic lymphocytic leukemia radiogenicity: a systematic review, *Cancer Causes & Control*, **18**(10): 1077-1093, Dec. 2007.

Sokolnikov, M.E., E.S. Gilbert, D.L. Preston, N.S. Shilnikova, V.V. Khokhryakov, E.K. Vasilenko, N.A. Koshurnikova. 2008. Lung, liver, and bone cancer mortality in Mayak workers. *Int J Cancer* **123**: 905-911. 2008.

Stewart, A., J. Webb, D. Hewitt. 1958. A survey of childhood malignancies. *Br. Med J.* **1**(5086): 1495-1508. 1958.

UNSCEAR. 2008. United Nations Scientific Committee on the Effects of Atomic Radiation, *Effects of Ionizing Radiation - - UNSCEAR 2006 Report to the General Assembly with Scientific Annexes. Volume I. Effects of Ionizing Radiation.* United Nations, New York. 2008.

UNSCEAR. 2000. United Nations Scientific Committee on the Effects of Atomic Radiation, *Sources, Effects, and Risks of Ionizing Radiation with Annexes, Volume II: Effects.* United Nations, New York. 2000.

.

U.S. EPA. 2008. *EPA Radiogenic Cancer Risk Models and Projection for the U.S. Population,* U.S. Environmental Protection Agency, Office of Radiation and Indoor Air, draft, December 2008, http://epa.gov/radiation/assessment/pubs.html. (the “Blue Book”)

U.S. EPA. 1999. ***“Cancer Risk Coefficients for Environmental Exposure to Radionuclides,”*** Federal Guidance Report No. 13, EPA 402-R-99-001, September 1999, 335 pages http://epa.gov/radiation/docs/federal/402-r-99-001.pdf

U.S. EPA. 1984. *Estimating Radiogenic Cancer Risks*, Washington, DC **(NOTE: Need full citation. Check with ORIA Staff/Drs. Clark, Puskin, Pawel et al. - - -KJK)**

U.S. EPA 1994. *Estimating Radiogenic Cancer Risks* ("Blue Book"), Washington, DC (EPA 402-R-93-076), June 1994: http://epa.gov/radiation/docs/assessment/402-r-93-076.pdf

U.S. EPA/ORIA. 2009. Memorandum entitled "Advisory Review of the Draft Document: *EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population,"* from Elizabeth A. Cotsworth, Director, Office of Radiation and Indoor Air to Vanessa Vu, Director, Science Advisory Board Staff Office, January 26, 2009

U.S. EPA/ORIA. 2008. "EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population," U.S. Environmental Protection Agency (EPA), Office of Radiation and Indoor Air (ORIA), Draft December 2008, 116 pages ("The Blue Book")
http://epa.gov/radiation/assessment/pubs.html

U.S. EPA/ORIA. 2006. "***Modifying EPA Radiation Risk Models Based on BEIR VII,"*** Draft *White Paper*, Prepared by Office of Radiation and Indoor Air, U.S. Environmental Protection Agency, August 1, 2006, 36 pages
http://yosemite.epa.gov/sab/sabproduct.nsf/8097D8CE7070C1E4852571DA0005C605/$File/rac_oria_white_paper_08-01-06.pdf

U.S. EPA/ORIA. 1999. ***"Cancer Risk Coefficients for Environmental Exposure to Radionuclides,"*** Federal Guidance Report No. 13, EPA 402-R-99-001, September 1999, 335 pages http://epa.gov/radiation/docs/federal/402-r-99-001.pdf

U.S. EPA/SAB. 2008. ***Advisory on Agency Draft White Paper Entitled "Modifying EPA Radiation Risk Models Based on BEIR VII,"*** EPA-SAB-08-006. January 31, 2008
http://yosemite.epa.gov/sab/sabproduct.nsf/FD9963E56C66E4FF852573E200493359/$File/EPA-SAB-08-006-unsigned.pdf

U.S. EPA/SAB. 2006. ***Advisory on Agency Draft White Paper Entitled "Modifying EPA Radiation Risk Models Based on BEIR VII,"*** EPA-SAB-08-006. January 31, 2008
http://yosemite.epa.gov/sab/sabproduct.nsf/FD9963E56C66E4FF852573E200493359/$File/EPA-SAB-08-006-unsigned.pdf

U.S. EPA/SAB. 1999. ***"An SAB Report: Estimating Uncertainties in Radiogenic Cancer Risk,"*** EPA-SAB-RAC-99-008, February 18, 1999
http://yosemite.epa.gov/sab/sabproduct.nsf/D3511CC996FB97098525718F0064DD44/$File/rac9908.pdf

U.S. EPA/SAB. 1994. ***"Evaluation of EPA's Proposed Methodology for Estimating Radiogenic Cancer Risks,"*** EPA-SAB-RAC-LTR-93-004, December 9, 1992
http://yosemite.epa.gov/sab/sabproduct.nsf/0A0E72B3E05BC8928525731C007830F3/$File/RADIOGENIC+CANCER+RAC-LTR-93-004_93004_5-8-1995_68.pdf

U.S. NAS/NRC. 2006. ***Health Risks from Exposure to Low levels of Ionizing Radiation, BEIR VII Phase 2,*** National Academies of Sciences (NAS), National Research Council, Committee to Assess Health Risks from Exposure to Low levels of Ionizing Radiation. 2006. 416 pages http://newton.nap.edu/catalog/11340.html#toc

U.S. NAS/NRC. 1980. National Academy of Sciences Committee on the Biological Effects of Radiation, *The Effects on Populations Exposed to Low Levels of Ionizing Radiation (BEIR III). National Academy of Sciences Report BEIR III*, National Academy of Sciences Press, Washington, DC, National Academy Press, 1980

Van Kaick, G., A. Dalheimer, S. Hornik, A. Kaul, D. Liebermann, H. Luhrs, A. Spiethoff, K. Wegener, H. Welch. 1999. The German Thorotrast study: Recent results and assessment of risks. *Radiation Research* **152**(6): S64-S71. 1999.

Vrijhead, M., E. Cardis, P. Ashmore, A. Auvinen, E. Gilbert, R.R. Habib, H. Malker, C.R. Muirhead, D.B. Richardson, A. Rogel, M. Schubauer-Berigan, H. Tardy, M. Telle-Lamberton. 2008. Ionizing radiation and risk of chronic lymphocytic leukemia in the 15-country study of nuclear industry workers. 15-Country Study Group. *Radiat. Res.* **170**(5): 661-5. 2008.

Yoshinaga, S., K. Mabuchi, A.J. Sigurdson, M.M. Doody, E. Ron. 2004. Cancer risks among radiologists and radiologic technologists: review of epidemiologic studies. *Radiology* **233**(2): 313-321. 2004.

Web-based Citations and Hotlinks

(NOTE: Under development. To be added, deleted and re-formatted as appropriate - - - KJK)

U. S. EPA (Environmental Protection Agency). 1994. *Estimating Radiogenic Cancer Risks* ("Blue Book"), Washington, DC (EPA 402-R-93-076), June, 1994: http://epa.gov/radiation/docs/assessment/402-r-93-076.pdf

U.S. EPA (Environmental Protection Agency) / OAR (Office of Air and Radiation). 1999. Federal Guidance Report (FGR)-13. *Federal Guidance Report 13: Cancer Risk Coefficients for Environmental Exposure to Radionuclides*, Washington, DC (EPA 402-R-99-001), September, 1999 http://epa.gov/radiation/docs/federal/402-r-99-001.pdf

U. S. EPA (Environmental Protection Agency) 1999a. *Estimating Radiogenic Cancer Risks Addendum: Uncertainty Analysis*, Washington, DC (EPA 402-R-99-003), May, 1999: http://epa.gov/radiation/docs/assessment/402-r-99-003.pdf

U.S. EPA. (Environmental Protection Agency). 1999b. *Update to the Federal Guidance Report No. 13* and *CD Supplement*: http://epa.gov/radiation/federal/techdocs.htm#report13

U.S. EPA. 2006. Office of Radiation and Indoor Air (ORIA), Draft *White Paper: Modifying EPA Radiation Risk Models Based on BEIR VII*, August 1, 2006 http://epa.gov/radiation/news/recentadditions.htm

U.S. EPA/ORIA. 2008. "EPA Radiogenic Cancer Risk Models and Projections for the U.S. Population," U.S. Environmental Protection Agency (EPA), Office of Radiation and Indoor Air (ORIA), Draft December 2008, 116 pages ("The Blue Book") http://epa.gov/radiation/assessment/pubs.html

U.S. NAS/NRC. 2006. BEIR VII. *Health Risks from Exposure to Low levels of Ionizing Radiation BEIR VII Phase 2*, National Academies of Sciences (NAS), National Research Council, Committee to Assess Health Risks from Exposure to Low levels of Ionizing Radiation, http://newton.nap.edu/catalog/11340.html#toc

FEDERAL REGISTER SOLICITING NOMINATIONS TO AUGMENT EXPERTISE ON THE RADIATION ADVISORY COMMITTEE (RAC), *Federal Register*, Vol. 73, No. 76, Friday, April 18, 2008, pp. 21129-21130 http://www.epa.gov/fedrgstr/EPA-SAB/2008/April/Day-18/sab8400.htm

BACKGROUND REPORTS AND ADVISORIES:

"EVALUATION OF EPA's PROPOSED METHODOLOGY FOR ESTIMATING RADIOGENIC CANCER RISKS," EPA-SAB-RAC-LTR-93-004, December 9, 1992 http://yosemite.epa.gov/sab/sabproduct.nsf/0A0E72B3E05BC8928525731C007830F3/$File/RADIOGENIC+CANCER+RAC-LTR-93-004_93004_5-8-1995_68.pdf

"AN SAB REPORT: REVIEW OF HEALTH RISKS FROM LOW-LEVEL ENVIRONMENTAL EXPOSURES TO RADIONUCLIDES (FRG-13 REPORT)," EPA-SAB-RAC-99-009, December 23, 1998
http://yosemite.epa.gov/sab/sabproduct.nsf/2EF0698AA08A29098525718F006532D8/$File/rac9909.pdf

"AN SAB REPORT: ESTIMATING UNCERTAINTIES IN RADIOGENIC CANCER RISK," EPA-SAB-RAC-99-008, February 18, 1999
http://yosemite.epa.gov/sab/sabproduct.nsf/D3511CC996FB97098525718F0064DD44/$File/rac9908.pdf

ADVISORY ON AGENCY DRAFT WHITE PAPER ENTITLED "MODIFYING EPA RADIATION RISK MODELS BASED ON BEIR VII," EPA-SAB-08-006. January 31, 2008
http://yosemite.epa.gov/sab/sabproduct.nsf/FD9963E56C66E4FF852573E200493359/$File/EPA-SAB-08-006-unsigned.pdf

AGENCY AND OTHER DOCUMENTS (AND HOTLINKS) RELATED TO ESTIMATING RADIOGENIC CANCER RISKS:

Blue Book: ***ESTIMATING RADIOGENIC CANCER RISKS***, EPA 402-R-93-076, June 1994
http://www.epa.gov/radiation/docs/assessment/402-r-93-076.pdf

and its Uncertainty Addendum: ***ESTIMATING RADIOGENIC CANCER RISKS ADDENDUM: UNCERTAINTY ANALYSIS***, EPA 402-R-99-003, May 1999
http://www.epa.gov/radiation/docs/assessment/402-r-99-003.pdf

The basis for the Blue Book SAB peer review is at:

"EVALUATION OF EPA's PROPOSED METHODOLOGY FOR ESTIMATING RADIOGENIC CANCER RISKS," EPA-SAB-RAC-LTR-93-004, December 9, 1992
http://yosemite.epa.gov/sab%5Csabproduct.nsf/0A0E72B3E05BC8928525731C007830F3/$File/RADIOGENIC+CANCER+RAC-LTR-93-004_93004_5-8-1995_68.pdf

The Uncertainty Addendum SAB peer review is at:

"AN SAB REPORT: ESTIMATING UNCERTAINTIES IN RADIOGENIC CANCER RISK," EPA-SAB-RAC-99-008, February 18, 1999
http://yosemite.epa.gov/sab%5Csabproduct.nsf/D3511CC996FB97098525718F0064DD44/$File/rac9908.pdf

FEDERAL GUIDANCE REPORT 13:

"Cancer Risk Coefficients for Environmental Exposure to Radionuclides," Federal Guidance Report No. 13, EPA 402-R-99-001, September 1999, 335 pages
http://epa.gov/radiation/docs/federal/402-r-99-001.pdf

NATIONAL ACADEMY OF SCIENCES BEIR VII REPORT:

U.S. NAS/NRC, 2006. ***Health Risks from Exposure to Low levels of Ionizing Radiation, BEIR VII Phase 2,*** National Academies of Sciences (NAS), National Research Council, Committee to Assess Health Risks from Exposure to Low levels of Ionizing Radiation, 2006, 416 pages
http://newton.nap.edu/catalog/11340.html#toc

AGENCY UPDATED DRAFT WHITE PAPER:

Modifying EPA Radiation Risk Models Based on BEIR VII, Draft *White Paper*, Prepared by Office of Radiation and Indoor Air, U.S. Environmental Protection Agency, August 1, 2006, 36 pages
http://yosemite.epa.gov/sab/sabproduct.nsf/8097D8CE7070C1E4852571DA0005C605/$File/rac_oria_white_paper_08-01-06.pdf

APPENDIX A – EDITORIAL COMMENTS

Minor (editorial) comments on the draft EPA document on Radiogenic Cancer Risk.

p.6: Insert acronyms:
UI Uncertainty interval
ICD ? (used on p.23)

p. 7, paragraph 2: This should mention the provision of estimates for alpha-emitters, X-rays etc. Also, kidney cancer should be added to the list in the 3rd sentence.

p. 7, paragraph 4: Sentence "Nevertheless … time after exposure." This is true, but for most cancers the estimates are more precise than those from any other study. This point might be worked into the paragraph. Another limitation that might be mentioned is the relevance for low dose rate exposure.

p.16, Section 2.1.5, line 2: Replace 'new' by 'recently observed'.

p. 20, 1st full paragraph: The study of British radiologists by Berrington et al. (Br. J. of Radiology 2001) might also be cited.

p. 20, 2nd full paragraph: An important paper on workers that needs to be cited is the recent update of the study of NRRW British nuclear workers (Muirhead et al. Brit. J. Cancer, 2009). The most important limitations (in my opinion) are not mentioned. These are lack of statistical power (imprecise risk estimates) and vulnerability to confounding when studying small risks. There are also more recent Chernobyl papers that might be cited including 2 papers on thyroid cancer (Cardis et al. JNCI 2005; Tronko et al. JNCI 2006) and 2 papers on leukemia incidence (Romanenko et al. Radiat. Res. 2008; Kesminiene et al. Radiat. Res. 2008).

p. 21, line 1: Kidney cancer should be added here.

p. 23, last 2 lines: Suggest revising as following: "… the BEIR VII committee found that the ERR per Gy decreased by about 25% per decade of age at exposure (for ages under 30) in the model …

p. 25, Table 3-2: For thyroid cancer, attained age (*a*) id not an effect modifier. The Ron et al. pooled analysis should also be cited. For leukemia, the ERR and EAR were *linear*-quadratic functions of dose.

p. 27, "Breast" paragraph: It would be helpful to indicate briefly the rationale for using only an EAR model for this site.

p.27, Table 3-3: Last letter in heading should be Greek eta, not 'H'.

p.28, Fig.3-2 and others: Always show units along axes.

p.41, Section 3.9.2: insert period after '9'.

p. 43: Line just below equation 3-21. The inequality is incorrect. When one multiplies the expression in 3-21 by $M^{(A)} - M^{(R)}$, the direction of the inequality will change when $M^{(A)} - M^{(R)}$ is negative.

p. 43, last paragraph: The wording here is confusing. Equation (3-20) seems to *assume* the $M^{(true)}$ that is between the EAR and ERR estimates.

p. 55, 3rd sentence: BEIR VII accounted for uncertainty in the age parameters for the all solid cancer estimate.

p.57, Table 3-13: Do the 90% UI values refer to Kidney or to combined Residual + kidney as in Table 3-11?

p. 59, paragraph 2: Another important difference is the approach to transport.

p. 62 ff: If there is sharing of the main effect parameters, I would think there should be sharing of the age parameters as well. Also, there should probably be allowance for correlation of the age at exposure and attained age parameters. (I have no idea what the impact of the changes might be.)

p.63, Table 4-1: Replace 2nd parameter heading (9it is the same as the 1st).

p.77, Table 4-4b: Insert 'age' in heading before '15'.

p.83, Table 4-5: Although heading says '95% uncertainty intervals', the values are similar to the 90% uncertainty intervals of Table 3-11. Check.

p. 88, 1st full paragraph: The more recent Sokolnikov et al. paper should also be cited here.

p. 90, 1st full paragraph: I suggest providing confidence intervals for these estimates to remind readers of the considerable uncertainty. This comment also applies to many other estimates presented in the report.

p. 90, 2nd full paragraph: We argued in the Gilbert et al. 2004 paper that the estimates of the ERR per Gy from plutonium and from radon were fairly comparable. You might want to check this paper (beginning 2nd column on p. 514).

APPENDIX B –ACRONYMS

(NOTE: Contains acronyms relevant specifically to the Blue Book Review. Please complete missing items as appropriate. - - - KJK)

A	Atomic
AM	Arithmetic Mean
BCC	Basal Cell Carcinoma
BEIR	Biological Effects of Ionizing Radiation (Pertains to committees of the Board of Radiation Effects, National Research Council of the National Academy (now the National Academies'), charged with assessing the Biological Effects of Ionizing Radiation
BEIR VII	The report entitled *"Health Risks from Exposure to Low Levels of Ionizing Radiation BEIR VII – Phase 2"* published (2006) by the Committee to Assess Health Risks from Exposure to Low levels of Ionizing Radiation of the Board on Radiation Effects Research, national Research Council of the National Academies
Bq	Becquerel
CLL	Chronic Lymphocytic Leukemia
Co	Chemical symbol for Cobalt (^{60}Co isotope)
CT scan	??
DDREF	Dose and Dose-Rate Effectiveness Factor
EAR	Excess Absolute Risk
EPA	Environmental Protection Agency (U.S. EPA)
ERR	Excess Relative Risk
eV	Electron Volts
FGR	Federal Guidance Report
GM	Geometric Mean
GSD	Geometric Standard Deviation (?)
Gy	Gray, SI unit of radiation absorbed dose (1 Gy is equivalent to 100 rad in traditional units)
H	Chemical symbol for Hydrogen (^{3}H isotope)
ICRP	International Commission on Radiological Protection
I	Chemical Symbol for Iodine (^{131}I isotope)
IR	Ionizing Radiation
IREP	Interactive Radio-epidemiology Program
k	Kilo (thousands)
kVp	Kilo Volts (p ?)
LAR	Lifetime Attributable Risk
LET	Linear Energy Transfer
LN	Linear Non-Threshold (also LNT)
LSS	Life-Span Study
mGY	Milli (one Thousandth) Gray
MCMC	Markov Chain Monte Carlo methods
Me	???
NAS	National Academy of Sciences
NCRP	National Council on Radiation Protection and Measurements

NIOSH	National Institute for Occupational Safety and Health
NMSC	Non-Melanoma Skin Cancer
NRC	National Research Council
OAR	Office of Air and Radiation (U.S. EPA/OAR)
ORIA	Office of Radiation and Indoor Air (U.S. EPA/OAR/ORIA)
Ra	Chemical symbol for Radium (Isotopes include ^{224}Ra, ^{226} Ra, ^{228}Ra, and ^{236}Ra)
RAC	Radiation Advisory Committee ((U.S. EPA/SAB/RAC)
RBE	Relative Biological Effectiveness
SAB	Science Advisory Board (U.S. EPA/SAB)
SEER	Surveillance, Epidemiology and End Results
Type I	Decision error (in this case on risk estimates). A decision error occurs when the *null hypothesis* is rejected when it is true. The probability of making a Type I decision error in called *alpha*.
Type II	Decision error (in this case on risk estimates). A decision error that occurs when the *null hypothesis* is accepted when it is false. The probability of making a Type II decision error is called *beta*.
Type III	Decision error (in this case on the age distribution)
UNSCEAR	United Nations Scientific Committee on the Effects of Atomic Radiation
US	United States of America – used interchangeably with USA
V	(???)
WinBUGS	Windows (for Microsoft windows programs) for Bayesian inference Using Gibbs Sampling analysis software
X-ray	

End of Document