POLICY ISSUE
(Information)

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FOR: The Commissioners

FROM: Luis A. Reyes
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SUBJECT: STAFF REVIEW OF THE NATIONAL ACADEMIES STUDY OF THE HEALTH RISKS FROM EXPOSURE TO LOW LEVELS OF IONIZING RADIATION (BEIR VII)

PURPOSE:

To provide an overview of the National Academies report entitled, "Health Risks from Exposure to Low Levels of Ionizing Radiation," and to inform the Commission regarding the potential implications of the report for U.S. Nuclear Regulatory Commission (NRC) regulations.

SUMMARY:

In COMSECY 96-005, dated April 2, 1996, the Commission responded to SECY 95-249 (dated October 3, 1995) and approved the staff's recommendation that the NRC should sponsor a National Academies study to examine the health effects of low dose radiation and upon completion of the study to provide recommendations to the Commission regarding the implications of the National Academies report for NRC regulations and for Federal Guidance. The staff has completed a review of the BEIR VII report and prepared this paper to summarize the significant findings.

The staff believes that the findings presented in the National Academies BEIR VII report contribute to our understanding of the health risks from exposure to ionizing radiation. The major conclusion is that current scientific evidence is consistent with the hypothesis that there is a linear, no-threshold dose response relationship between exposure to ionizing radiation and the development of cancer in humans. This conclusion is consistent with the system of radiological protection that the NRC uses to develop its regulations. Therefore, the NRC's regulations continue to be adequately protective of public health and safety and the environment. Consequently, none of the findings in the BEIR VII report warrant initiating any immediate change to NRC regulations or Federal Guidance.

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BACKGROUND:

Since 1972, the National Academies has published a series of reports on the Biological Effects of Ionizing Radiation (BEIR) which augment other National Academies reports (dating back to 1956) on the health effects of low level radiation. At the request of the NRC, the Environmental Protection Agency, and the Department of Energy (DOE), the National Academies initiated in 1996 the first phase of a two-phase study to conduct a comprehensive review of the health risks associated with exposure to low-doses of ionizing radiation. When completed, this would be the seventh in a series of National Academies reports by a BEIR committee (BEIR VII). The purpose of the first phase of the study was to review the scientific literature and decide whether there was sufficient new information to warrant a full study. The National Academies concluded in the phase one report that it was an opportune time to proceed with a comprehensive re-analysis of the health risks associated with low levels of ionizing radiation because substantial new information had become available.

In initiating the second phase of the BEIR VII study in 1998, the sponsoring agencies asked the National Academies to conduct a comprehensive review of all biological and biophysical data regarding the health effects attributable to exposure to low doses of ionizing radiation. For the purpose of this review, low dose was defined as exposures between 0 and 100 mSv (10 rem) or 100 mGy (10 rads). The BEIR VII Committee also was asked to limit its review to data related to low linear energy transfer (LET) radiation (e.g., x-rays and γ-rays) and low doses of neutron radiation.

The sponsoring agencies asked the National Academies to consider factors (e.g., age, gender, dose rate, diet) that may influence individual response to radiation exposure and to develop models that describe the causes of both cancer and non-cancer diseases attributable to radiation exposure. The sponsoring agencies would then use this information to assess the health risk to humans of exposure to low levels of ionizing radiation.

The National Academy Press released a prepublication copy of the BEIR VII report to the public on June 29, 2005. In response to COMSECY 96-005, the staff has reviewed that report and prepared this paper to summarize the report and "provide recommendations to the Commission regarding the implications of BEIR VII for NRC regulations, for Federal Guidance, and for risk harmonization." The Discussion section of this paper summarizes the significant findings from the BEIR VII report.

DISCUSSION:

The primary finding of the BEIR VII Committee is that "the current scientific evidence is consistent with the hypothesis that there is a linear, no-threshold dose-response relationship between the exposure to ionizing radiation and the development of cancer in humans." The Committee reports that most of the data reviewed supports this overall conclusion. However, details presented in the body of the report suggest that this conclusion is not definitive. In particular, the Committee could not definitively exclude the possibility of a threshold for radiation effects lower than 0.1 Sv (10 rem) of lifetime exposure in human studies and 20 mGy (2 rads) in DNA studies.

Assessing the health risks associated with exposure to low doses of ionizing radiation is difficult because methods have not yet been developed that can deliver very low dose, low-LET ionizing radiation to a specific target. Similarly, techniques have not yet been developed that can detect and quantify any adverse or beneficial changes in cells or tissues that are associated with low dose radiation exposure. However, new information that has become available since the 1990 publication of the BEIR V report has improved our understanding of the health risks associated with radiation exposure. For reasons of practicality and with some exceptions, the Committee reviewed information that had been published through early 2004. An information cut-off date was established to allow the Committee to finalize the BEIR VII report. Consequently, many research findings published after the information cut-off date (e.g., studies funded by the Department of Energy's Low Dose Radiation Research Program) were not

included in the BEIR VII report.

Epidemiologic Data

The BEIR VII Committee examined several sources of epidemiologic data, including medical exposures of patients, occupational exposures of physicians and nuclear industry workers, and studies of groups of persons exposed to low levels of ionizing radiation (e.g., Chernobyl cleanup workers). The Japanese atomic bomb survivors from the cities of Hiroshima and Nagasaki are the single most important source of epidemiologic data that the BEIR VII Committee used to evaluate the risks of exposure to ionizing radiation at low (< 0.1 Sv or 10 rem) and moderate exposures (< 1 Sv or 100 rem). A group, or cohort, of atomic bomb survivors was established in 1950 using population census information to study the effects of ionizing radiation. This group, named the Life Span Study (LSS) cohort, is characterized by the following information:

- The available demographic information for the cohort encompasses 120,000 persons of both sexes and all ages.
- It was possible to estimate dose for approximately 87,000 members of the cohort who were present in Hiroshima or Nagasaki at the time of the bombings. The remainder lived in the cities, but were not present at the time of the bombings.
- Each member of the cohort was assigned a radiation exposure with values ranging from zero to several Sievert.
- Excellent medical data on cancer and non-cancer diseases has been collected for the cohort members.

Three major changes have occurred since 1990. First, an additional 12 years of follow-up medical data are available. Second, cancer incidence data for the cohort are available (previously, only mortality data was available). The impact of these two developments has been to reduce several sources of uncertainty in the assessment of cancer risk among the atomic bomb survivors. Third, the dosimetry system (DS86) used to assign radiation exposure to the atomic bomb survivors was replaced with an improved dosimetry system (DS02). Upon reviewing this information, the BEIR VII Committee made the following observations and conclusions:

- The DS02 estimates of neutron dose to cohort members do not differ greatly from the DS86 estimates.
- The health risk per Sievert for solid cancer and leukemia decreased by about 10 percent when estimated using the new dosimetry system.
- The new LSS cohort data provided additional evidence of a radiation-associated excess for all solid cancers at doses down to around 100 mSv (10 rem).
- The balance of scientific evidence tends to favor a simple proportional relationship between low radiation dose and cancer risk. The Japanese atomic bomb data are best characterized as a linear no-threshold dose response, although some low dose non-linearity is not excluded. The LSS dose response for leukemia is curvilinear with a statistically significant increase in leukemia observed at doses around 200 mSv (20 rem).
- It is unlikely that a threshold exists for the induction of cancer, but the occurrence of radiation-induced cancer at low doses will be small.
- The change in dosimetry systems have very little effects on factors that influence individual response to ionizing radiation exposure (e.g., gender, age at exposure, attained age since exposure, and time since exposure).

The BEIR VII Committee uses radiation cancer risk estimates derived from the Japanese atomic bomb data to estimate radiation risk for the U.S. population. However, it is not necessarily straightforward to extend the risk estimates from the Japanese atomic bomb survivors to the U.S. population because the survivors of 1945 differ from the 21st century U.S. population. For example, the LSS cohort comprises

Japanese subjects exposed to radiation under wartime conditions and the deprivations associated with a world war. Thus, the baseline (or natural) risks for developing cancer in any particular organ differ between Japanese and U.S. citizens (often as a result of dietary or environmental factors), and the BEIR VII Committee conceded that it was unclear how to account for those differences. Equally important, the incidence rates for several cancer sites have changed since 1950 as the Japanese culture has become more westernized. To account for these differences, the Committee used different radiation risk transport models to estimate organ-specific cancer risk in the U.S. population. However, the models used to transfer or "transport" cancer risk estimates to the U.S. population are not very precise. In some instances, the Committee augmented the Japanese atomic bomb data with medical information obtained from U.S. patients who received radiation therapy (e.g., for thyroid, breast, stomach and lung cancer). For most cancer sites, the Committee's selection of a given transport model or combination of models was based on collective judgment. For many tissues, the uncertainty for cancer incidence and mortality estimates is very large with subjective 95 percent confidence intervals greater than an order of magnitude. The statistical uncertainty in the radiation risk estimates may obscure the potential impact of factors (e.g., age or gender at exposure) that affect individual radiation sensitivity.

Dose and Dose Rate Effectiveness Factor

The BEIR VII Committee considered the effect of dose rate on estimating radiation risk. The Committee derived the estimated health risks from radiation exposure for the LSS cohort on the basis of individuals exposed to a single, acute exposure. These risk estimates are not applicable for individuals who receive multiple exposures or are exposed to radiation at very low dose rates for periods of several days, months, or years. A dose and dose rate effectiveness factor (DDREF) is used to account for the different radiation exposure conditions. The BEIR V Committee in 1990 recommended using a dose rate effectiveness factor of 2 for populations or persons exposed to small doses at low dose rates. In order to determine the DDREF value that should be recommended, the BEIR VII Committee employed a combined Bayesian analysis of dose response curvature for cancer risk using animal radiobiology data and medical data from the LSS cohort. The Committee concluded that the DDREF values that could be used to adjust linear risk estimates for Japanese atomic bomb survivors range from 1.1 to 2.3. Using their collective judgment, the Committee selected a value of 1.5 as the DDREF for assessing health risks for solid tumors. However, the Committee acknowledged that there is considerable statistical uncertainty in the DDREF selection.

Risk Coefficient for Cancer

The Committee's preferred estimate for lifetime attributable risk of mortality for all solid cancers and leukemia is 5×10^{-2} per Sv (5×10^{-4} per rem) and 6×10^{-3} per Sv (6×10^{-5} per rem), respectively. The magnitude of estimated risks for total cancer mortality or leukemia is similar to estimates derived by the BEIR V Committee, the International Commission on Radiation Protection (ICRP), and the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR). The BEIR VII Committee states that the new data and analyses have reduced sampling uncertainty, but the uncertainties remain very large with regard to transporting risk from the Japanese atomic bomb survivors to the U.S. population, and estimating risk for exposure at low doses and dose rates.

Heritable Genetic Effects

Adverse hereditary health effects that could be attributed to radiation exposure have not been observed in studies of Japanese children whose parents were atomic bomb survivors. However, studies of mice and other organisms have produced extensive data showing that radiation-induced cell mutations in sperm and eggs can be passed on to offspring. The BEIR VII Committee opined that there is no reason to believe that such mutations could not also be passed on to human offspring. For low or chronic doses of low-LET irradiation, the Committee assessed the genetic risks to be very small [30 to 47 cases per million first generation progeny per cGy (rad)] compared to the baseline or natural rates of genetic

diseases (738,000 cases per million) in the population.

Mechanistic Studies

Epidemiologic studies are unable to provide direct evidence of any dose response relationship at very low doses [0 to 100 mSv (10 rem)] because of the lack of sufficient statistical power to detect a health effect. Consequently, scientists are studying the effects of ionizing radiation in other systems such as single cells or in rodents. The Committee examined the relationship between radiation exposure and the induction of damage to DNA in cells. The Committee reviewed processes through which DNA damage is repaired or misrepaired, the subsequent appearance of gene and chromosomal mutations, and the development of cancer, to ascertain the dose response relationship for exposures less than 100 mGy (10 rads). The Committee acknowledged that the mechanisms that lead to adverse health effects after ionizing radiation exposure are not fully understood.

The data that the BEIR VII Committee reviewed greatly strengthened their view that there are intimate links between the dose-dependent induction of DNA damage in cells and the development of cancer. When a photon or a single particle passes through a cell, the ionizing radiation produces several types of damage in DNA. The most important type of damage is
formed at what are called “locally multiply damaged sites” – clusters of lesions or damage at a single site on a chromosome. These complex lesions are unique to radiation exposure and are not associated with normal metabolic oxidative processes. The number of locally multiply damaged sites created in a cell increase with both dose and LET. Experimental results in studies of chromosomal aberrations, malignant transformation, or gene mutations induced by relatively low total doses or low doses per fraction suggest that the dose-response relationship over a range of 20 to 200 mGy (2 to 20 rads) is generally linear. The BEIR VII Committee was uncertain whether a linear dose response relationship continues between 0 and 20 mGy (2 rads). In fact, the Committee noted that “the statistical power of the data was not sufficient to exclude the theoretical possibility of a dose threshold for radiation effects.”

The BEIR VII Committee reviewed a large amount of phenomenological data for studies investigating adaptive response, low dose hypersensitivity, bystander effects, genomic instability, and radiation hormesis. The body of data suggests either an enhancement or reduction in radiation effects and, in some cases, the phenomena appear to be restricted to special experimental circumstances. Without a better understanding of the mechanism of action, the Committee could not predict how these phenomena will influence low-dose, low-LET dose response relationships.

IMPACT ON NRC REGULATIONS:

The current system of radiation protection used by the NRC is based on the assumption that there is a linear, no-threshold dose response relationship for exposure to ionizing radiation and the development of cancer. That is to say, for every incremental increase in radiation exposure, there is an incremental (albeit very small) increase in the likelihood of developing radiation induced cancer. The major conclusion in the National Academies report is that current scientific evidence is consistent with the linear, no-threshold hypothesis. This conclusion is consistent with the NRC’s system of radiological protection. Therefore, the general conclusion of the BEIR VII Committee supports the NRC’s continued use of this assumption for low dose radiation exposure and the NRC’s regulations continue to be adequately protective of public health and safety and the environment. Consequently, none of the findings in the BEIR VII report warrant any immediate change to NRC regulations or Federal Guidance.

The BEIR VII Committee also estimated lifetime risk for both cancer incidence and cancer mortality for leukemia and all solid cancers. These radiation risk estimates are numerically similar to risk estimates provided in BEIR V and in more recent UNSCEAR and ICRP reports. Despite the apparent similarity in estimated lifetime risk of solid cancer and leukemia, the technical basis used to develop the estimated risk by each organization is significantly different. The UNSCEAR and ICRP values were calculated

using the DS86 dosimetry system, Japanese cancer mortality data, and a DDREF of 2 to estimate risk to the global population. The BEIR VII Committee used the DS02 dosimetry system, Japanese cancer incidence data, and a DDREF of 1.5 to estimate risk to the U.S. population. After considering the different methodologies used to estimate cancer risk, the staff does not propose any changes in how it estimates cancer risk for ionizing radiation exposure.

The BEIR VII Committee used a DDREF of 1.5 to estimate health risks for solid cancer. NRC currently uses a DDREF of 2 based on recommendations of the ICRP (Publication 60), the National Council on Radiation Protection and Measurements (Report 116), and the National Academies (BEIR V). Changing to a DDREF of 1.5 in the face of considerable statistical uncertainty appears unwarranted at this time, but will be reconsidered again when the ICRP publishes its next set of radiation protection recommendations.

An issue that may warrant additional consideration is the potential influence of gender on radiation sensitivity. The BEIR VII Committee's preferred estimate of lifetime attributable risk for cancer incidence and cancer mortality (Table 12-13) suggests that females are more sensitive than males to radiation exposure. Yet, the 95 percent subjective confidence intervals associated with estimated lifetime cancer risk for males and females suggest that the apparent gender difference may not be significant statistically. Consequently, the BEIR VII Committee combined the two risk estimates and cited an average value which also was done by the BEIR V committee. A potential gender difference was not discussed in the BEIR VII report. The staff will continue to monitor this issue as the ICRP finalizes its new radiation protection recommendations and as additional epidemiologic information is made available.

FUTURE STAFF ACTIONS:

The BEIR VII report does not support the need for the fundamental revision to ICRP radiological protection recommendations. However, it will provide additional technical basis for the ICRP to consider as it revises its draft 2005 recommendations on radiological protection. The staff will continue to monitor the ICRP's activities, review documents when they become available, and provide comments directly to the ICRP. The staff also will participate in other forums, such as the Expert Group of the Nuclear Energy Agency or the National Academies Board on Nuclear and Radiation Sciences, to express the NRC's views.

Finally, the staff will continue to monitor the research findings developed and released from the Low Dose Radiation Research Program funded by Department of Energy. Additional data regarding adaptive response, low dose hypersensitivity, bystander effects, genomic instability, and radiation hormesis will become available from the DOE research program which will clarify the contributions of these phenomena to cell and tissue damage, thus allowing better assessment of the health risks from exposure to ionizing radiation.

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