DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

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Dear ABRWH members,

Notice of intent to change the NIOSH-IREP lung cancer risk model for estimating probability of causation under EEOICPA

As you know, there are two different versions of IREP. NIOSH-IREP is the version maintained by NIOSH. A separate version (NIH-IREP) is maintained by the National Cancer Institute (NCI.) NIH-IREP was developed primarily to serve the needs of the Department of Veterans Affairs in adjudicating cancer claims filed by veterans exposed to radiation during military service, whereas the risk models in NIOSH-IREP are intended to fit the characteristics and radiation exposures incurred by civilian nuclear weapons workers.

Perhaps the most significant difference between NIOSH-IREP and NIH-IREP occurs in the treatment of lung cancer risk for exposure to radiation other than radon. Initially, these risk models were identical in the two versions of IREP. However, NCI revised the NIH-IREP lung model in late 2003 based on both newly published and unpublished (1) data from the Japanese atomic bomb survivor cohort, including the incorporation of different assumptions about the interaction between cigarette smoking and lung cancer.

This lung model revision was followed in mid-2004 by a modification to the NIH-IREP computer code for exposures to alpha radiation. NCI modified the computer code again in September 2005, this time to adjust the population transport function (the parameters that affect the transfer of risk from the Japanese population to the U.S. population) in the NIH-IREP lung risk model. The purpose of the 2004 and 2005 modifications was to ensure consistency with the NIH-IREP documentation (*Report of the NCI-CDC Working Group to Revise the 1985 NIH Radioepidemiological Tables)*, published by NCI in 2003. Online links to the NCI report and to the NIH-IREP computer program are provided on the NIOSH/OCAS Web site: www.cdc.gov/niosh/ocas . (To access the NCI/NIH links, navigate to the "Probability of Causation—NIOSH-IREP" page and scroll down to the "Other Related Materials" section, located at the bottom of the page.)

In the revised NIH-IREP lung model, risk is adjusted for age at exposure and age at diagnosis. The NIOSH-IREP lung model does not adjust for these age-dependent factors. Further, the NIH-IREP lung model relies less on a multiplicative interaction than does NIOSH-IREP in accounting for the interaction between cigarette smoking and lung cancer. Consequently, the same inputs entered into NIH-IREP and NIOSH-IREP produce substantially different probabilities of causation for some exposure profiles. In terms of probability of causation, the main effect of the NCI revisions is that NIH-IREP is more favorable to smokers and NIOSH-IREP is more favorable to non-smokers. Other effects (age and gender-related, for example) vary in accordance with the circumstances of a case and are more difficult to generalize.

We began evaluating the new NIH-IREP lung model in 2004 for its applicability to workers covered under EEOICPA. To assist with this evaluation, SENES Oak Ridge, Inc. provided NIOSH with a detailed assessment of the differences between the two IREP lung models (2). The SENES assessment concluded with a recommendation to replace the NIOSH-IREP lung model with the new NIH-IREP model or, alternatively, to consider programming NIOSH-IREP to run both models. (In the latter option, the higher probability of causation would determine the claim outcome.)

To help resolve this issue, we obtained input from four outside experts, posing the following question to each: "In your expert scientific judgment, should NIOSH adopt the NIH-IREP lung cancer risk model for exposures other than radon for use in NIOSH-IREP? If so, should the model be adopted intact, or should NIOSH modify it in some way to better fit the characteristics and radiation exposures of nuclear weapons workers covered under EEOICPA? Alternatively, should NIOSH-IREP be programmed to run both lung cancer models and to report only the higher probability of causation? Please provide the rationale for your conclusion." (3)

The four experts recruited by NIOSH are: David J. Brenner, PhD, Professor of Radiation Oncology and Public Health, Columbia University School of Public Health; Faith G. Davis, PhD, Professor of Epidemiology and Biostatistics, University of Illinois at Chicago, School of Public Health; David B. Richardson, PhD, Assistant Professor of Epidemiology, University of North Carolina School of Public Health; and Jonathan M. Samet, MD, MS, Professor and Chairman, Department of Epidemiology, Johns Hopkins University School of Public Health.

Each expert reviewed the question independently of the other reviewers. Faith Davis recommended adopting the NIH-IREP model, noting that since it is based on more recent evidence, it represents an improvement over the current NIOSH-IREP model (4). Jonathan Samet and David Richardson, concluding that the evidence is not compelling enough to support the exclusive use of either model, recommended that we run both models and use the higher probability of causation (5, 6). David Brenner argued that the state of knowledge remains inconclusive with respect to the interaction between smoking and external radiation, and recommended modifying NIH-IREP by introducing alternate interaction assumptions (7). SENES prepared a detailed analysis and summary of the four expert opinions (8). That report and all other documents referenced in this letter are enclosed.

Perhaps the only real consensus among the four reviewers is that none recommends the exclusive retention of the NIOSH-IREP model. Also striking is the diversity of opinion as to how to properly characterize and model the interaction between cigarette smoking and radiation. NIOSH recognizes that the NIH-IREP lung risk model utilizes additional years of follow-up of the Japanese survivor cohort, but also notes the substantive points raised by our expert reviewers. Thus, we conclude that the current state of scientific knowledge of this issue is ambiguous, and that there are sufficient reservations about the NIH-IREP model to justify an alternative approach.

After considerable evaluation and discussion, we propose to program NIOSH-IREP to run both lung cancer risk models and to report only the higher probability of causation. A notice to this effect will be included in the Federal Register notice for the October 2005 ABRWH meeting. NIOSH will fully brief the Board at this upcoming meeting, and will make no change to NIOSH-IREP until the Board

has considered the proposal and provided input. Should this change be implemented, all previous non-compensable lung cancer claims would be reevaluated.

Sincerely,

Larry J. Elliott, MSPH, CIH
Director
Office of Compensation
Analysis and Support

cc:
L. Wade
L. Shields

Enclosures:

(1) Land CE and Pierce DA. *Likelihood profile for parameter alpha used in computation of statistical uncertainty for ERR/Sv in NIH-IREP lung cancer model*. Personal communication from Charles Land, NIH/NCI, to NIOSH, February 3, 2004.

(2) Apostoaei AI and Trabalka JR, SENES Oak Ridge, Inc. *Differences in the estimation of lung cancer risk between NIOSH-IREP and NIH-IREP*. September 20, 2004.

(3) NIOSH/OCAS. *Evaluation of NIH-IREP lung cancer risk model for application to NIOSH-IREP*. (Instructions and summary of IREP lung model evaluation provided by NIOSH to outside experts), undated; E-mailed to reviewers on November 26, 2004.

(4) Davis FG. *Response to NIOSH questions*. Expert opinion solicited by NIOSH, February 10, 2005.

(5) Samet, JM. *Evaluation of two models for projecting lung cancer risk: NIOSH-IREP and NIH-IREP*. Expert opinion solicited by NIOSH, February 22, 2005.

(6) Richardson DB. *Should NIOSH adopt the NIH-IREP model for lung cancer for use in the EEOICPA?* Expert opinion solicited by NIOSH, February 28, 2005

(7) Brenner DJ. *Lung Cancer: Interaction of radiation exposure with smoking. What to do in IREP?* Expert opinion solicited by NIOSH, June 28, 2005.

(8) SENES Oak Ridge, Inc. *How should NIOSH estimate risk of lung cancer in workers covered under EEOICPA in the face of uncertainties in the interaction between smoking and low-LET radiation*. (Analysis and summary of expert opinions),