July 14, 1999

EPA-SAB-RAC-ADV-99-010

Honorable Carol M. Browner
Administrator
U.S. Environmental Protection Agency
401 M. Street, S.W.
Washington, D.C. 20460

Re: Advisory on Proposed EPA Methodology for Assessing Risks from Indoor Radon Based on BEIR VI: White paper

Dear Ms. Browner:

The enclosed Advisory was developed by the Radiation Advisory Committee (RAC) of the Science Advisory Board (SAB) in response to a request dated February 22, 1999 from Mr. Stephen D. Page, Director of the Office of Radiation and Indoor Air (ORIA) to provide advice on the application in a "White Paper" of the National Academy of Science's (NAS) Biological Effects of Ionizing Radiation Committee report (BEIR VI). In particular, the request to the RAC seeks advice on the following charge questions:

a) Is the overall approach of using the BEIR VI age-concentration model acceptable?

b) What advice does the RAC have on the refinements and extensions we (ORIA staff) are considering?, and

c) Have we (ORIA staff) adequately accounted for the sources of uncertainty?

The RAC held a public meeting on March 24, 25, and 26, 1999 at which it was briefed by, and had technical discussions with ORIA staff, as well as a writing session by the Committee. The advisory resulting from these meetings responds both to the three Charge questions briefly discussed below, as well as addressing other issues identified during the public meetings.

Overall, the Committee was impressed with the quality and focus of the ORIA effort as presented to us in the draft "White Paper." In general, ORIA has proposed a reasonable method for using the National Research Council (NRC)/ National Academy of Sciences (NAS) findings from BEIR VI to form an Agency radon risk model. The authors should be commended for a very thorough effort in considering most aspects of this complex risk assessment. The following comments are intended to help ORIA

improve a very good product, and to help ORIA sharpen its approach and communicate its recommendations more clearly. Our response to the charge questions and issues beyond the charge are highlighted and summarized below.

      a)   Question 1: <u>Is the overall approach of using the BEIR VI age-concentration model acceptable?</u>

The Committee recommends use of a model that provides risk estimates intermediate between those of the concentration and duration models. This recommendation is supported by the predictions of other models discussed in BEIR VI, which also provide intermediate risk estimates. However, the Committee chose not to recommend any specific method for modeling radon risks, in the belief that ORIA is better equipped to make that decision.

      b)   Question 2: <u>What advice does the RAC have on the refinements and extensions we (ORIA staff) are considering?</u>

The Committee generally supports the extensions of the BEIR VI models that ORIA proposes to make the EPA radon model most useful for Agency purposes. In particular, the Committee supports expanded treatment of smoking prevalence by age and urges ORIA to continue to investigate how to distinguish between the risks for current smokers and former smokers. The Committee also supports the change of the definition of risk from "excess" to "etiologic" through the inclusion of radon-related lung cancers that would be incurred in persons who would have died later from lung cancer related to other causes. ORIA should also investigate expressing risk in terms of years of life lost, rather than simply counting cases of early mortality.

      c)   Question 3: <u>Have we (ORIA staff) adequately accounted for the sources of uncertainty?</u>

While ORIA has discussed many of the important uncertainties in the radon risk estimates, extending the BEIR VI discussion in some areas and providing quantitative uncertainty estimates for some of the input variables, many of the uncertainties remain unquantified. The White Paper, at this stage of its development, provides little feeling for the overall uncertainties in the risk estimates stemming from all these input uncertainties. The Committee, therefore, recommends additional effort to identify, discuss, and quantify uncertainties to the extent possible with available resources. Further, identifying the input uncertainties of the risk estimates contributing most to the uncertainties would help in guiding future research.

      d)   Beyond the Charge: <u>The need to use the radon risk model for situation-specific assessments.</u>

The Committee also provided some advice beyond the Charge in Section 4 of

this advisory. The Agency should be sure that the final radon risk model can be used for situation-specific assessments that require a user-specific mix of sex, age, and smoking status in the studied population. Further, ORIA should provide easily understood tools that would allow the model to be used outside ORIA -- even by the general public -- to estimate radon risks for a variety of situations. However, ORIA should be sure to provide cautions and caveats about the interpretation of risk calculations and about the degree of uncertainty in the modeling procedures.

The RAC appreciates the opportunity to provide this advisory to you and we hope that it will be helpful. We look forward to the response of the Assistant Administrator for Air and Radiation to the advisory in general and to the specific comments and recommendations in this letter in particular.

Sincerely,

/s/

Dr. Joan M. Daisey, Chair
Science Advisory Board

/s/

Dr. Stephen L. Brown, Chair
Radiation Advisory Committee
Science Advisory Board

NOTICE

This report has been written as part of the activities of the Science Advisory Board, a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide balanced, expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency and, hence, the contents of this report 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 or commercial products constitute a recommendation for use.

ABSTRACT

On March 24-26, 1999, the Science Advisory Board's Radiation Advisory Committee conducted an advisory for the Office of Radiation and Indoor Air (ORIA) on a White Paper concerning proposed methodologies for assessing risks from indoor radon, which was based on the National Academy of Sciences/National Research Council Biological Effects of Ionizing Radiation (BEIR) VI report.

The Committee found that ORIA has proposed a reasonable method for extending the findings from BEIR VI to form an Agency radon risk model, and made a thorough effort in considering most aspects of this complex task. The comments offered are intended to help ORIA improve a good product, sharpen its approach, and communicate its recommendations more clearly.

A model that would provide risk estimates between those of the concentration and duration models was recommended by the Committee, although an exact method was not proposed. This recommendation is supported by other models discussed in BEIR VI, which yield intermediate risk estimates.

The Committee generally supports modifications of the BEIR VI models intended to improve the usefulness of the EPA radon model, including expanded treatment of smoking prevalence by age and continued investigation on distinguishing the risks of current and former smokers. While ORIA identified and quantified numerous important uncertainties in the radon risk estimates, further identification, discussion, and quantification is desirable.

The final radon risk model should be made usable for assessments that require specific mixes of sex, age, and smoking status. Further, easily used tools should be provided so that the model can be used outside of ORIA to estimate radon risks for a variety of situations.

KEY WORDS: cancer risks, indoor radon exposures, radon models, radon risk

U.S. ENVIRONMENTAL PROTECTION AGENCY
SCIENCE ADVISORY BOARD
RADIATION ADVISORY COMMITTEE
March 24-26, 1999

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[1]   Drs. Poston and Hoel did not attend the RAC's March review meeting. Dr. Poston provided written comments, and Dr. Hoel reviewed the draft advisory after the March meeting.

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1. EXECUTIVE SUMMARY

Radon is well established as a cause of lung cancer in miners (particularly uranium miners) through the inhalation of its radioactive decay products. Radon decay products in indoor air are also widely assumed to cause lung cancer. However, the available epidemiology for residential exposures to radon is ambiguous and does not provide a solid quantitative basis for evaluating the magnitude of the lung cancer risk. As a result, the quantitative analysis of the miner data has been extrapolated from radon decay product exposures in mines to lower residential exposures.

The methods used to perform this extrapolation from mines to indoor air have been debated, however. The National Research Council (NRC) of the National Academy of Sciences (NAS) in March, 1999 released the report entitled "Health Effects of Exposure to Radon" ("BEIR VI") on the risk of indoor radon[2]. The Report discusses several mathematical models capable of making the extrapolation, with an equal preference for two models that produce somewhat different estimates of the population lung cancer burden attributable to indoor radon: the "concentration" model and the "duration" model. Both models also consider the effects of age, sex, and smoking status--never smoker (NS) vs. ever smoker (ES). For the relatively low levels of radon exposure encountered in homes, the concentration model predicts about 40% greater risk per unit of cumulative exposure. Using data on the average levels of radon in homes and the characteristics of the 1995 U.S. population with respect to age, sex, and smoking status, the NRC estimated the cumulative cancer burden (lung cancer deaths per year) from radon in homes with the two models.

EPA's Office of Radiation and Indoor Air (ORIA) is in the process of deciding how to use the NRC findings in its own risk assessments for radon decay products. ORIA must decide whether to adopt one of the two NRC models, to create a hybrid model, to adopt one of the other models discussed by the NRC but not preferred, or to create its own model. If ORIA selects an existing model, it must decide what modifications, if any, are necessary to adapt the model for Agency use. ORIA has produced a "White Paper" (EPA. 1999) discussing the issues of model selection and adaptation and presenting its preliminary conclusions about each issue. It has tentatively chosen to use the concentration model with three important modifications regarding smoking prevalence by age, accounting for radon-related cancers in the national cancer statistics, and identification of premature death in persons who would have later died of lung cancer.

ORIA requested that the Radiation Advisory Committee (RAC, or "the Committee") of the Science Advisory Board (SAB) provide advice on its radon modeling

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[2] Whenever the Committee refers to the health efects of radon, the role of the radon decay products is implicit.

efforts by answering three charge questions. The Committee's responses to the questions appear in Section 3 of this Advisory and are summarized below. In general, ORIA has proposed a reasonable method for using the NRC findings to form an Agency radon risk model. The authors should be commended for a very thorough effort in considering most aspects of this complex risk assessment.

1.1 Question 1.   Is the overall approach of using the BEIR VI age-concentration model acceptable?

The Committee believes that the differences in the two primary BEIR-VI models would have vanished if the NRC had used a continuous rather than a discretized representation of radon exposure rates, durations of exposure, and cumulative exposures. Therefore, the ORIA rationale for choosing the concentration model on the basis of biological plausibility and simplicity of use is not compelling. If ORIA could base its risk assessment on a continuous model, a choice between models would not be necessary. Because that option may not be feasible in the near term, the Committee recommends that ORIA adopt a model that provides risk estimates intermediate between those of the concentration and duration models. This recommendation is supported by the predictions of other models discussed in BEIR VI, which also provide intermediate risk estimates. The Committee chose not to recommend any specific method for modeling radon risks, in the belief that ORIA is better equipped to make that decision.At a minimum, ORIA should examine the strengths and limitations of the categorizations within each model and develop a rationale and consensus on which categories and ranges should be chosen.

1.2 Question 2.   What advice does the RAC have on the refinements and extensions we (ORIA staff) are considering?

The Committee generally supports the modifications to the BEIR VI models that ORIA proposes to make the EPA radon model most useful for Agency purposes. In particular, we support the expanded treatment of smoking prevalence by age and urge ORIA to continue investigating how to distinguish between the risks for current smokers and former smokers. We also support the change of the definition of risk from "excess" to "etiologic" through inclusion of radon-related lung cancers that would be incurred in persons who would have died later from lung cancer related to other causes. ORIA should also investigate expressing risk in terms of years of life lost, rather than simply counting cases of early mortality.

1.3 Question 3.   Have we (ORIA staff) adequately accounted for the sources of uncertainty?

ORIA has discussed many of the important uncertainties in the radon risk estimates, extending the BEIR VI discussion in some areas and providing quantitative uncertainty estimates for some of the input variables. However, many of the

uncertainties remain unquantified, and the White Paper at this stage of development provides little feeling for the overall uncertainties in the risk estimates stemming from all these input uncertainties. The Committee, therefore, recommends additional effort to identify and quantify uncertainties to the extent possible with available resources. Although we recognize the difficulties of such an effort, some guidance on the overall reliability of the estimates would be welcome. Identifying the input uncertainties contributing most to the uncertainties in the radon risk estimates through some kind of sensitivity analysis would help in guiding future research. Most important, it would provide the public with an indication of the uncertainties associated with prediction of radon-caused lung cancer deaths.

1.4 Beyond the Charge

The Committee also provided some advice beyond the Charge as presented in Section 4. In brief, the Agency should be sure that the final radon risk model can be used for situation-specific assessments that allow for a user-specified mix of sex, age, and smoking status in the population of concern. Further, it should provide easily understood tools that would allow the model to be used outside ORIA--even by the general public--to estimate radon risks for a variety of situations. However, ORIA should be sure to provide cautions and caveats about the interpretation of risk calculations and about the degree of uncertainty inherent in the modeling procedures and results.

The White Paper is not intended for general distribution and assumes a high level of expertise and familiarity with BEIR VI that would not be found in most audiences. When ORIA produces its official risk assessment methodology report, more detailed explanations should be provided, especially on those issues where EPA's approaches are substantial extensions of those of BEIR VI.

2. INTRODUCTION

2.1 Background

Radon is well established as a cause of lung cancer in miners (particularly uranium miners) through the inhalation of its radioactive decay products ("radon progeny"). The epidemiologic evidence from studies of miners is supported by results from animal studies and radiobiological data. Radon decay products in indoor air are also widely assumed to cause lung cancer. The available epidemiology for residential exposures to radon is ambiguous. Although a meta-analysis of a group of residential studies does provide some support for the assumption that radon in indoor air contributes to the risk of lung cancer (Lubin and Boice. 1997), these studies do not provide a solid quantitative basis for evaluating the magnitude of the lung cancer risk. As a result, the quantitative analysis of the miner data has been extrapolated from mine exposures to lower residential exposures.

The methods used to perform this extrapolation from mine air to indoor air have been debated, however. The National Research Council (NRC) of the National Academy of Sciences in March, 1999 released the report "Health Effects of Exposure to Radon" ("BEIR VI") on the risk of indoor radon[3]. The report discusses several mathematical models capable of making the extrapolation, with an equal preference for two models that produce somewhat different estimates of the population lung cancer burden attributable to indoor radon. One model, the "concentration" model, uses the average level of exposure (in working levels - WL) along with cumulative exposure (in working level-months - WLM) to predict risk, while the other, the "duration" model, uses duration of exposure (in years) along with WLM. Both models also consider the effects of age, sex, and smoking status--never smoker (NS) vs. ever smoker (ES). For the relatively low levels of radon exposure encountered in homes (generally much less than 0.5 WL), the concentration model predicts about 40% greater risk per unit of cumulative exposure. Using data on the average levels of radon in homes and the characteristics of the 1995 U.S. population with respect to age, sex, and smoking status, the NRC also estimated the cumulative cancer burden (lung cancer deaths per year) from radon in homes with the two models.

EPA's Office of Radiation and Indoor Air (ORIA) is currently in the process of deciding how to use the NRC findings in its own risk assessments of radon. ORIA must decide whether to adopt one of the two NRC models, to create a hybrid model, to adopt one of the other models discussed by the NRC but not preferred, or to create its own model. If ORIA selects an existing model, it must decide what modifications, if any, are necessary to adapt the model for Agency use. ORIA has produced a "White

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[3] Whenever the Committee refers to the health effects of radon, the role of the radon decay products is implicit.

Paper" discussing the issues of model selection and adaptation and presenting its preliminary conclusions about each issue (EPA. 1999). It has tentatively chosen to use the concentration model, modified to account for the following:

1. age-specific smoking prevalence data;
2. early deaths in people who would later have died from lung cancer not associated with radon; and
3. an adjustment to remove radon-attributable cancer deaths from the baseline lung cancer risk derived from national cancer mortality statistics so that the application of the relative risk concentration model will be consistent.

ORIA is also extending the uncertainty analyses provided in the BEIR VI report.

After considering the comments in this Advisory and perhaps from other observers, ORIA will produce one or more reports similar to the "Blue Book" (EPA. 1994) that will describe its radon risk methodology and its application to various problems.

On February 22, 1999, the Director of ORIA, Mr. Stephen D. Page, requested an advisory of Dr. Donald G. Barnes, Director of the SAB, on the white paper. The RAC engaged in the advisory at its March 24-26, 1999 public meeting. The Committee prepared the initial draft advisory during the March public meeting. In the course of the review, the Committee also identified other issues beyond the charge. These issues deal principally with uses and documentation of the EPA radon model.

2.2 Charge to the SAB

ORIA requested that the Radiation Advisory Committee ("the Committee") of the Science Advisory Board (SAB) provide advice on its radon modeling efforts by answering the following three charge questions:

Question 1. Is the overall approach of using the BEIR VI age-concentration model acceptable?

Question 2. What advice does the RAC have on the refinements and extensions we (ORIA staff) are considering?

Question 3. Have we (ORIA staff) adequately accounted for the sources of uncertainty?

3. RESPONSE TO THE CHARGE

In general, ORIA has proposed a reasonable method for using the NRC findings to form an Agency radon risk model. The authors should be commended for a very thorough effort in considering most aspects of this complex risk assessment. The following comments are intended to help ORIA sharpen its approach and communicate its recommendations more clearly.

3.1 Question 1: Is the overall approach of using the BEIR VI age-concentration model acceptable?

The Committee is generally supportive of ORIA's proposal to selecta single radon risk model rather than maintaining two separate models for future analyses. Use of both models could well cause confusion among those outside the scientific community. Based on information presented in BEIR VI and the White Paper, the estimates of the U.S. lung cancer burden due to residential radon are somewhat different when using the concentration model vs. the duration model--both of which are methods for taking into account the inverse exposure rate effect. The concentration model appears to be more conservative in the sense that it estimates approximately 40% more annual deaths nationwide, a difference that might be politically significant even if not statistically significant. ORIA needs to consider the importance of such a perceived difference.

While ORIA has presented two arguments to support its selection of the concentration model over the duration model for a variety of risk assessment purposes, neither argument is unassailable. The argument based on biological plausibility assumes that radon acts principally as an initiator of cancer. The possibility that radon has cancer promoting activity (e.g., through cell killing and subsequent cell proliferation) should not be dismissed. The argument based on simplicity falters if exposure rate is interpreted as average radon decay product concentrations (working levels) over an extended duration of exposure, as it appears the NRC used for each miner in its epidemiologic evaluation.

The estimates from both risk models seem to depend on the cut points selected for exposure and exposure rate in the analysis of the miner data. If the cut points had been selected differently, both the concentration and duration models could have yielded different results. A model such as the Cox proportional hazards model (Cox. 1972) can be constructed incorporating both cumulative exposure and either exposure rate or duration as continuous variables representing different aspects of protracted exposure. The choice between the latter variables should yield identical likelihoods, due to the fact that cumulative exposure in WLM is simply the product of intensity of exposure (measured in WL) and duration of exposure in months. Therefore, the use of multiplicative relative risk models, such as those used in BEIR VI, means that inclusion

of either duration or concentration makes the other unnecessary. The primary reason that the BEIR VI concentration and duration models differ in their estimates of the overall risks appears to be that each of these variables was categorized independently and their product is not necessarily equal to cumulative exposure. If ORIA could base its risk assessment on a continuous model, a choice between models would not be necessary.

The rationale in the White Paper for choosing the concentration model, therefore, becomes arbitrary. We have already questioned the biological argument and the simplicity argument. Orally, ORIA also offered the argument that the concentration model would be more easily understood by the general public.   Although the argument has some merit, it is in itself not a compelling reason to choose the concentration model to represent the inverse dose-rate effect.

If using a continuous radon risk model is not feasible in the near term, the Committee recommends that ORIA adopt a model that produces estimates intermediate between the concentration and duration models. For example, the constant relative risk (CRR) model fitted to miners with relatively low exposures or the meta-analysis model of the residential studies, both estimated in BEIR VI, produce risk estimates greater than the duration model but less than the concentration model. Both of these models are also appealing since they represent exposures more relevant to the indoor radon problem. However, the Committee recognizes that the latter models do not include coefficients that modify risk for attained age and time since exposure, which reduces their appeal for estimating risk using the EPA lifetable approach. Rather than recommend a specific model for use by EPA, the Committee prefers to defer the final model choice to EPA, with the recommendation that the weight of evidence seems to indicate that the most accurate estimates are between those produced by the duration and concentration models.

The Committee notes that cancer risk theory predicts differing risks for the same cumulative exposure depending on the timing and pattern of exposure, with the direction of the differences depending on the mechanism of carcinogenesis (e.g., initiation vs. promotion) (Crump and Howe, 1984). As proposed, the concentration model is probably better at dealing with time-varying exposures than are the other proposed models, but all are deficient in some respect and further research in this arena would be useful. The use of average exposure rates over periods of time in WLM/month may have caused some bias in the radon risk estimates. If the variation in the estimated average exposure rates was randomly distributed about the true exposure rates in each mine, the bias would be toward lower risks[4]. If the variation was systematic (e.g., exposure rates declining with time for most miners), the bias might be

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[4] BEIR VI actually did use time-varying exposures by calculating each miner's cumulative exposure at specific age intervals. Bias toward the null would occur if WLM estimates were unbiased but subject to random misclassification.

in the other direction.

3.2 Question 2: What advice does the RAC have on the refinements and extensions we (ORIA staff) are considering?

3.2.1 Overview

The proposed methodology for calculating radon risk described in the White Paper is very sophisticated (EPA. 1999). It builds upon the BEIR VI report conclusions (NRC. 1998). The White Paper takes the information about radon risk that was developed by the NRC and puts it into a form that can be used by the EPA for a variety of purposes including, but not limited to, updating its public information aimed at reducing residential radon exposures. For instance, ORIA improved the usefulness of the radon risk estimate by the inclusion of smoking patterns from the data supplied by the Department of Health and Human Services.

The refinements EPA has used in deriving the risk numbers appear to be reasonable, although in light of the level of uncertainty in the basic model at low radon concentrations, some of these refinements may have little effect on the effective range of the risk estimates. However, the Committee found it difficult to determine how much of the increase in estimated cases of lung cancer in the US between the 1992 EPA estimate and the various examples given in the White Paper is due simply to the increase in size and change in composition of the population on which the risk is projected, and how much of the increase is due to increased risk per person.

3.2.2 Baseline Adjustment

The Committee had difficulty understanding ORIA's adjustment to the baseline risks to account for the contribution of radon to the current lung cancer statistics. The Committee agrees that ORIA is correct to avoid double counting of risks in the relative risk approach. However, when the adjustment is applied, it effectively makes the baseline cancer rates applicable to a hypothetical population exposed to a radon level of zero in the home.[5] It does not correct for the ambient (outdoor) radon level. Because no population exists with a zero exposure to radon, the results are difficult to understand, interpret, and communicate. It would be easier to understand a baseline adjustment consistent with the state of the art in radon mitigation, which would bring the radon level in residences to a credible but non-zero level.

3.2.3 Smoking Patterns

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[5]Although BEIR-VI was directed specifically at residential radon, its methods can be used, with small modifications, to predict risks from workplace radon.

The Committee strongly supports an ORIA effort to incorporate a category for former smokers. The general U.S. population has a higher prevalence of former smokers than in the 11 cohorts of miners used in the BEIR VI report. Also, the relative risk for lung cancer due to smoking declines with time from cessation of smoking. This decrease should be reflected in lower numbers of excess lung cancers if these estimates are used in ORIA's life table approach. This approach has the added benefit of demonstrating to the public that the best strategy includes reducing indoor radon levels as well as eliminating or reducing cigarette smoking.

EPA proposes to add a discussion on how changes in smoking patterns might impact estimates of risk. It is even more important to discuss how changes in radon exposure through the installation of a mitigation system could affect risk.

3.2.4 Etiologic Definition

The NRC used an "excess" definition of risk in which only the excess of lung cancer cases over those which would have occurred through other causes are counted. ORIA is proposing to shift to an "etiologic" definition in which cases of radon-induced lung cancer are counted even if they occur in people who would have died of lung cancer (from other causes) later on. Because the etiologic definition takes into account the burden of earlier occurrence of cancer, the Committee supports this change.

It is interesting that for the example of the female NS (page 15, Fig.3), virtually all of the lung cancer mortality for ages up to 50 to 55 years is attributable to radon. There is a school of thought that years of life lost, or even quality-adjusted life years (QALY) are more appropriate parameters with which to gauge detriment than is simply the number of premature deaths (Holmes, 1995). With this in mind, the apparent fact that lung cancer deaths attributable to radon begin 10 - 15 years earlier than those from remaining causes should perhaps be highlighted. Certainly, the Committee supports the presentation of the radon risk as the probability of dying prematurely from a radon-induced lung cancer.

3.3 Question 3:   Have we (ORIA staff) adequately accounted for the sources of uncertainty?

Although the discussion of uncertainties is a good start and many of the sources of uncertainty are adequately treated, some sources of uncertainty and their importance have not been adequately discussed. The White Paper does not provide a good sense of the overall uncertainty of the risk estimates in quantitative terms or which of the component uncertainties is most important. In some cases, even the qualitative identification and discussion of uncertainties could be improved.

For example, the results of the Cohen study are dismissed using the arguments that ecologic studies are not valid for establishing causation (due to possible

confounding), and also that the results are biologically implausible and inconsistent with residential case-control studies.   Cohen (Cohen. 1990) has attempted to account for confounding by smoking and other factors to the extent possible using population data. The RAC recognizes that ecologic studies have a limited ability to address confounding, because data on individuals are not available; however, the results of such studies should be acknowledged in a discussion of uncertainties. At low exposure levels, the case-control studies, in general, seem to show very little effect. Finally, the assertion of biological implausibility ignores the possibility that at low levels, radiation may stimulate the immune system (hormesis) (Sakamoto, Miyamoto and Watabe. 1987). Although the Committee is not advocating the hormetic hypothesis or other threshold or nonlinear exposure-response relationships, from the evidence now available, a threshold exposure (i.e., a level of exposure below which radon has no effect) cannot be excluded. Therefore, we believe the White Paper should acknowledge in its uncertainty assessment the possibility that radon may not increase lung cancer risks at very low levels of exposure.

More discussion would also be useful on the uncertainties attributable to potential misestimation of miner's exposures, and on how changes in smoking patterns or cigarette composition would affect calculated risks. With respect to miner's exposures, not only are there errors in average exposure estimates (which may cause bias, as noted in the White Paper), but individuals with the same average exposure may have different timing of exposure, and hence different lung cancer risks. Moreover, the relevance of the Chinese cohort data seems questionable, for a variety of reasons. Finally, susceptibility due to either genetic or environmental factors might be different in miners than in the general population, and this possibility contributes to uncertainties in the residential risk estimates.

With respect to smoking patterns, there is great variability between occasional and heavy smokers. Although the Committee realizes that it may not be possible to factor this variability into the model, perhaps data are available to at least characterize the extent of variability in smoking patterns. There is also uncertainty about the relative risk of radon for former smokers, and about radon risks to passive smokers. Finally, differences in lung dose per WLM exposure could vary by age, sex, and smoking status.

As other examples, reductions in radon exposure not only will change the distribution of exposures used in the cancer burden estimates, but may also require the adjustment in the risk coefficients that account for the contribution of the baseline radon exposure to observed lung cancer rates. Moreover, if the equilibrium fraction for radon progeny correlates with the radon level in homes, residential risk estimates would be affected.

It is extremely important that the sources of uncertainty be discussed in some detail so that the reader can understand the assumptions made in the model, the

range of possible values for each parameter, and--at least qualitatively--the impact of these uncertainties on the resulting estimates. Although the Committee realizes that quantification will often be difficult if not impossible, ORIA should attempt a sensitivity analysis to identify which of the input uncertainties contribute most to the overall uncertainties in the risk estimates.

Finally, although uncertainty is discussed in Section VI, statements of uncertainty are not provided in the rest of the document. While it is clear that the numbers in the White Paper are for illustration only and do not represent EPA policy at this time, qualitative expressions of uncertainties should be associated with numerical estimates in any future descriptions or applications of this methodology that are intended for broader distribution.

4. COMMENTS BEYOND THE CHARGE

4.1 Uses of the EPA Radon Model

Although the White Paper provides several examples of uses to which the radon risk model could be put, its only numeric example is an estimate of the lung cancer burden (deaths per year) attributable to residential radon. Much of the discussion of model choice and modifications seems to focus on this use. However, the models will undoubtedly be used for situation-specific assessments as well, with possibly even more important policy implications. It therefore seems desirable to provide the users with the ability to input their own mix of sex, age, and smoking status, rather than to have them be forced to use the national mix at some specific point in time.

However the risk model is finally formulated, it would be desirable for ORIA to provide tools that would allow it to be used outside ORIA--even by the general public--to estimate radon risks for a variety of situations. The tools should be easy to understand and use, but they should be accompanied by cautions about the interpretation of risk calculations and about the degree of uncertainty inherent in the modeling procedures and their results to minimize the potential for misuse of the risk estimates. Guidance should be provided on uses of the models that would be inappropriate or misleading.

4.2 Documentation of the Model

The White Paper is generally quite readable for an audience familiar with the radon risk literature. However, it assumes a high level of expertise and familiarity with BEIR VI that would not be found in most audiences. When ORIA produces its official risk assessment methodology report, more detailed explanations should be provided, especially on those issues where EPA's approaches are substantial extensions of those of BEIR VI. Further, explanations need to be clearer and better justified, especially concerning why EPA chose the "concentration" versus the "duration" model, as well as the methodology for adjusting baseline lung cancer death rates for the existing distribution of residential radon levels. The latter concept seems to have been made more difficult than necessary, and several of the Committee members were confused by the discussion. Although it does not appear that the White Paper itself will be distributed widely, it will be important to keep these points in mind to the extent that this document serves as the basis for later documents and as a reference for health professionals in communicating with the public. Moreover, derivation of some of the equations used would be helpful to the critical reader. For example, equation (4)--determination of lung cancer rates for non-smokers from population lung cancer rates--would be clearer if a short derivation were included either in the text or as an appendix.

The quantity "exposure rate" and its units are not used consistently in the

document. In Table 2, and on page 14 (Section 3b), the units for exposure rate are WL; however, on page 13, in an example used to bolster arguments against the duration model, exposure rate is expressed in WLM/y. Furthermore, ORIA needs to clarify that the actual quantity used in BEIR VI is WLM/ month, not the instantaneous concentration as expressed by WL. A related question regards the duration model. If exposure rate is expressed in WL, are comparisons between exposures in mines and dwellings with this model comparable, given that occupancy times for mines (~24%) and dwellings (assumed to be 70%) differ by nearly a factor of three? Equal radon decay product concentrations in mines and dwellings will lead to quite different average exposure rates when the averages are taken over a day or more.

The definitions of smoking status (ever smoker, never smoker, and former smoker) need to be sharpened to avoid ambiguity. Number of cigarettes smoked daily or in total, duration of smoking, age at first smoking, and time since cessation of smoking could be used to define the categories. Moreover, the uncertainties introduced by these category definitions need to be discussed. Using only two or three categories for a continuum of behavior introduces the same kinds of difficulties as defining the increments of age or exposure rates used in the risk equations. How should "passive" smokers (e.g., children or spouses of heavy smokers) be classified?

Although the title and the Introduction clearly state that the White Paper is intended to address methodology, the document ends abruptly. Perhaps the fact that this is just methodology should be recapped at the end, and there should be a paragraph or two that says what EPA will do next. The three uses of the methodology as outlined in the Introduction should be repeated and expanded upon there.

After releasing its methodology report, a next step would be to prepare a paper for a peer-reviewed journal such as *Health Physics.* This Committee has recommended previously that EPA be more active in their activities within the radiation protection societies. EPA can gain much credibility by making the radiation safety professionals more aware of these solid scientific contributions.

APPENDIX A- DETAILED COMMENTS

A- 1 Comments on Units , Terminology, Tables, and Figures

a)   The Uncertainty Analysis section of the White Paper refers to "errors in dosimetry." These are not really errors in dosimetry, but errors in exposure estimates.

b)   On page 3: There needs to be more of an explanation of Working Level. How does it equate to pCi/L?

c)   Be sure all details such as units, etc. are given in Tables and Figures to make these self-explanatory.

d)   Tables and figures need to be labeled more clearly...for example, where table titles say "number", the symbol # or the word "number" should also appear immediately adjacent to the appropriate column or row.   Every attempt should be made to facilitate a reader's correct and timely interpretation of the tables.

e)   The risk estimates in Table 7 should be multiplied by 10^{-4}.

A- 2 Recommendations for Clarifying the Report

a)   In Section D, it is stated that the NAS preferred models are applicable to any population. Is this really the case? What about populations with compositions different from the US average? Populations within the U.S. may differ substantially in age and sex distribution, smoking prevalence, race or ethnicity, and other factors potentially influencing risk.

b)   On page 6, more explanation for the value of 0.9, by which β is adjusted downward, would be useful.

c)   On page 26, the basis for assuming a constant rate of change is not explained. Given only two data points from which to extrapolate, a linear extrapolation might just as well be postulated.   Having decided to do a constant rate of increase projection, a formula for the more general case should be given, rather than just a numerical example. It could take the form:

$$P(y) = P(y_0) \bullet \left(\frac{P(y_1)}{P(y_0)} \right)^{(y-y_1)}$$

Moreover, exactly how the prevalence rates were adjusted downward "to

A- 1

be in agreement with estimates from the OSH" is not clear.

d)   On page 32 (Section C2), the White Paper states that the rate of lung cancer in females is approaching that in males. However, female lung cancer mortality rates are still less than one half those of males. (EPA. 1994).

e)   On page 4, more explanation of why the "inverse dose rate" effect makes biological sense is needed.

f)   On page 3 (paragraph 2), the statement that "...the right hand side...is multiplied by a factor K..." requires further explanation/justification.

g)   On page 3 (paragraph 3), some explanation of "...life table techniques..." would be helpful: how they are used, why it makes sense to use them here. This could be done in a footnote.

h)   On page 3 (paragraph 3), the White Paper states that the methodology "...subtracted off the estimated radon-induced lung cancer deaths..." Further explanation is needed.

i)   On page 5 (paragraph 1), the White Paper states that "...the dose to target cells…was typically about 30% lower for a residential exposure as compared to an equal WLM exposure in mines." Some additional (short) explanation of how NAS reached this conclusion would be helpful (e.g., footnote, appendix, etc.).

j)   On page 6 (paragraph 2), the White Paper states that attributable risk "... is only weakly dependent on lung cancer rates." Why?

k)   On page 9 (paragraph 1), the White Paper states that "...BEIR VI did not provide numerical estimates of the risk per WLM." This is an important point. Why did BEIR VI decide not to do this? Was it beyond their charge? Did they feel that the information was too weak to support such a move? A word of explanation as to why EPA needs to do this would be important.

l)   On page 13 (paragraphs 3-4) the White Paper states that "...we prefer the concentration model..." The White Paper needs to provide more than the two-paragraph explanation currently devoted to this--perhaps some discussion of the likely convergence of the 2 models would be helpful. How different are the results of these 2 models likely to be?

m)   On page 19 (paragraph 1), the White Paper contrasts "AR" and "... the

risk per WLM ..." There are several epidemiologic approaches used in the document, which makes the document confusing. Perhaps a glossary with a brief discussion of how each is used and which is the most pertinent/revealing for this discussion would be helpful (or just making the text clearer regarding the utility of each measure).

n)   On pages 30-31, the discussion of uncertainties in miner data is nicely done. However, the Committee members were not all familiar with "submultiplicative" (page 31, paragraph 4) as a scientific term.

o)   On page 9, please explain item 2.

p)   On page 13 (paragraph 3), this discussion could be strengthened with reference to observations of an inverse dose rate effect in experiments with alpha emitters in laboratory animals. However, observations at high exposure levels do not necessarily imply similar behavior in the residential radon exposure range. In the proposed model, risk per WLM does not increase further below 0.5 WL. The possibility that the increase could either continue or reverse should be discussed in the uncertainties section. The relationship between the inverse dose rate effect and dose or dose rate could be discussed.

q)   On page 32 (Section 2), could there be a difference in dosimetry between males and females?

r)   The assumption of few new smokers after age 21 should be documented.

s)   On page 33 (paragraph 2), what about the relatively short life-spans of the Chinese miners?

t)   On page 34 (last paragraph), the Committee recollects that in some of the animal experiments cited, radon and smoking exposures generally occurred on the same day in both groups (smoking followed by radon or vice versa). If this is the case, then they would not be very relevant for assessing the relative susceptibility of children to radon if they became smokers many years later. ORIA should check this point.

APPENDIX B- DETAILED EDITORIAL COMMENTS

a) On page 2, the citation (NAS, 1990) is not in the references. Should it be NAS (1988)?

b) On page 14, "0.69 for a $\leq$ 75 y" should be "0.69 for a $\geq$ 75 y".

c) On page 29 (paragraph 2), the White Paper states that "...the committee's preferred uncertainty estimates were obtained from the CRR model." This model should have been introduced earlier in the document as another model with which EPA staff does not agree.

d) On page 10 (next to last line), should this be $h^{pop}(a)$?

e) On page 29 (line 2), omit one "these."

g) On page 32 (line 2), the statement should say "There are very few data".

APPENDIX C- GLOSSARY OF TERMS AND ACRONYMS

ADV	Advisory
BEIR	Biological Effects of Ionizing Radiation
Ci	Curie
CRR	Constant Relative Risk
EPA	U.S. Environmental Protection Agency (U.S. EPA, EPA, or "the Agency")
ES	Ever Smoker
L	Liter
NAS	National Academy of Sciences
NRC	National Research Council
NS	Never Smoker
ORIA	Office of Radiation and Indoor Air (U.S. EPA)
p	Pico (one trillionth, e.g., 10^{-12} Ci is a picocurie)
QALY	Quality-Adjusted Life Years
RAC	Radiation Advisory Committee (of the U.S. EPA/SAB/RAC)
SAB	Science Advisory Board (of the U.S. EPA/SAB)
U.S.	United States
vs	Versus
WL	Working Levels
WLM	Working Level-Month
y	Year

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AN SAB ADVISORY: ASSESSING RISKS FROM INDOOR RADON

AN ADVISORY BY THE RADIATION ADVISORY COMMITTEE ON PROPOSED EPA METHODOLOGY FOR ASSESSING RISKS FROM INDOOR RADON