

SAB Working Review Draft Advisory dated December 12, 2006 for Radiation Advisory Committee Edits – Do Not Cite or Quote. This review draft is a work in progress, does not reflect consensus advice or recommendations, has not been reviewed or approved by the Science Advisory Board’s Charter Board, and does not represent EPA policy.



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

--- Working Review Draft ---

EPA-SAB-RAC-ADV-07-xxx

The Honorable Stephen L. Johnson
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Subject: Advisory on Agency Draft White Paper entitled “*Modifying Radiation Risk Models Based on BEIR VII,*”

Dear Administrator Johnson:

--- Letter to be Completed ---

NOTICE

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This advisory has been written as part of the activities of the EPA Science Advisory Board (SAB), a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The SAB is structured to provide balanced, expert assessment of scientific matters related to problems facing the Agency. This advisory has not been reviewed for approval by the Agency and, hence, the contents of this advisory do not necessarily represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names of commercial products constitute a recommendation for use. Reports and advisories of the SAB are posted on the EPA website at <http://www.epa.gov/sab>.

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FY 06 Roster
U.S. Environmental Protection Agency (EPA)
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SCIENCE ADVISORY BOARD STAFF

Dr. K. Jack Kooyoomjian, Designated Federal Officer, US EPA, Science Advisory Board (1400F), 1200 Pennsylvania Avenue, NW, Washington, DC, 20460

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9

10 **MEMBERS**

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12 NM
13

14 **Dr. Thomas B. Borak**, Professor, Department of Environmental and Radiological Health
15 Sciences, Colorado State University, Fort Collins, CA
16

17 **Dr. Antone L. Brooks**, Professor, Radiation Toxicology, Washington State University Tri-
18 Cities, Richland, WA
19

20 **Dr. Brian Dodd**, Consultant, Las Vegas, NV
21

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23

24 **Dr. William C. Griffith**, Associate Director, Institute for Risk Analysis and Risk
25 Communication, Department of Environmental and Occupational Health Sciences, University of
26 Washington, Seattle, WA
27

28 **Dr. Helen A. Grogan**, Cascade Scientific, Inc., Bend, OR
29

30 **Dr. Richard W. Hornung**, Director of Biostatistics and Data Management, Cincinnati
31 Children’s Hospital Medical Center, Division of General and Community Pediatrics, Cincinnati,
32 OH
33

34 **Dr. Jonathan M. Links**, Professor, Department of Environmental Health Sciences, Bloomberg
35 School of Public Health, Johns Hopkins University, Baltimore, MD
36

37 **Mr. Bruce A. Napier**, Staff Scientist, Radiological Science & Engineering Group, Pacific
38 Northwest National Laboratory, Richland, WA
39

40 **Dr. Daniel O. Stram**, Professor, Department of Preventive Medicine, Division of Biostatistics
41 and Genetic Epidemiology, Keck School of Medicine, University of Southern California, Los
42 Angeles, CA
43

44 **Dr. Richard J. Vetter**, Radiation Safety Officer, Professor of Biophysics, Mayo Clinic,
45 Rochester, MN
46

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2 **Dr. K. Jack Kooyoomjian**, Designated Federal Officer, US EPA, Science Advisory Board
3 (1400F), 1200 Pennsylvania Avenue, NW, Washington, DC, 20460

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**U.S. Environmental Protection Agency
Science Advisory Board**

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--- (Roster to be Inserted in Later Drafts) ---

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1. EXECUTIVE SUMMARY

--- (To be prepared in a Later Draft, once consensus language is agreed upon --- KJK) ---

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2. INTRODUCTION

2.1 Background

In 1994, the EPA published a report, referred to as the “Blue Book,” which lays out the EPA’s methodology for quantitatively estimating radiogenic cancer risks (U.S. EPA. 1994) <http://epa.gov/radiation/docs/assessment/402-r-93-076.pdf>. A follow-on report made minor adjustments to the previous estimates and presented a partial analysis of the uncertainties in the numerical estimates (U.S. EPA. 1999a) <http://epa.gov/radiation/docs/assessment/402-r-99-003.pdf>. Finally, the Agency published Federal Guidance Report 13 (U.S. EPA. 1999) <http://epa.gov/radiation/docs/federal/402-r-99-001.pdf> 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. These were later updated (U.S. EPA. 1999b) <http://epa.gov/radiation/federal/techdocs.htm#report13>.

The National Research Council recently released *Health Risks from Exposure to Low levels of Ionizing Radiation BEIR VII Phase 2* which primarily addresses cancer and genetic risks from low doses of low LET radiation (BEIR VII) (U.S. NAS/NRC. 2006) <http://newton.nap.edu/catalog/11340.html#toc>). In the EPA draft *White Paper: Modifying EPA Radiation Risk Models Based on BEIR VII*, the Agency proposes changes to the EPA’s methodology for estimating radiogenic cancers, based on the contents of BEIR VII (U.S. EPA. 2006a). The Agency expects to adopt the models and methodology recommended in BEIR VII, but believes that certain modifications and expansions are desirable or necessary for the EPA’s purposes.

2.1.1 Request for EPA Science Advisory Board (SAB) Review

The Radiation Advisory Committee (RAC) was initially briefed on the draft White Paper topic at its public planning meeting of December 21, 2005 which was held at the National Air and Environmental Radiation Laboratory (NAERL) in Montgomery, Alabama (see 70 Fed. Reg. 69550, November 16, 2005). ORIA issued its external draft White Paper entitled “*Modifying EPA Radiation Risk Models Based on BEIR VII*,” on August 1, 2006 (U.S. EPA. 2006a). The charge questions to the SAB were formally submitted on August 31, 2006 (U.S. EPA. 2006b).

The SAB RAC met in a public teleconference meeting on September 6, 2006 and conducted a face-to-face public meeting on September 26, 27 and 28, 2006 for this advisory (see 71 Fed. Reg. 45545, August 9, 2006). Additional public conference calls took place on November 28, 2006 and December 18, 2006 (see 71 Fed. Reg., 62590, October 26, 2006 and add additional meetings as appropriate - - - KJK). 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>).

1 **2.2 Proposed EPA Adjustments and Extensions to BEIR VII Models**

2
3 **2.2.1 Current EPA Cancer Risk Models**

4
5 For most cancer sites, radiation risk models are derived primarily from epidemiologic
6 data from the Life Span Study (LSS) of the atomic bomb survivors. The EPA’s models for
7 esophageal, stomach, colon, lung, ovarian, bladder, leukemia, and “residual” cancers were
8 adapted from the models published by Land and Sinclair based on a fit to the linear, no-threshold
9 fit to the LSS data (Land and Sinclair. 1991).

10
11 For each solid tumor site, gender, and age-at-exposure interval, there is a model
12 providing a coefficient for the excess relative risk (ERR) per gray (Gy) for cancer mortality,
13 which is assumed to be constant beginning at the end of a minimum latency period until the end
14 of life. Land and Sinclair present two sets of models known as the “multiplicative” and the
15 “National Institutes of Health (NIH)” models that differ in how one “transports” risk from the
16 Japanese LSS population to the United States population. In the multiplicative model, it is
17 assumed that the ERR/Gy is the same in all populations, whereas, in the NIH model, it is
18 assumed that the excess absolute risk (EAR) is the same in different populations for the limited
19 period of epidemiological follow-up. Given the scarcity of information on how radiogenic
20 cancer risk varies between populations having differing baseline cancer rates, the EPA
21 previously adopted an intermediate geometric mean coefficient “GMC” model for each site,
22 where the ERR coefficients were taken to be the geometric mean of the corresponding ERR
23 coefficients for both the multiplicative and the NIH models (U.S. EPA. 1994).

24
25 For leukemia, the treatment of the temporal response in the models was more complex,
26 but the approach for transporting risk to the U.S. population was analogous. Following the
27 approach of Land and Sinclair, the EPA also developed a GMC model for kidney cancer from
28 the LSS data. The EPA’s models for other sites, including breast, liver, thyroid, bone, and skin
29 were based on various authoritative reports (NCRP. 1980; NRC. 1988; ICRP. 1991a, b; Gilbert.
30 1991). Based primarily on ICRP recommendations at that time, for low doses and dose rates,
31 each coefficient was reduced by a factor (DDREF) of two from that which would be obtained
32 from a Linear Non Threshold (LNT) fit to the LSS data.

33
34 **2.2.2 BEIR VII Models**

35
36 BEIR VII cancer site-specific models derived from the LSS differ from those of Land and
37 Sinclair in several notable ways: (1) they are derived primarily from data on cancer incidence
38 rather than cancer mortality; (2) mathematical fitting is performed to better reflect the functional
39 dependence of solid cancer risk on age at exposure and attained age, (i.e., age at diagnosis of a
40 cancer or age at death due to cancer depending on the end-point of interest); (3) a weighted
41 average of risk projection models is used to transport risk from the LSS to the U.S. population;
42 (4) a value for the DDREF of 1.5 is estimated from the LSS and laboratory data; (5) quantitative
43 uncertainty bounds are provided for the site-specific risk estimates in BEIR VII.

1 For breast cancer and thyroid cancer, BEIR VII risk models are based on pooled analyses
2 of data from the LSS cohort, together with data from epidemiologic studies of medically
3 irradiated cohorts (Preston et al. 2002; Ron et al. 1995).

4 5 **2.2.3 Proposed EPA adjustments and Extensions to BEIR VII Models**

6
7 In the draft *White Paper: Modifying EPA Radiation Risk Models Based on BEIR VII*
8 (U.S. EPA. 2006a), the Agency’s Office of Radiation and Indoor Air (ORIA) outlined proposed
9 changes in the EPA’s methodology for estimating radiogenic cancers, based on the contents of
10 BEIR VII and some ancillary information. For the most part, the Agency expects to adopt the
11 models and methodology recommended in BEIR VII; however, the Agency believes that certain
12 modifications and expansions are desirable or necessary for the EPA’s purposes.

13
14 One significant extension to be considered is the estimation of risks from exposures to
15 higher LET radiations, especially to alpha particles, but also to lower energy photons and beta
16 particles. An important expansion proposed by EPA to be considered is the estimation of risks
17 from exposures to alpha particles, and also to alpha emitters deposited in the lung and the bone.
18 BEIR VII does not present any risk estimates for radiogenic bone cancer. The EPA proposes to
19 estimate bone cancer risk from data on radium injected patients.

20
21 BEIR VII does not provide quantitative estimates of risk for skin cancer. It does not fully
22 address prenatal exposures. BEIR VII presents a model for estimating the risk of the radiogenic
23 thyroid cancer incidence, but not of mortality due to radiogenic thyroid cancer.

24
25 The EPA proposes to use somewhat different population statistics from BEIR VII.
26 Consideration is given to an alternative model for estimating radiogenic lung cancer. For breast
27 cancer, the EPA proposes an alternative method for estimating mortality, which takes into
28 account changes in incidence rates and survival rates over time.

29
30 At this point in its activity on this topic, the EPA is seeking advice from the Agency’s
31 Science Advisory Board’s Radiation Advisory Committee (RAC) on the application of BEIR
32 VII’s cancer risk estimates and on issues relating to these modifications and expansions. After
33 receiving the advisory review, the Agency plans to implement changes in their methodology
34 through the publication of a revised Blue Book, which it would expect to submit to the SAB’s
35 RAC or a specialty panel supplementing the RAC for final review. The revised Blue Book could
36 then serve as a basis for an updated version of FGR-13.

37 38 **2.2.4 Uncertainty Estimates**

39
40 BEIR VII provides quantitative uncertainty bounds for each of its risk coefficients,
41 however, no uncertainty was assigned to the form of the dose-response relationship. It was
42 implicitly assumed that the dose-response relationship followed the hypothetical dose-response
43 curve depicted in Figure 10-1. This shows a progression of linear approximations, with different
44 slopes within different dose ranges. The relationship between these different slopes provides the
45 definition of the dose and dose-rate effectiveness factor (DDREF). This progression allowed the
46 BEIR VII Committee to place uncertainty on bounds of the DDREF. Mechanisms pertaining to

1 the biological effects of low-level ionizing radiation are being investigated, which could
2 eventually mandate a different dose-response model, potentially resulting in large changes in
3 estimates of risk at low doses. Assigning probabilities to alternative models would be highly
4 subjective at this time. The EPA does not propose to quantify the uncertainty pertaining to low-
5 dose extrapolation, but it would provide a brief discussion of the issue.

6 7 **2.2.5 Level of Review**

8
9 There are various levels of reviews which EPA can request from the SAB. These include
10 reviews, advisories, and commentaries. The request from EPA-ORIA was for an “advisory”
11 review of the draft White Paper. ORIA was interested in vetting ideas with a group of scientific
12 experts on how to incorporate the changes in cancer risk models described by BEIR VII and to
13 extend the BEIR VII models to areas not specifically addressed by the BEIR VII committee.
14 ORIA described it as kind of a “mid-course correction” which would allow the RAC to provide
15 advice on a series of questions which would guide the agency in incorporating the latest
16 scientific thinking into their risk estimates. The RAC was not asked to provide policy direction,
17 therefore the RAC did not consider the implications to EPA standards which may be an outcome
18 of the changes to the risk estimates. The RAC only considered the scientific evidence which
19 support the risk models for radiogenic cancer.

20 21 **2.2.6 Specific Charge to the Committee**

22
23
24 1) *BEIR VII provides incidence models for many cancer sites as a basis for calculating the*
25 *risk from low-dose, low-LET radiation. Please comment on EPA’s application of this overall*
26 *approach as described in the draft White Paper.*

27
28 2) *In addition to the overall approach described in BEIR VII, the draft White Paper presents*
29 *specific modifications and extensions. Please comment on the soundness of the following*
30 *proposals:*

- 31
32 a. *Calculation of the risk to the life table (stationary) population instead of the actual*
33 *U.S. population (see Sections II.A.-C.); this is consistent with our current approach.*
34
35 b. *Use of more recent incidence and mortality data from SEER and/or other sources*
36 *(see Section II.D.); BEIR VII used a previous version of SEER data for the years*
37 *1995-1999.*
38
39 c. *Method for combining BEIR VII’s models for projecting risk from Japanese A-bomb*
40 *survivors to U.S. population (see Section II.E.). In contrast to BEIR VII, we propose*
41 *to combine the two risk models before integration to calculate the lifetime*
42 *attributable risk.*
43
44 d. *Adoption of an alternative model for radiogenic lung cancer risk which may better*
45 *account for the effects of smoking than the BEIR VII approach (see Section II.G.).*
46

- 1 e. *Method for calculating breast cancer mortality risk, accounting for the relatively long*
2 *time from detection until death (see Section II.H.).*
3
- 4 f. *Proposed approaches for extending risk estimates to radiations of different LET’s - in*
5 *particular, deriving site-specific risk estimates for alpha or x radiations based on*
6 *models derived from the A-bomb survivors, who were primarily exposed to gamma*
7 *rays (see Section III).*
8
- 9 g. *Estimation of risks for sites not specified in BEIR VII, specifically bone and skin, for*
10 *which we propose to update our current approaches (see Sections III.A. and V,*
11 *respectively).*
12
- 13 h. *Estimation of risk due to prenatal exposure. EPA’s current lifetime risk estimates do*
14 *not include risk from prenatal exposure, and BEIR VII does not provide them. The*
15 *draft White Paper uses ICRP recommendations to project its risks of childhood*
16 *cancers induced by in utero exposure. Please comment on the soundness of the*
17 *approach described in the draft White Paper to apply ICRP as described in Section*
18 *IV.*
19
- 20 3) *BEIR VII provides quantitative uncertainty bounds for each of its risk coefficients. EPA*
21 *proposes to adopt this methodology with some additional discussion of the uncertainties not*
22 *quantified in BEIR VII. Please comment on the adequacy of this approach (see Section II.K.).*
23
- 24 4) *In Section VI, the draft White Paper discusses some issues relating to radiogenic thyroid*
25 *cancer. Does the RAC have any specific suggestions for dealing with this risk; e.g., does the*
26 *RAC have any advice on gender specificity, effectiveness of iodine -131 compared to gamma*
27 *rays, or estimation of thyroid cancer mortality?*

3. PHILOSOPHY OF APPROACH TO THE CHARGE

3.1 Responding to the Agency’s Specific Request

In providing advice to the Agency, the RAC had to consider the important distinction between the current state of scientific knowledge and the need for a practical, operational public health approach to radiation protection and standards setting. In this Advisory, the RAC wishes to comment on both issues.

For the purposes of providing estimates of the risks of radiation-induced cancers as a basis for setting radiation protection standards, the RAC endorses EPA's proposal to base its approach on BEIR VII. Specifically, the RAC endorses the use of an LNT model for low dose risk estimation. By “low dose,” the RAC follows BEIR VII’s definition; that is, doses below 100 mSv (0.1 Sv), in the context of low LET radiation. In endorsing the use of an LNT model for low-dose risk estimation, the RAC wishes to emphasize that the specific LNT model applied below 100 mSv differs from that applied at higher doses, with a smaller slope. The ratio of slopes is the DDREF, whose use the RAC endorses. In essence, the RAC endorses the overall approach to radiogenic cancer risk estimation in BEIR VII, as typified in Figure 10-1.

With respect to recent advances in the scientific knowledge of radiation biology and carcinogenesis, the RAC wishes to emphasize that considerable uncertainties remain in the risk estimates for radiation-induced cancers, especially at low doses and low-dose rates. As BEIR VII acknowledges, the epidemiological data below 100 mSv (0.1 Sv) are not sufficient by themselves for risk estimation, and considerable cellular and animal data suggest complexities beyond the simple application of an LNT model. The RAC also wishes to emphasize the additional complexities introduced with varying RBE and dose rate. Thus, while the RAC endorses EPA’s use of the LNT model, we recommend that the Agency continue to monitor the science underlying the biophysical models of radiation damage and dose-response in the low-dose range to link low dose effects with increased cancer risk.

Additional discussion of the on-going research findings is in Appendix A.

3.2 Acknowledgement

The document “*Modifying EPA Radiation Risk Models Based on BEIR VII*,” August 1, 2006 was well written and provided much needed background. Similarly, with the BEIR VII report, presentations by the ORIA staff and other information provided to the RAC in the course of the public meetings were found to be helpful. During the meetings, the ORIA staff worked diligently to augment their draft *White Paper* with additional pieces of information that the RAC felt were necessary to assist with the advisory. The staff took care to honor all the RAC’s requests and demonstrated their patience as members sought to understand all that went into the modified procedures being proposed.

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4. RESPONSE TO CHARGE QUESTION 1: APPLICATION OF THE OVERALL APPROACH AS DESCRIBED IN THE DRAFT WHITE PAPER

4.1 Response to Charge Question 1:

BEIR VII provides incidence models for many cancer sites as a basis for calculating the risk from low-dose, low-LET radiation. Please comment on EPA’s application of this overall approach as described in the draft White Paper.

The Radiation Advisory Committee (RAC) agrees with the EPA that the BEIR VII methodologies using incidence models and data should be used wherever possible. The RAC accepts the EPA’s use of BEIR VII methodologies for deriving risk estimates for cancers of the stomach, colon, liver, prostate, uterus, ovary, bladder, and other solid tumors. However if one of the four following conditions apply, then the RAC agrees that the EPA is warranted in modifying the BEIR VII methodologies. The four possible conditions are:

- 1) Information and data are needed about subject matter not addressed in BEIR VII;
- 2) More recent or more relevant data exist which could improve or otherwise influence the risk estimates;
- 3) Compelling evidence suggests the use of a more appropriate scientific method; or
- 4) The EPA’s implementation requirements for practicality or applicability necessitate an adaptation or other alternative to BEIR VII methodologies.

The RAC grouped all of the charge issues according to these conditions. For example, under condition one, RAC considered prenatal exposures, bone and skin cancers, x- and alpha-particle radiations and tritium as areas not addressed by BEIR VII, and for which the EPA has a need to derive a basis for risk estimates. An example of applying condition two is the use of the most recent SEER data would improve the risk estimate. Examples of condition three are issues where a more appropriate scientific method was considered, i.e. in development of lung and breast cancer risk estimates and the estimation of uncertainty. An example of condition four is the use of a stationary or a standard population.

The RAC concludes that the EPA’s use of the gray (Gy) as the unit of radiation absorbed dose is appropriate and agrees that modifying factors should be applied to the risk rather than dose.

The RAC’s approach to giving advice to the EPA is predicated on the basic premise that the risk estimates are for use in assessing population or average individual risk, rather than risk to a specific individual. This is because specific individuals may be more or less susceptible to radiation-induced cancer than the average individual.

1 **5. RESPONSE TO CHARGE QUESTION 2: WHITE PAPER**
2 **MODIFICATIONS AND EXTENSIONS**
3

4 **5.1 Response to Charge Question # 2**

5 *In addition to the overall approach described in BEIR VII, the draft White Paper presents*
6 *specific modifications and extensions. Please comment on the soundness of the following*
7 *proposals:*
8

- 9 a. *Calculation of the risk to the life table (stationary) population instead of the actual U.S.*
10 *population (see Sections II.A.-C.); this is consistent with our current approach.*
- 11
- 12 b. *Use of more recent incidence and mortality data from SEER and/or other sources (see*
13 *Section II.D.); BEIR VII used a previous version of SEER data for the years 1995-1999.*
14
- 15 c. *Method for combining BEIR VII’s models for projecting risk from Japanese A-bomb*
16 *survivors to U.S. population (see Section II.E.). In contrast to BEIR VII, we propose to*
17 *combine the two risk models before integration to calculate the lifetime attributable risk.*
18
- 19 d. *Adoption of an alternative model for radiogenic lung cancer risk which may better*
20 *account for the effects of smoking than the BEIR VII approach (see Section II.G.).*
21
- 22 e. *Method for calculating breast cancer mortality risk, accounting for the relatively long*
23 *time from detection until death (see Section II.H.).*
24
- 25 f. *Proposed approaches for extending risk estimates to radiations of different LET’s - in*
26 *particular, deriving site-specific risk estimates for alpha or x radiations based on models*
27 *derived from the A-bomb survivors, who were primarily exposed to gamma rays (see*
28 *Section III).*
29
- 30 g. *Estimation of risks for sites not specified in BEIR VII, specifically bone and skin, for*
31 *which we propose to update our current approaches (see Sections III.A. and V,*
32 *respectively).*
33
- 34 h. *Estimation of risk due to prenatal exposure. EPA’s current lifetime risk estimates do not*
35 *include risk from prenatal exposure, and BEIR VII does not provide them. The draft*
36 *White Paper uses ICRP recommendations to project its risks of childhood cancers*
37 *induced by in utero exposure. Please comment on the soundness of the approach*
38 *described in the draft White Paper to apply ICRP as described in Section IV.*
39

1 **5.2 Response to Charge Question # 2a**

2
3 *Calculation of the risk to the life table (stationary) population instead of the actual U.S.*
4 *population (see Sections II.A.-C.); this is consistent with our current approach.*

5
6 The RAC agrees that the proposed estimation of radiogenic cancer risks for the U.S.
7 population based on a standard stationary population based on the year 2000 deathrate, or fixed
8 cohort is a reasonable adaptation of the BEIR VII approach. Specifically, it avoids the potential
9 for changes over time in the baseline cancer rates among the actual U.S. population that may be
10 associated with changes in its racial, ethnic, cultural or other characteristics known to influence
11 population disease rates. It also is consistent with the EPA’s established approach to cancer risk
12 estimation from exposures to chemicals.
13

14 **5.3 Response to Charge Question #2b**

15
16 *A Use of more recent incidence and mortality data from SEER and/or other sources (see*
17 *Section II.D.); BEIR VII used a previous version of SEER data for the years 1995-1999.*

18
19 The RAC agrees that the EPA’s proposed use of the most current cancer-specific
20 incidence and mortality rates available is an appropriate and scientifically valid adaptation of the
21 BEIR VII approach.
22

23 It is anticipated that incidence or mortality data for the years 1998-2002 will be available
24 for the final calculations of radiogenic cancer incidence risk estimates from NCI’s SEER
25 program. In contrast, only data from this program for 1995-1999 were available to BEIR VII.
26

27 Although other potential sources of valid, nationally representative data will be
28 considered by the EPA, the RAC considers that the most current SEER data are adequate and
29 preferred for consistency with the BEIR VII approach. The EPA may want to consider the latest
30 vital statistics report produced from the 2000 census for mortality rates if they become available
31 before the final report is produced.
32

33 **5.4 Response to Charge Question #2c**

34 *Method for combining BEIR VII’s models for projecting risk from Japanese A-bomb*
35 *survivors to U.S. population (see Section II.E.). In contrast to BEIR VII, we propose to*
36 *combine the two risk models before integration to calculate the lifetime attributable risk.*

37
38 The RAC notes that there is considerable uncertainty in the application of risk estimates
39 developed from the Japanese atomic bomb survivors to the U.S. population. This uncertainty
40 results from different genetic and lifestyle characteristics of the two populations and differences
41 in the baseline cancer risks. The RAC agrees with the EPA’s proposed approach for projecting

1 risk estimates from the Japanese A-bomb survivors to the U.S. population by combining the age-
2 specific results from the EAR and ERR models using the weighted geometric mean before
3 calculating the lifetime attributable risk. This approach is a modification of that used in BEIR
4 VII but is consistent with the method used previously by the EPA in FGR13. The RAC notes that
5 the EPA method has the advantage of allowing the risk results from separate exposures to be
6 integrated, enabling the risk from chronic lifetime exposure to be calculated.
7

8 **5.5 Response to Charge Question #2d**

9 *Adoption of an alternative model for radiogenic lung cancer risk which may better account*
10 *for the effects of smoking than the BEIR VII approach (see Section II.G.).*
11

12
13 The lung cancer risk estimates reported by BEIR VII are primarily based on analyses of
14 the LSS data. These estimates were not adjusted for cigarette smoking which is potentially an
15 important confounder and/or effect modifier. This problem of lack of adjustment for cigarette
16 smoking is further compounded by the fact that lung cancer incidence rates are lower in Japan
17 than the U.S. and the lung cancer incidence rate ratio of males to females is considerably higher
18 in Japan than in the U.S. The BEIR VII Committee was aware of this problem and chose to deal
19 with it by using a risk transport model that more heavily weighted the EAR estimates relative to
20 ERR estimates, i.e. assigning the weight of 0.7 for EAR and 0.3 for ERR. The BEIR VII
21 Committee justified this approach based on mechanistic arguments and the fact that a 2003 paper
22 by Pierce found that the interaction between low LET radiation and smoking was consistent with
23 an additive effect in the LSS population. This weighting scheme results in a lifetime attributable
24 risk (LAR) that is roughly twice as great in women as compared to men.
25

26 The EPA white paper took issue with the BEIR VII lung cancer risk estimates. EPA was
27 concerned that the lack of adjustment for cigarette smoking and birth cohort effects would result
28 in an overestimate of risk in the U.S. population as well as female to male incidence rate ratio
29 that was too high. EPA proposed to use a pure EAR model for lung cancer, equivalent to a
30 weighting of 1.0 for EAR and 0.0 for ERR risk models.
31

32 The RAC requested additional work on this problem from the EPA consisting of the
33 following tasks:
34

- 35 ● Compare results of the calculation of LAR using BEIR VII weighting to 100% EAR model
36 and to alternative weighting schemes and/or the use of arithmetic, AM, or geometric, GM,
37 means.
- 38 ● Consider how the additive ERR model for smoking and radiation provides evidence for the
39 appropriate weighting scheme.
- 40 ● Consider papers additional to Pierce (2003) on the nature of the smoking /radiation
41 interaction.
42
43
44

1
 2 Based upon EPA’s response to these requests, the RAC produced the following table
 3 illustrating the effect upon LAR estimates for lung cancer incidence of several different
 4 weighting schemes for the EAR and ERR risk models. The columns labeled WP and BEIR VII
 5 reflect differences in how the weighting was applied. BEIR VII used a weighted average of the
 6 final age-adjusted ERR and EAR estimates on a log scale, while EPA first weighted each age-
 7 specific stratum and then combined the weighted age-specific risk estimates. Inspection of the
 8 table reveals that the difference in application of the weights produced very small changes in the
 9 WP and BEIR VII LAR estimates. The weighting of 0.0 for ERR proposed by EPA produces
 10 LAR estimates that are somewhat smaller than the weight of 0.3 for ERR chosen by BEIR VII,
 11 most notably for females. The RAC also notes that the evidence for a purely additive model is
 12 not compelling based upon the literature review performed by EPA. There is some support for
 13 an interaction between radiation exposure and cigarette smoking that is intermediate between
 14 additive and multiplicative, similar to the weighting scheme selected by BEIR VII.

15
 16 Accordingly, due to a lack of compelling evidence to depart from the weighting approach
 17 used by BEIR VII, the RAC recommends that EPA should not employ alternative weighting
 18 schemes. The RAC also notes that, although differences between the EPA proposed estimates
 19 and BEIR VII are relatively small, the EPA LAR estimates are consistently lower than those
 20 reported in BEIR VII. Changes to BEIR VII that reduce published risk estimates would be
 21 controversial, especially given that the differences would be well within the level of uncertainty.

Table 1: Comparison of the White Paper (WP) and BEIR VII Method for Combining EAR and ERR LAR Projections for Lung Cancer Incidence.¹

	Combination Method RR weight ² = 0.0		Combination Method RR weight ³ = 0.3		Combination Method RR weight = 0.5		Combination Method RR weight = 0.7		Combination Method RR = 1.0	
	WP	BEIR VII	WP	BEIR VII	WP	BEIR VII	WP	BEIR VII	WP	BEIR VII
Sex										
Male	179	179	186	193	195	203	206	213	230	230
Female	344	344	401	428	460	495	541	573	714	714

NOTE: Number of cases per 100,000 persons exposed to 0.1 Gy. Results do not incorporate DDREF adjustment.

¹Results are shown for stationary populations and SEER incidence data for the years 1998-2002.

²Weight for projection based on EPA proposal

³Weight for projection using BEIR VII

1 **5.6 Response to Charge Question #2e**

2 *Method for calculating breast cancer mortality risk, accounting for the relatively long time*
3 *from detection until death (see Section II.H.).*
4

5 The RAC notes that the EPA adopts BEIR VII’s approach to estimating the risk of breast
6 cancer in females that differs from that used by BEIR VII to estimate the risks for the majority of
7 other solid cancers. However, the EPA identified issues relative particularly to the changing
8 clinical course of breast cancer in conjunction with a relatively long survival period, and
9 questions some aspects of BEIR VII’s risk estimation method for this site-specific cancer. The
10 EPA thus has identified several alternative methods for estimating the relative risk for radiogenic
11 breast cancer in an effort to take into account some of the temporal features that can influence
12 the cancer’s clinical course and hence the risk estimates. The RAC concurs with the EPA’s
13 decision to explore these alternative methods.
14

15 Specifically, the RAC likes the EPA’s proposal to relate current breast cancer mortality
16 rates to retrospective incidence rates rather than current incidence rates to better reflect the
17 influence of life style changes, earlier breast cancer detection and treatment that could influence
18 survival and hence mortality rates over an extended period.
19

20 The RAC notes the potential of development of second cancers during the cancer survival
21 period. Such an event could be spontaneous or related to treatment of cancer. In the case of
22 breast cancer, it could impact mortality reporting and loss of deaths attributed to breast cancer.
23

24 The RAC suggests that the EPA explore the feasibility of using the BEIR VII with the
25 proposed method (above) with retrospective lagging incidence rates relative to current mortality
26 rates.
27

28 **5.7 Response to Charge Question #2f**

29 *Proposed approaches for extending risk estimates to radiations of different LET’s - in*
30 *particular, deriving site-specific risk estimates for alpha or x radiations based on models*
31 *derived from the A-bomb survivors, who were primarily exposed to gamma rays (see Section*
32 *III).*
33

34 A significant extension requiring subject matter not addressed in BEIR VII is guidance
35 on how to deal with the estimation of risks from exposures to higher LET radiation, especially
36 alpha particles and lower energy photons and beta particles. Knowledge of these risks is required
37 particularly for dealing with the possible health risks from chronic irradiation from alpha, beta,
38 or gamma emissions from internally deposited radionuclides. A key feature of the low-LET
39 radiation exposures used in the analyses available in the BEIR VII report, especially those based
40 on the Japanese atomic bomb survivors, is that they involved a very brief, whole-body exposure
41 to radiation from an external source. In such a situation, all of the organs and tissues of the body
42 were irradiated and the long-term risks to these organs and tissues have been studied directly.
43 When dealing with internally deposited radionuclides, the situation is different because the

radionuclide is likely to be distributed non-uniformly in the body, with only a few organs and tissues receiving most of the dose. This can change the spectrum of cancers produced and may decrease the effectiveness per unit of dose. Also, because of the possible long-term retention of some long-lived radionuclides, the dose can continue to accumulate at a low dose rate over months or years. Dealing with these differences is important but not necessarily straightforward as discussed below.

Higher LET Radiation

A. Alpha Particles

The EPA white paper discusses three possible approaches to estimating the lifetime health risks from internally deposited alpha-emitting radionuclides. These three approaches are to use:

a) Data from human populations exposed to alpha-emitting radionuclides.

There are good carcinogenic risk data available for the following organs and tissues:

- Bone cancer from radium dial painters and radium chemists exposed to $^{226,228}\text{Ra}$;
- Bone Cancer from ankylosing spondylitis patients exposed to ^{224}Ra ;
- Liver cancer from patients given Thorotrast (^{232}Th) as an imaging agent;
- Leukemia from patients given Thorotrast (^{232}Th) as an imaging agent;
- Lung cancer from uranium miners who inhaled ^{222}Rn and progeny; and
- Lung cancer from Mayak Russian workers who inhaled ^{239}Pu .

Since the lung, liver, bone and bone marrow are the major organs at risk for internally deposited, alpha-emitting radionuclides, these populations provide important information on carcinogenic risk for alpha-emitting radionuclides.

b) Data from life-span studies of laboratory animals exposed via various routes of exposure to graded activity levels of alpha-emitting radionuclides.

There are sizeable data bases available for different species of laboratory animals exposed to different beta-, gamma- or alpha-emitting radionuclides by various routes and studied for their lifetimes. These studies provide much information on the life-span health effects but the number of variables involved including species, route of exposure, animal husbandry and other factors make it difficult to extrapolate the risk results directly to human populations in a consistent manner. However, they do provide useful information on radionuclides for which no human data are available. Such studies also help define the influence of dose distribution and the relative effectiveness of high- and low-LET radiations in those cases where studies of the high and low LET emissions were studied in a parallel manner under similar conditions.

c) The most recent cancer risk data from the RERF studies of atomic bomb survivors exposed to low-LET radiation multiplied by a general RBE_M factor for alpha particles.

1 This third, more general, approach assumes that an appropriate value for RBE_M is known
2 and that it is appropriate to use this value with the cancer risk seen after a brief, high dose-rate
3 exposure received by the atomic bomb survivors to estimate cancers risks in a broad range of
4 organs and tissues for which no data are available for alpha-particle exposure.

5
6 As discussed in Section III.A.3, Summary and Recommendations of the White Paper, the
7 EPA proposes to multiply site-specific gamma-ray cancer risk estimates by an RBE of 20 to
8 derive corresponding estimates of cancer risk from alpha radiation, with two exceptions:

- 9
10 a) An RBE = 1-3 for leukemia induced by alpha emitters deposited in bone; and
11 b) Continued use of models derived from BEIR VI to estimate lung cancer risk from
12 inhaled radon progeny.

13
14 The RAC recognizes the problems that the EPA has to deal with in adding consideration
15 of alpha-emitting radionuclides to the information already provided for low-LET radiation in the
16 BEIR VII report. This particular issue is one example of the need for a practical, operational
17 public health approach to radiation protection and standards setting mentioned earlier in this
18 Advisory. On this basis, the RAC is supportive of the use of a generally accepted RBE_M value
19 such as the 20 that they are using currently. For those radionuclides for which human cancer risk
20 data are available for the lung, liver, bone, or bone marrow, the RAC recommends that this
21 information be used directly whenever possible. For other organs and tissues, the RAC is
22 supportive of the general approach of using the low-LET cancer risk from BEIR VII multiplied
23 by RBE_M .

24 25 **B. Low-energy Photons and Electrons**

26
27 The EPA White Paper suggests that the relative biological effectiveness (RBE) for
28 medical x rays is about 2 – 2.5. However, x rays are not unique from gamma rays except for
29 their production. Any risk estimate associated with exposure to photons needs to be correlated
30 with energy rather than the method of production.

31
32 Reviews by ICRU (1986) and Kocher et al. (2005) show that RBEs for low energy
33 photons, < 30 keV, and low energy electrons, <15 keV, are higher than one when compared to
34 higher energy x rays and ^{60}Co gamma rays. A probability distribution by Kocher et al. (2005)
35 showed a median radiation effectiveness factor (REF) of approximately 2.4 for photons less than
36 30 keV and for ^3H beta particles. Thus, an effectiveness factor for these low energy radiations in
37 the range of 2 to 2.5 seems reasonable.

38 39 **5.8 Response to Charge Question #2g**

40 *Estimation of risks for sites not specified in BEIR VII, specifically bone and skin, for which we*
41 *propose to update our current approaches (see Sections III.A. and V, respectively).*

42
43 The RAC recognizes that although the BEIR VII committee chose not to provide risk
44 estimates for non-melanoma skin cancer (NMSC) induced by ionizing radiation, EPA has an

1 operational need for such estimates. This presents ORIA with certain methodological challenges
2 given the high incidence and low mortality rates of NMSC among the US general population and
3 the limitations of available data.

4
5 The RAC supports EPA's proposed use of the 1991 ICRP model to estimate the incidence
6 and mortality risks of radiogenic NMSC taking into account more recent findings that most of
7 the NMSCs attributable to low to moderate doses of LET ionizing radiation are of the basal cell
8 (BCC) type (Shore 2001), and that the incidence rates of BCC have been increasing substantially
9 in recent decades among the general population (Karagas et al. 1999).

10
11 However, the RAC concurs with EPA that because of the high background incidence
12 rates and low mortality due to NMSC, it is inappropriate to include risk estimates for radiogenic
13 NMSC in the estimate of the total risk for radiogenic cancer. The RAC also notes that as ionizing
14 radiation is not considered to be a risk factor for melanoma skin cancer there is no rationale for
15 risk estimation in this instance.

16
17 Data for mortality due to bone cancer following exposure to ²²⁶Ra, ²²⁸Ra and ²²⁴Ra are
18 available for humans. These data provide a basis for estimating risks from these isotopes that
19 distribute uniformly in the bone. They also should be compared to the derived risks using the A-
20 bomb data and help define the magnitude of the RBE and radiation weighting factor used. The
21 induction of bone cancer by radioisotopes that produce non-uniform surface deposition in the
22 bone need to be considered as being in a different class from the isotopes that are uniformly
23 deposited in the bone. For isotopes for which there are no human data, the animal data may help
24 in determining the factors necessary to relate the risk from an isotope like ²³⁹Pu or the beta-
25 emitting ⁹⁰Sr to that derived from the A-bomb data combining DDREF with radiation weighting
26 factors.

27 28 **5.9 Response to Charge Question #2h**

29 *Estimation of risk due to prenatal exposure. EPA’s current lifetime risk estimates do not*
30 *include risk from prenatal exposure, and BEIR VII does not provide them. The draft White*
31 *Paper uses ICRP recommendations to project its risks of childhood cancers induced by in*
32 *utero exposure. Please comment on the soundness of the approach described in the draft*
33 *White Paper to apply ICRP as described in Section IV.*

34
35 The RAC concludes that it would be reasonable for the EPA to base its risk estimates for
36 *in utero* radiation exposure on those recommended by the ICRP.

37
38 Rationale:

- 39 • BEIR VII does not provide risk estimates for *in utero* exposure to radiation, and the EPA
40 needs an estimate for its guidance documents;
- 41
42 • Few human data exist on which to base an estimate of radiogenic cancer risk for *in utero*
43 exposure to radiation. The primary sources of data are the Oxford Survey of Childhood
44 Cancer (Mettler and Upton, 1995, Steward et al. 1958, Mole 1990, Doll and Wakeford

1 1997) and studies of Japanese atomic bomb survivors exposed during pregnancy
2 (Delongchamp et al, 1997). When all sources of uncertainty are taken into account, the
3 risk estimates from these studies are not incompatible with each other (Wakeford & Little
4 2002). ICRP has provided an absolute risk estimate for cancer risk of $6 \times 10^{-2} \text{ Gy}^{-1}$ from
5 ages 0-15 after *in utero* irradiation (ICRP 2001a; ICRP 2001b); and
6
7 • Even though the risk from *in utero* exposure is a minor component of the overall
8 radiogenic cancer risk, a discussion of it should be included for completeness.
9
10
11

6. RESPONSE TO CHARGE QUESTION 3: UNCERTAINTIES NOT QUANTIFIED IN BEIR VII

Charge Question 3: *BEIR VII provides quantitative uncertainty bounds for each of its risk coefficients. EPA proposes to adopt this methodology with some additional discussion of the uncertainties not quantified in BEIR VII. Please comment on the adequacy of this approach (see Section II.K.).*

The RAC strongly endorses the EPA-ORIA’s desire to estimate uncertainty bounds for its radiogenic cancer risk estimates. Indeed, given the range of possible operational uses of the risk estimates, as much effort should go into estimating the uncertainty bounds as into producing the central or point risk estimates themselves.

Ideally, the uncertainty analysis would involve the development of a probability density function for (site-specific) estimated risk, rather than confidence intervals around a central or point risk estimate. Such an approach, which has previously been considered by other national and international committees, would facilitate risk estimation based on other than the average risk. For example, such an approach might facilitate the identification of a minimum cost-of-errors (or ‘loss’) risk estimate for operational use (e.g., in risk-informed regulation). However, the RAC believes that such an approach is not likely to be practically achievable, and endorses the EPA-ORIA’s approach (central risk estimate with uncertainty bounds, following BEIR VII).

The uncertainty bound estimates should incorporate, to the extent possible, *all* sources of error and/or uncertainty, including the three main sources identified in BEIR VII (sampling variability in the LSS data, transport of risk from LSS to U.S. population, and the appropriate value for DDREF **at both high and low doses of low-LET radiation** (or, equivalently, the **appropriate use of the LNT** dose-response model used for low-dose extrapolation)), but also considering other sources of error and/or uncertainty identified by the EPA-ORIA (including dosimetry (of which neutron RBE is a factor), disease detection, correct disease classification, temporal patterns, and appropriate RBE values). By “consider,” the RAC means that the EPA-ORIA should attempt to estimate, in a preliminary fashion, the relative magnitude of the contribution of the additional sources of error or uncertainty they identified to the overall uncertainty. Of importance, it is useful to try to estimate the independent contribution of these additional sources, most of which are likely partially correlated with those sources identified in BEIR VII. One possible way of estimating the magnitudes is via some modest simulation studies. Only if the independent contribution of any of these additional sources of error is potentially significant in magnitude should that source be included in the uncertainty analysis. In any event, the methods of uncertainty analysis should follow BEIR VII.

There is some value to producing two sets of uncertainty bounds, one representing the bounds on the (site-specific) central or point risk estimate for the method of combining the RR and AR that the EPA finally chooses to use, the other representing combinations ranging from 100% RR through 100% AR. The former gives a measure of the uncertainty of the central risk estimate derived from the method specifically used, and the latter gives an indication of the range in which the true value (independent of method) likely resides.

1
2 In coming to these recommendations, the RAC considered several additional
3 complications that could influence uncertainty. To begin with, **the significant biological**
4 **responses from the LSS** and other epidemiological data cover a finite range of individual doses.
5 The uncertainties associated with risk estimates are smallest within that range of doses **where**
6 **significant changes in cancer frequency can be detected.** At doses significantly above this
7 range, radiogenic cancer risk estimates are not meaningful, because acute fatalities dominate. At
8 doses below this range, there is, by definition, no directly demonstrated effect in humans, and
9 risk estimates must be based, explicitly or implicitly, on an assumed **LNT** dose-response model
10 and method of extrapolation from known, higher-dose/higher-response data. In such a situation,
11 lower-dose risk estimates may have larger relative uncertainties than higher-dose risk estimates
12 because of this extrapolation.

13
14 Said another way, assumptions about the biophysical model for radiogenic cancer
15 influence the choice of dose-response model, and errors in the assumptions and subsequent
16 choice of method of extrapolation amplify errors in the central or point risk estimates. The
17 biophysical model for radiogenic cancer intrinsic to LNT implies direct DNA damage to a single
18 cell as the initiating event, followed by clonal expansion. **It is well established that the initial**
19 **DNA damage increases linearly with dose. However, it is also well known that the**
20 **biological processing of that damage is non-linearly dependent on dose. Since dose-**
21 **dependent changes in gene and protein expression,** adaptive response, genomic instability,
22 and bystander effects **have been demonstrated in many biological systems,** they can change
23 the shape of the dose-response function at low doses. *(Such effects are likely only important*
24 *(relative to LNT) at low doses.) Perhaps we could delete this.* Of importance, the specific nature
25 of the original damage, and the mechanisms involved in the biological processing of that damage
26 change with dose. It is thus likely an oversimplification to suggest that only the magnitude of
27 somatic genetic changes is dose-dependent. It is further likely that errors in risk estimates
28 progressively increase (relatively) as dose decreases if these additional elements of the
29 biophysical model are more prominent at low doses.

30
31 Having said that, BEIR VII specifically considered adaptive response, genomic
32 instability, and bystander effects, and concluded that there is insufficient evidence to explicitly
33 add these effects to the dose-response model. The EPA-ORIA proposes **at the present time** to
34 follow BEIR VII **and use the LNT for calculation of radiation risk.** In the absence of
35 compelling scientific evidence to do otherwise, the RAC endorses the EPA-ORIA’s plan in this
36 regard. The RAC does recommend, however, that the EPA-ORIA include a (qualitative)
37 discussion of **modern molecular biological** concepts in its final report. As a cautionary note,
38 **we recommend that the EPA discuss** the application of its **LNT** risk estimates in very low-
39 dose settings **where there are no human cancer data and where the doses are a fraction of**
40 **the ever present background radiation exposure.**

41
42 It is important to note that there is indeed opportunity to include uncertainties in the
43 model – that is, uncertainties in high-dose versus low-dose behavior – in the overall uncertainty
44 analysis. In BEIR VII and the EPA-ORIA’s proposed approach to uncertainty estimation, this
45 “additional” uncertainty is contained within the uncertainty in the value for DDREF, since

1 DDREF is only invoked at lower doses. The RAC thus strongly endorses the EPA-ORIA’s
2 intention to include uncertainty in DDREF in the overall uncertainty analysis.
3

4 **The RAC suggests the need for an additional dose-rate effectiveness factor at higher**
5 **total doses delivered at low dose rates where the DDREF does not apply. In these higher**
6 **dose ranges the influence of dose-rate can be marked and a dose rate factor would much**
7 **higher than the 1.5 recommended by BEIR VII. This large dose rate factor can be very**
8 **important in predicting the biological damage in the event of nuclear accidents or terrorist**
9 **activities where large populations could be exposed to large doses at low dose-rates**

10
11 Uncertainties are also a function of time into the future, being smallest in the near time
12 frame. This is due to several factors, including changes in future (actual) populations (as opposed
13 to a ‘stationary population’), future background cancer incidence, and future medical advances
14 (since the case fatality rate may decrease as a result of better treatment interventions in the
15 future). Uncertainties thus become greater as the risk estimates are applied further into the future.
16 The RAC recommends that EPA-ORIA include a (qualitative) discussion of these concepts in its
17 final report.
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7. RESPONSE TO CHARGE QUESTION 4: ISSUES RELATING TO RADIOGENIC THYROID CANCER NOT QUANTIFIED IN BEIR VII

Charge Question 4: *In Section VI, the draft White Paper discusses some issues relating to radiogenic thyroid cancer. Does the RAC have any specific suggestions for dealing with this risk; e.g., does the RAC have any advice on gender specificity, effectiveness of iodine -131 compared to gamma rays, or estimation of thyroid cancer mortality?*

The RAC believes that it is premature to offer any advice to ORIA on this issue. A major review of radiogenic thyroid cancer is planned by the National Council on Radiation Protection and Measurements. This should be considered by ORIA as more recent or more relevant data which could improve the risk estimates provided by BIER VII.

REFERENCES CITED

--- (references to be added & cited as appropriate) ---

Breckow, Joachim. Linear-no-threshold is a radiation protection standard rather than a mechanistic effect model. *Radiat. Environ. Biophys* (2006) 44:257-260.

Delongchamp RR, K Mabuchi, Y Yoshimoto, DL Preston. Cancer mortality among atomic bomb survivors exposed *in utero* or as young children. *Radiation Research* 147: 385-395, 1997.

Dodd, Brian. 1990. “The Validity of Population Dose and Cancer Risk Coefficients in the Determination of Latent Cancer Fatalities,” HPS Newsletter, April, 1990.

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

Federal Register Notice Citations:

FR, Vol. 70, No. 220, November 16, 2005, pp. 69550-69551; and

FR, Vol. 71, No. 153, August 9, 2006, pp. 45545-45546;

FR, Vol. 71, No. 207, October 26, 2006, pp. 62590-62591

Gilbert. 1991 (To be provided by RAC KJK)

International Commission on Radiological Protection. 1991a. Recommendations of the International Commission on Radiological Protection. ICRP Publication 60. *Ann ICRP* 21 (1-3).

International Commission on Radiological Protection. 1991b. The Biological basis for Dose Limitation in the Skin. ICRP Publication 59. *Ann ICRP* 22(2).

International Commission on Radiological Protection. Pregnancy and Medical Radiation Volume 31/1, *Annals of the ICRP*, Publication 84, Pergamon Press, 2001a.

International Commission on Radiological Protection. Doses to the Embryo and Fetus from Intakes of Radionuclides by the Mother. *Annals of the ICRP*, Publication 88. Pergamon Press. 2001b.

ICRU. 1986 (To be provided by RAC KJK)

Japanese A-Bomb Survivors (See Section 4.9 --- To be provided by RAC KJK)

Karagas et al. 1999 (To be provided by RAC.... KJK)

Kocher et al. 2005 (To be provided by RAC.... KJK)

1 Land CE and WK Sinclair. 1991. The relative contributions of different organ sites to the total
2 cancer mortality associated with low-dose radiation exposure. In: *Risks associated with Ionising*
3 *Radiations*. Annals of the ICRP 22(1).
4
5 Mettler, FA and AC Upton, Medical Effects of Radiation. pp 331-334. W.B. Saunders,
6 Philadelphia, 1995.
7
8 Mole R. Childhood cancer after prenatal exposure to diagnostic x-ray examinations in Britain. Br
9 J Cancer 62: 152-168, 1990.
10
11 NCRP 1980. *Induction of Thyroid Cancer by Ionizing Radiation*. NCRP Report No 64. Bethesda,
12 MD: National Council on Radiation Protection and Measurements.
13
14 NRC 1988. *Health Effects of Radon and Other Internally Deposited Alpha-Emitters (BEIR IV)*.
15 Washington, DC: National Academy Press.
16
17 Oxford Survey of Childhood Cancer, see Mettler and Upton.
18
19 Pierce. 2003 (To be provided by RAC.... KJK)
20
21 Preston, DL, A Mattsson, E Holmberg, R Shore, NG Hildreth, and JD Boice Jr. 2002. Radiation
22 effects on breast cancer risk: a pooled analysis of eight cohorts. *Radiation Research* 158: 220-
23 235.
24
25 Ron E, JH Lubin, RE Shore, K Mabuchi, B Modam, L Pottern, AB Schneider, MA Tucker, and
26 JK Boice. 1995. Thyroid cancer after exposure to external radiation; a pooled analysis of seven
27 studies. *Radiation Research* 141: 259-277.
28
29 Shore. 1990 (To be provided by RAC.... KJK)
30
31 Shore. 2001 (To be provided by RAC.... KJK)
32
33 Steward A, Webb J, Hewitt D. A survey of childhood malignancies. Br Med J 1: 1495-1508,
34 1958.
35
36 U. S. EPA (Environmental Protection Agency). 1994. *Estimating Radiogenic Cancer Risks*
37 (“Blue Book”): <http://epa.gov/radiation/docs/assessment/402-r-93-076.pdf>
38
39 U.S. Environmental Protection Agency (EPA), Office of Air and Radiation (OAR). 1999.
40 “Federal Guidance Report 13. *Cancer Risk Coefficients for Environmental Exposure to*
41 *Radionuclides*,” Washington, DC (EPA-402-R-99-001),
42 <http://www.epa.gov/radiation/docs/federal/402-r-00-001.pdf>
43
44 U.S. EPA/OAR. 1999. Federal Guidance Report (FGR)-13. *Federal Guidance Report 13:*
45 *Cancer Risk Coefficients for Environmental Exposure to Radionuclides:*
46 <http://epa.gov/radiation/docs/federal/402-r-99-001.pdf>

1
2 U. S. EPA (Environmental Protection Agency) 1999a. *Addendum: Uncertainty Analysis*:
3 <http://epa.gov/radiation/docs/assessment/402-r-99-003.pdf>
4
5 U.S. EPA. (Environmental Protection Agency) 1999b. *Update to the Federal Guidance Report*
6 *No. 13 and CD Supplement*: <http://epa.gov/radiation/federal/techdocs.htm#report13>
7
8 U.S. EPA SAB. 2002. “*Panel Formation Process: Immediate Steps to Improve Policies and*
9 *Procedures: An SAB Commentary*,” EPA-SAB-EC-COM-02-003, May 17, 2002.
10
11 U.S. Environmental Protection Agency, Office of Radiation and Indoor Air (ORIA). 2006a
12 “*Modifying EPA Radiation Risk Models based on BEIR VII*,” Draft White Paper, Prepared by:
13 ORIA, U.S. Environmental Protection Agency, August 1, 2006
14 <http://epa.gov/radiation/news/recentadditions.htm>
15
16 U.S. EPA, Office of Radiation and Indoor Air (ORIA). 2006b. Memorandum from Elizabeth A.
17 Cotsworth, Director, ORIA to Vanessa Vu, Director, Science Advisory Board Staff Office,
18 entitled “*Advisory Review of the Draft ‘White Paper: Modifying EPA Radiation Risk Models*
19 *Based on BEIR VII*,” August 31, 2006
20
21 U.S. NAS/NRC. 2006. *BEIR VII. Health Risks from Exposure to Low levels of Ionizing*
22 *Radiation BEIR VII Phase 2*, National Academies of Sciences (NAS), National Research
23 Council, Committee to Assess Health Risks from Exposure to Low levels of Ionizing Radiation,
24 <http://newton.nap.edu/catalog/11340.html#toc>
25
26 Wakeford & Little. 2002 (To be provided by RAC KJK)
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Web-based Citations and Hotlinks

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U. S. EPA (Environmental Protection Agency). 1994. *Estimating Radiogenic Cancer Risks* (“Blue Book”): <http://epa.gov/radiation/docs/assessment/402-r-93-076.pdf>

U. S. EPA (Environmental Protection Agency) 1999a. *Addendum: Uncertainty Analysis*: <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>

FGR-13. *Federal Guidance Report 13: Cancer Risk Coefficients for Environmental Exposure to Radionuclides*: <http://epa.gov/radiation/docs/federal/402-r-99-001.pdf>

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>

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>

1 **APPENDIX A – THOUGHTS PERTAINING TO ON-GOING RESEARCH**
2 **AND PARADIGMS ASSOCIATED WITH BIOLOGICAL RESPONSES TO**
3 **LOW DOSES OF RADIATION**

4 (NOTE: This Appendix needs references cited - - - KJK)

5
6 BEIR VII uses a biophysical model that suggests that each and every ionization increases
7 the probability of a DNA breakage and that this results in a linear increase in the risk for
8 mutations and also cancer (BEIR VII or other citations needed here). This model is dependent
9 on independent action of the cells, lack of cell communication and a linear link between initial
10 DNA damage and the development of disease. Recent research has been conducted to provide
11 solid data on the response of molecules, cells, tissues and organisms to very low doses of
12 radiation (Ref is needed here). This research has demonstrated that several of the assumptions
13 used in the BEIR VII biophysical model are not valid.
14

15 Many new biological phenomena have been observed following low doses of radiation.
16 For example, it has been demonstrated that following exposures to low doses of radiation there
17 are unique changes in gene and protein expression which are related to new biological effects
18 that were not recognized when the BEIR VII biophysical models were developed. These new
19 biological effects include radiation induced apoptosis and adaptive responses as well as
20 bystander effects, and genomic instability (Ref is needed here). It has been determined that
21 genetic background plays a major role in the magnitude and impact of these biological responses
22 to radiation (Ref is needed here).
23

24 Two different types of adaptive responses have been identified (Ref is needed here). The
25 first is where low doses of radiation decrease the amount of damage observed relative to
26 background levels. The second is where a small “priming dose” of radiation given before a high
27 acute “challenge dose” results in a decreased response relative to the high dose alone (Ref is
28 needed here). In many studies of the adaptive response different sets of genes are activated
29 following either high or low doses of radiation, thus suggesting unique biological responses as a
30 function of dose and as a function of genetic background in cells that are capable of adaptive
31 responses. Cells and tissues that demonstrate an adaptive or protective response following low
32 dose exposures have repair and stress genes up regulated. Identification of these genes is
33 providing a scientific basis for defining metabolic pathways activated by radiation and
34 determining mechanisms of action. Low-dose activation of protective mechanisms like changes
35 in cell cycle, support the existence of non-linear dose-response relationships for low-LET
36 radiation.
37

38 Using recently developed microbeams and other technology to expose individual cells
39 and study the response of the “hit” cells and the response of neighboring cells demonstrated the
40 presence of “bystander effects.” These effects demonstrate that a cell traversed by an alpha
41 particle or “hit” by a focused low LET beam communicate with neighboring cells and can
42 produce changes in “non-hit” cells. These changes have been shown to be both “harmful” and
43 “protective” and are most marked following exposure to high-LET radiation (Ref is needed
44 here). This impacts current use of “hit-theory” in defining radiation risk since the radiation
45 target is much larger than the individual cell. The research demonstrates that cells communicate

1 within each tissue so that the assumption of independence of action of individual cells used in the
2 BEIR VII biophysical model do not hold. Since non-hit cells show biological responses, it is
3 not appropriate to calculate radiation dose to individual cells or cell types in tissues. It also
4 makes it more difficult to define the biological target for the interaction of radiation with cells
5 and the induction of cancer. The data suggest that tissues and organs respond as a whole rather
6 than as the sum of the number of cells “hit”, and that the dose should be calculated to the whole
7 organ/tissue rather than to individual cells (Ref is needed here). This has been demonstrated
8 both in whole animals and in many cell systems.

9
10 Tissue interactions have been shown to modify the expression of cellular and molecular
11 damage and to be critical in the expression of cancer. This damage as well as cancer incidence
12 can be modified with treatment after radiation exposure. (Ref is needed here). Research has been
13 conducted to understand cell/cell and cell/tissue interactions and how they modify cancer
14 frequency (Ref is needed here). Data from this research verified that the initial DNA damage
15 increases linearly with radiation dose but that even the initial DNA damage and repair is
16 modified by radiation type, dose and dose-rate. But more importantly it has shown that
17 biological repair of this damage as well as other the cellular and organ responses are very non-
18 linear over the low dose region. These new findings have important significance for
19 understanding the adequacy of regulatory standards.

20
21 Radiation-induced genomic instability is seen at a high frequency in cells many cell
22 divisions after the radiation exposure. The instability results in increased frequency of
23 mutations, chromosome aberrations, and cell killing. Radiation-induced genomic instability
24 seems to be one of the early stages in the carcinogenesis process and has been seen both *in vitro*
25 and *in vivo*. Genomic instability suggests there are frequent radiation-induced changes following
26 radiation, not rare mutational events. These observations challenge the importance of the role
27 that initial mutations play in radiation-induced cancer (Ref is needed here). The BEIR VII
28 biophysical model suggests that since DNA damage increases as a linear function of dose that
29 there must be a linear increase in cancer risk.

30
31 The magnitude of the response for all of these new phenomena have been shown to be
32 dependent on the genetic background of the cells, tissues and organisms in which they are being
33 measured. With a better definition of the range of inter-individual variability and the
34 development of tools that make it possible to identify individuals that are sensitive and resistant
35 to both early and late effects of radiation. However, currently it is not possible to identify
36 radiation resistant or radiation sensitive individuals or to use this information in a regulatory
37 framework.

38
39 These recent scientific advances provide a scientific basis for the observed non-linear
40 dose-response relationships seen in many biological systems (Ref is needed here). These new
41 biological findings that make it necessary for the field of radiation biology to adopt new
42 paradigms associated with the biological responses to low doses of radiation and to modify the
43 models used to support the extrapolation of dose-response relationships into dose regions where
44 it is not possible to measure changes in cancer in human populations.

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APPENDIX B – BIOSKETCHES

**U.S. ENVIRONMENTAL PROTECTION AGENCY
SCIENCE ADVISORY BOARD
RADIATION ADVISORY COMMITTEE (RAC)**

--- (To be Added in Quality Review Draft) ---

APPENDIX C – ACRONYMS

1		
2		
3	A-Bomb	<u>A</u> tom <u>B</u> omb
4	AM	<u>A</u> rithmet <u>M</u> ean
5	AR	<u>A</u> bsolut <u>R</u> isk
6	BCC	<u>B</u> asal <u>C</u> ell <u>C</u> arcinoma
7	BEIR	<u>B</u> iological <u>E</u> ffects of <u>I</u> onizing <u>R</u> adiation
8	BEIR VII	<i>Health Risks from Exposure to Low Levels of Ionizing Radiation BEIR VII</i>
9		<i>Phase 2</i>
10	CDC	<u>C</u> enters for <u>D</u> isease <u>C</u> ontrol
11	CFR	<u>C</u> ode of <u>F</u> ederal <u>R</u> egulations
12	Co	Chemical symbol for cobalt (⁶⁰ Co isotope)
13	DDREF	<u>D</u> ose and <u>D</u> ose- <u>R</u> ate <u>E</u> ffectiveness <u>F</u> actor
14	DFO	<u>D</u> esignated <u>F</u> ederal <u>O</u> fficer
15	DNA	<u>D</u> eoxyribonucleic <u>A</u> cid
16	EAR	<u>E</u> xcess <u>A</u> bsolut <u>R</u> isk
17	EPA	<u>E</u> nvironmental <u>P</u> rotection <u>A</u> gency (U.S. EPA)
18	ERR	<u>E</u> xcess <u>R</u> elativ <u>R</u> isk
19	FR	<u>F</u> ederal <u>R</u> egister
20	FGR-13	Federal <u>G</u> uidance <u>R</u> eport <u>13</u>
21	GM	<u>G</u> eometric <u>M</u> ean
22	GMC	<u>G</u> eometric <u>M</u> ean <u>C</u> oefficient
23	GSD	<u>G</u> eometric <u>S</u> tandard <u>D</u> eviation
24	Gy	<u>G</u> ray
25	H	Chemical symbol for <u>H</u> ydrogen (³ H isotope)
26	I	Chemical symbol for <u>I</u> odine (¹³¹ I isotope)
27	ICRP	<u>I</u> nternational <u>C</u> ommission on <u>R</u> adiological <u>P</u> rotection
28	ICRU	<u>I</u> nternational <u>C</u> ommission on <u>R</u> adiation <u>U</u> nits and Measurements, Inc.
29	IREP	<u>I</u> nteractive <u>R</u> adio <u>E</u> pidemiological <u>P</u> rogram
30	keV	<u>k</u> ilo <u>e</u> lectron <u>V</u> olts
31	LAR	<u>L</u> ifetime <u>A</u> ttributible <u>R</u> isk
32	LET	<u>L</u> inear <u>E</u> nergy <u>T</u> ransfer
33	LNT	<u>L</u> inear <u>N</u> on <u>T</u> hreshold
34	LSS	<u>L</u> ife <u>S</u> pan <u>S</u> tudy
35	mSv	<u>m</u> illi- <u>S</u> ievert
36	NAS	<u>N</u> ational <u>A</u> cademy of <u>S</u> ciences (U.S. NAS)
37	NCHS	<u>N</u> ational <u>C</u> enter for <u>H</u> ealth <u>S</u> tatistics
38	NCI	<u>N</u> ational <u>C</u> ancer <u>I</u> nstitute
39	NCRP	<u>N</u> ational <u>C</u> ouncil on <u>R</u> adiation <u>P</u> rotection and Measurements
40	NIH	<u>N</u> ational <u>I</u> nstitutes of <u>H</u> ealth
41	NIOSH	<u>N</u> ational <u>I</u> nstitute for <u>O</u> ccupational <u>S</u> afety and <u>H</u> ealth
42	NMSC	<u>N</u> on- <u>M</u> elanoma <u>S</u> kin <u>C</u> ancer
43	NRC	<u>N</u> ational <u>R</u> esearch <u>C</u> ouncil
44	OAR	<u>O</u> ffice of <u>A</u> ir and <u>R</u> adiation (U.S. EPA/OAR)
45	ORIA	<u>O</u> ffice of <u>R</u> adiation and <u>I</u> ndoor <u>A</u> ir (U.S. EPA/OAR/ORIA)

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2	PAG	<u>P</u> rotective <u>A</u> ction <u>G</u> uide
3	Pu	Chemical symbol for <u>P</u> luto <u>n</u> ium (²³⁹ Pu Isotope)
4	QA	<u>Q</u> uality <u>A</u> ssurance
5	QC	<u>Q</u> uality <u>C</u> ontrol
6	QA/QC	<u>Q</u> uality <u>A</u> ssurance/ <u>Q</u> uality <u>C</u> ontrol
7	R	<u>R</u> oentgen
8	Ra	Chemical symbol for <u>R</u> adium (Isotopes include ²²⁴ Ra, ²²⁶ Ra, ²²⁸ Ra, and ²³⁶ Ra)
9	RAC	<u>R</u> adiation <u>A</u> dvisory <u>C</u> ommittee (U.S. EPA/SAB/RAC)
10	rad	Traditional unit of <u>r</u> adiation absorbed dose in tissue (a dose of 100 rad is
11		equivalent to 1 gray (Gy) in SI units)
12	RBE	<u>R</u> elative <u>B</u> iological <u>E</u> ffectiveness
13	REF	<u>R</u> adiation <u>E</u> ffectiveness <u>F</u> actor
14	rem	<u>R</u> adiation equivalent in <u>m</u> an; traditional unit of effective dose equivalent (equals
15		rad x tissue weighting factor) (100 rem is equivalent to 1 Sievert (Sv))
16	R/h	<u>R</u> oentgen per <u>h</u> our; traditional measure of exposure rate
17	Rn	Chemical symbol for Radon
18	RR	<u>R</u> elative <u>R</u> isk
19	SAB	<u>S</u> cience <u>A</u> dvisory <u>B</u> oard (U.S. EPA/SAB)
20	SCC	<u>S</u> quamous <u>C</u> ell <u>C</u> arcinoma
21	SEER	<u>S</u> urveillance, <u>E</u> pidemiology, and <u>E</u> nd <u>R</u> esults
22	SI	<u>I</u> nternational <u>S</u> ystem of Units (from NIST, as defined by the General Conference
23		of Weights & Measures in 1960)
24	Sr	Chemical Symbol for <u>S</u> trontium (⁹⁰ Sr Isotope)
25	Sv	<u>S</u> ievert, SI unit of effective dose equivalent in man (1 Sv is equivalent to 100 rem
26		in traditional units)
27	UNSCEAR	<u>U</u> nited <u>N</u> ations <u>S</u> cientific <u>C</u> ommittee on the <u>E</u> ffects of <u>A</u> tom <u>i</u> c <u>R</u> adiation
28	US	<u>U</u> nited <u>S</u> tates
29	WLM	<u>W</u> orking <u>L</u> evel <u>M</u> onths
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