



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

September 5, 1986

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Hon. Lee M. Thomas
Administrator
U.S. Environmental Protection
Agency
401 M Street, SW
Washington, D.C. 20460

OFFICE OF
THE ADMINISTRATOR

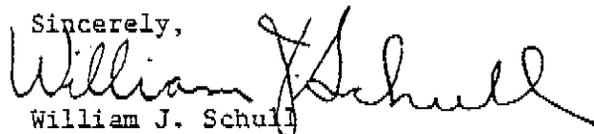
Dear Mr. Thomas:

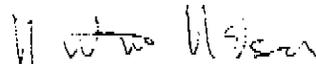
The Science Advisory Board's Radiation Advisory Committee was requested by the Office of Research and Development to review the scientific merit of a proposal to conduct an epidemiological study of radon in indoor air. The Board accepted this request and formed a Radioepidemiology Subcommittee to carry out the review. The Subcommittee has submitted its report in which it responded to two overriding scientific issues:

- o Can further epidemiological study contribute to an understanding of the risks of lung cancer associated with household exposures? The Subcommittee concludes that scientific uncertainties in current epidemiological studies (chiefly studies of uranium miners) could be further reduced through direct investigations of the domestic population.
- o Is the proposed study under review by the Office of Research and Development, entitled Health Effects of Waterborne Radon, appropriately designed to address this risk? For reasons cited in the attached report, the Subcommittee concludes that it is not appropriately designed.

The Subcommittee's report has been approved by both the Radiation Advisory Committee and the Executive Committee of the Science Advisory Board. We hope that our conclusions will assist the Agency in determining the merit of the proposed study and are prepared to provide any additional assistance that is requested. We request that the Agency formally respond to the report and indicate which recommendations the Office of Research and Development plans to accept or reject, providing the reasons in cases where the Subcommittee's advice is not accepted.

Sincerely,


William J. Schull
Chair, Radiation Advisory Committee
Science Advisory Board


Norton Nelson
Chair, Executive Committee
Science Advisory Board

Review of a Proposed Study--Health Effects of Waterborne Radon
Radioepidemiology Subcommittee
Radiation Advisory Committee

On February 18, 1986 Dr. Hugh McKinnon, the Acting Director of the Office of Health Research in the Office of Research and Development (ORD), requested the Radiation Advisory Committee to review a proposed epidemiological study of indoor radon. The EPA's Office of Drinking Water and the Office of Radiation Programs also requested the review. The questions the Agency wished the Committee to address included:

1. Can further epidemiological study contribute to an understanding of the risks of lung cancer associated with household radon exposures?
2. If so, is the proposed study under consideration by the Office of Health Research, Health Effects of Waterborne Radon, appropriately designed to determine this risk?

At its January 21-22, 1986 meeting, Mr. Gunther Craun of ORD's Health Effects Research Laboratory briefed the Committee on the background and content of the proposed study. At this meeting, the Committee formed a Radioepidemiology Subcommittee, chaired by Mr. Seymour Jablon of the National Research Council, to carry out the review. The Subcommittee met on April 18, 1986 in Denver for briefings by the investigators proposing the study. The Subcommittee provided written comments and short verbal summary of its activities at the June 20, 1986 Radiation Advisory Committee meeting. The contents of this letter report were subsequently developed, circulated and unanimously approved by mail.

The Subcommittee concludes that further epidemiological studies could clarify our understanding of the risks of lung cancer associated with radon in indoor air. Appropriately designed and well conducted epidemiological studies of those segments of the general population exposed to indoor radon are urgently needed.

There are at least two important questions that epidemiological studies can address: do radon exposures in indoor air pose a significant health risk and, if so, what is the magnitude of that risk? While the Subcommittee believes that exposure to radon in indoor air may be the most significant radiation exposure that affects the health of the general population, this conclusion is based on the extrapolation to the general population of lung cancer risks derived from studies of uranium miners. This extrapolation implies that a substantial fraction of all lung cancers in non-smokers may be attributable to radon exposures from indoor air. Because the actual radon exposures experienced by some miners and some families exposed to radon in the home may be quite similar, this is not primarily an issue of extrapolation from high radon doses to low, but of extrapolation between two human populations, in different environmental settings, that differ in ways that are known to affect the likelihood of certain diseases occurring.

While the Subcommittee is confident that these miner studies support the conclusion that radon causes lung cancer in humans, studies addressing the relationship between lung cancer and radon in domestic populations are only now being proposed and/or conducted. The differences between occupationally exposed miners and people exposed to radon at home may be sufficient to yield different risks of lung cancer for the domestic population. Mines typically contain other pollutants in addition to radon. The same may be said for homes, but the mixtures of other pollutants and levels of radon exposure in the two environments may not be the same. Miners and the population exposed to radon at home also differ in such factors as age, sex, ethnicity, race, smoking habits, nutritional practices, activity levels and general health. These differences in target populations and exposure patterns

make a study directed specifically at residential exposures very worthwhile. Such a study can reduce many of the uncertainties inherent in the present extrapolation from uranium miners to the general public.

Such a study must, of course, be appropriately designed and conducted to successfully measure these differences in risk between the mining and home environments. It is important to note that improperly designed studies of factors that may adversely affect public health pose a real danger because, by failing to identify risks that actually are present, such studies provide false reassurance. Such studies, especially those with small populations and uncertain dosimetry, may obscure effects which are quite real. While the scientific community is familiar with the fact that a negative study in a small population does not necessarily mean there is no problem, it is wasteful to conduct a study with little chance of answering the questions asked.

The Subcommittee's critical comments on the proposed study of the Health Effects of Waterborne Radon should not be construed by the reader to mean that epidemiological studies of radon in the home are not needed, but as an indication that those studies which are conducted should be designed to have adequate power to answer the important scientific questions.

The Subcommittee members confined their review to a single proposal, but they are individually familiar with other proposed and ongoing radon studies. For example, members are aware that the National Cancer Institute and the New Jersey Department of Health are undertaking a study that includes a larger population with lung cancer. Completed 30-page questionnaires are already available on each person which address diet, occupation, and smoking (both active and passive). Each individual was a long-term resident of a

single household and each of these homes will be measured for radon. Other studies are planned or underway in Pennsylvania, Sweden, Canada and China.

The fact that other studies of indoor radon are being conducted does not imply that a study sponsored by EPA would be unproductive. In a new research area, multiple studies with different populations, exposure levels, and investigators are especially useful. The results, if complementary, greatly strengthen the conclusions.

The study the Subcommittee was asked to review, Health Effects of Waterborne Radon, was proposed by investigators at the Maine Medical Center. What potential does the Maine study have for making a unique contribution to the current understanding of radon in homes? Two possibilities have arisen. One is that, by assessing a middle range of radon exposures, a successful study in Maine, together with studies in Pennsylvania (where the levels of radon in homes are thought to be higher) and in New Jersey (where the levels of radon are thought to be lower), could provide complementary results that would clarify the present understanding of risks associated with various levels of radon exposure.

The other possibility is that the study will add to what is known about the risks posed by radon in water. As is made clear by the title of the proposal, Health Effects of Waterborne Radon, the study was originally spurred by the observation that many wells serving as sources of household water in Maine are characterized by high levels of waterborne radon. However, the preliminary work by the investigators has shown that, even in Maine, radon in water is usually a minor contributor to radon in indoor air. While the title and the water measurements indicate the motivation for the study, it must now be evaluated exclusively in terms of

its utility as an investigation of lung cancer in women in relation to indoor air concentrations of radon.

Given the importance of evaluating the lung cancer risks that result from radon in household air, the key question is whether the proposed study in Maine gives reasonable assurance of providing useful information on this subject. The Subcommittee's conclusion is that it will not.

Although the proposal is for a case-control study, which is the design of choice for addressing this issue, there are certain overriding problems with the study that seriously compromise its potential utility. The Subcommittee highlights the following difficulties:

1. There are two problems with the proposed location: 1) the number of cases available is barely adequate and will not allow for dropping a possibly substantial number for whom dosimetry is inadequate; and 2) there is the related difficulty of measuring exposure for that portion of the study population that has lived in multiple dwellings. Consequently, estimates of levels of individual radon exposures will be especially uncertain.
2. The study is designed to answer the question, "Is there an increased risk of lung cancer in white women who are exposed to radon in the home?" It is not primarily aimed at the question of how these risks differ from those encountered in studies of miners. The Subcommittee recognizes that there are some divergent views in the scientific community on whether radon exposures in indoor air do, in fact, pose a significant health risk--a question which would be addressed by the proposed study. The Subcommittee believes,

however, that the critical scientific question concerns the determination of levels of risk in relation to levels of household exposures. The proposal does not address this issue and is not of sufficient quality to have a high likelihood of testing the null hypothesis.

3. The assumptions and sample size calculations underlying the selection of 600 cases and 800 controls in the proposal were not appropriate or adequate to address the question of levels of risk posed above. Whether an absolute or relative risk model is used, whether continuous or dichotomous exposures are employed, and which question the study addresses all affect the number of cases needed in the study and the desirable distribution between cases and controls. The overall number of people in the study may actually be adequate to address levels of risk associated with radon in indoor air, but the proposal is not as clear on this issue as a study of this importance warrants. A study of radon in indoor air is important, as is the need to ensure that there is a reasonable probability that the study can answer the questions posed. The Subcommittee is not convinced that this study, as currently designed, can meet this need.
4. Although the investigating team appears to have most of the necessary combination of scientific skills, the in-house statistical expertise is weak.
5. The difficulties and uncertainties in estimating radon exposures over thirty years are large. The proposal gave no estimate of the accuracy

or precision needed for estimating even total annual exposure based on short-term integrated sampling. The individual estimates of exposure to radon over thirty years are to be made from recalled activity patterns and current measurements of radon levels in homes which may have been altered over that time. The uncertainties in the exposure estimates may be so large, and the expected increase in the number of cancers in the study population so small, as to obscure the effects of radon on lung cancer rates. Errors in estimates of individual exposures will bias downward the risk estimates calculated and, if sufficiently large, may obscure them completely. Because the difficulties posed by historical exposure assessment are large for radon studies generally, spending the time now to conduct methodological studies for assessing radon exposure would provide a sound basis for the conduct of better epidemiological studies on this subject at a later date.

6. The effort to characterize radon in water does not seem useful since, according to the proposal itself, radon in water is not a significant source of radon in houses even when levels of radon in water are elevated.
7. The appropriate scientific method of dealing with deceased individuals is a matter of some controversy among epidemiologists. Simply excluding them from the study risks introducing selection bias if deceased persons systematically differ from living cases in terms of exposure or confounders. On the other hand, the use of proxies for controls (as proposed) risks introducing differential misclassification bias. This loss of validity is of particular concern for cigarette smokers

since smoking is a major cause of lung cancer, and comparable information on this point is especially important. A third alternative, using deceased controls for proxy interviews risks introducing other forms of selection bias and adding further misclassification, while not guaranteeing that the misclassification will now be non-differential. There are no universal guidelines. The alternatives need to be considered very carefully.

8. The proposed dietary questionnaire appears to be too brief to obtain satisfactory data concerning retinol and beta-carotene. This approach is unlikely to be informative and would appear not to be worth the effort.

Individual members of the Subcommittee also made a number of detailed recommendations that have been made available to the Office of Research and Development. While supporting the need for epidemiological studies on radon in indoor air, the Subcommittee recommends that the Agency not undertake the study reviewed in this report as it is presently planned.

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