May 15, 1996

Mr. Eugene Durman, Senior Policy Advisor
Office of Radiation and Indoor Air
U.S. Environmental Protection Agency
401 M Street, S.W.
Washington, DC 20460

Dear Mr. Durman:

Enclosed is a redline and strikeout version of the draft Scope of Work for a BEIR VII Scoping Study. I apologize for the delay in providing our comments, but additional time was needed for me to fully take into account the great interest in the study throughout the Nuclear Regulatory Commission. If you have questions regarding these comments, please call Judi Greenwald at (301) 415-6635.

Sincerely,

[ORIGINAL SIGNED BY]

Michael F. Weber, Acting Deputy Director
Division of Waste Management
Office of Nuclear Material Safety and Safeguards

Enclosure: As stated

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UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

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BEIR VII "SCOPING STUDY"
Draft Work Scope
May 2, 1996

BACKGROUND

Since publication of the 1990 BEIR V Committee report, "Health Effects of Exposure to Low Levels of Ionizing Radiation," new information has become available ~~on the Japanese atomic bomb survivors and other~~ regarding cohorts exposed to ionizing radiation at low doses and dose rates. Studies at the molecular and cellular level have ~~pointed the way towards~~ contributed to a better understanding of carcinogenesis and may eventually lead to an improved basis for estimating radiation risks at low doses and dose rates. In addition, there is new information on the effects of low-level radiation in producing risk decrements of both mortality and cancer, and other non-cancer effects ~~other than cancer~~.

To be credible, it is critical that federal radiation protection measures and risk assessments be based on the best current science. Although the emergence of new epidemiological data and progress in understanding the biological basis for carcinogenesis is expected to continue in coming years, an ~~update~~ extension of BEIR V may be desirable at this time. Before proceeding with a full-scale National Academy (BEIR VII) review and analysis aimed at updating the existing state of understanding and quantification of risks from low dose, low-LET radiation, it would be advantageous to conduct a preliminary study that would examine the range of potential issues that could be addressed, along with an assessment of the usefulness of available sources of new information in order to define the most useful scope for BEIR VII.

PROPOSED PLAN OF ACTION

The Board on Radiation Effects Research will organize a small expert panel to investigate what issues a BEIR VII study might usefully address in depth. The scoping study should address each of the issues/areas outlined below and any others the panel deems relevant. In conducting its review, the panel should consider the current availability of data not evaluated by the BEIR V committee and the expectation of significant additional data during the period of the BEIR VII review. The panel should provide a final letter report that: (1) recommends which of these issues could profitably be addressed in depth in a BEIR VII study, (2) provides a basis for these recommendations, (3) lists primary sources of data that might be used, (4) assesses whether or not a detailed analysis of each issue could have a significant effect on the quantification or validity of radiation risk estimates, and (5) indicates what scientific disciplines would be required to adequately address each of them.

Enclosure

OUTLINE OF AREAS TO BE ADDRESSED IN SCOPING STUDY

In considering issues to be addressed in future BEIR studies, the panel should at least review the following:

1. Cancer risk estimatation at low doses

The form of the low dose response ~~below~~ in the dose range directly accessible to human epidemiological studies, including the evidence for or against linearity and thresholds ~~at or near background levels of exposure~~

Adjustments to organ-specific risk estimates at low dose rates, e.g. as expressed by a Dose Rate Effectiveness Factor (DREF)

Significance—or nonsignificance— of "hormetic effects," i.e., risk decrements in human populations resulting from enhanced prevention, repair, or removal of DNA damage in the exposed biosystem,[1] ~~(e.g., adaptive response, immune system stimulation) to the dose response for cancer induction~~

2. Numerical risk estimation

Alternative biologically based[2] models for projecting radiation-induced cancer risks in the U.S. population, for workers and the general population

Quantification of uncertainties in radiation risk estimates

Resolution of claimed inconsistencies in risk estimates derived from different epidemiological studies

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[1] UNSCEAR 1994 Annex B contains a discussion of various mechanisms for adaptive responses, such as, prevention by increased radical detoxification (page 205), repair by activated genes and their enzyme products (page 199), removal by apoptosis (pages 199, 208), and immune system changes (page 206).

[2] The following biologically based models include both the normal very high background of intrinsic metabolic DNA alterations (2.4×10^5/cell/day) as well as the alterations produced by ionizing radiation (approximately 20/cell/cGy), and the adaptive responses of the biosystem to radiation.

- A Cytodynamic Two-Stage Model that Predicts Radon Hormesis (Decreased, then Increased Lung-Cancer Risk vs. Exposure, Dr. Kenneth T. Bogen, Lawrence Livermore National Laboratory, University of California, February, 1996
- The meaning of the α-Term in the Dose-Risk Function for Late Radiation Effects, Ludwig E. Feinendegen, Medical Department, Brookhaven National Laboratory, Upton, NY, and US Department of Energy, Washington, DC

3. Existence of sensitive subgroups

Genetic predisposition to radiogenic cancer

Exposures to other agents that modify the effect of radiation (other than agents administered for this purpose)

Risks from prenatal exposures

In reviewing these and other issues, the sources of data considered should include (but not be limited to) the following:

- Japanese atomic bomb survivors data

  Cancer incidence and mortality data available subsequent to BEIR V analysis with emphasis on exposures at low doses and dose rates

  Dependence of risk on cancer site, age at exposure, age at observation, time since exposure, gender, city, and dose

  New dosimetric information, particularly pertaining to neutron doses at Hiroshima

  Evidence pertaining to possible low level radiation induction of noncancer effects (mortality, genetic, teratological, cardiovascular, cataracts, etc.) ~~by radiation~~

- Other epidemiological low level data that has been cited as a basis for risk estimation at low levels of exposure

  Medically irradiated cohorts

  Populations exposed to chronic doses: (1) groups exposed in the former Soviet Union, (2) nuclear workers in the U.S. and other countries, and (3) other population groups for which studies have been reported (e.g., residents of high background areas).

  Evidence for carcinogenicity of I-131

- Laboratory studies pertaining to mechanisms of radiation carcinogenesis

  Occurrence of various types of DNA damage produced by radiation and intrinsic normal metabolism.

  Efficiency of biosystem in prevention, repair, and removal of DNA damage and its functional dependence on dose and dose rate

  Importance of specific gene changes caused by radiation or other agents in carcinogenesis

Influence of cell cycle on radiation-induced cellular changes and repair

In assessing what issues can be profitably addressed, the panel shall also consider recent reviews conducted by UNSCEAR, NRPB, ICRP, NCRP, and other organizations since the issuance of BEIR V. Should the panel recommend that it is not appropriate to evaluate specific issues at this time, the report should, if possible, indicate what additional data would be needed to make such an evaluation appropriate.