Evaluation of NIH-IREP Lung Cancer Risk Model for Application to NIOSH-IREP

Background

The Energy Employees Occupational Illness Compensation Program Act of 2000, as amended (EEOICPA), provides a lump sum payment of $150,000 plus medical benefits to any covered U.S. nuclear weapons worker diagnosed with cancer if that cancer is determined to have been "at least as likely as not" caused by occupational exposure to ionizing radiation. The Department of Health and Human Services (HHS) is charged with developing and updating, as warranted, the scientific guidelines for assessing eligibility for compensation. The Office of Compensation Analysis and Support (OCAS) of the National Institute for Occupational Safety and Health (NIOSH) performs this function for HHS.

HHS regulations (42 CFR Part 81) published in May 2002 established the guidelines for determining "probability of causation" under EEOICPA. Probability of causation, a term derived from the epidemiological concept of "assigned share," is defined for purposes of compensation as the risk of cancer due to occupational exposure to ionizing radiation (i.e., excess relative risk, or "ERR") divided by the total risk of cancer (1 + ERR.) Under EEOICPA, each cancer claim is individually evaluated via a computerized set of quantitative cancer risk assessment models. These risk models are embodied in a Web-based computational software package called NIOSH-IREP (Interactive Radio-Epidemiological Program.) Employing Monte Carlo simulation sampling to account for the uncertainties of dose estimation, risk modeling, and the stochastic nature of cancer induction, NIOSH-IREP calculates the probability (expressed as a percentage) that a cancer was caused by radiation exposure incurred by a covered employee while in the performance of duty.

A probability of causation of 50% or greater means that the claim merits compensation, i.e., that the cancer was "at least as likely as not" induced by radiation exposure. Each probability of causation result is unique, based upon data entered into NIOSH-IREP for that particular claim. Determinants of probability of causation include the type of cancer, amount and type of radiation dose, and other relevant factors (such as smoking history, if the cancer is of the lung, trachea, or bronchus.) In order to err on the side of the claimant, the upper 99th percentile credibility limit (akin to confidence limit) of probability of causation determines compensability. That is, if the upper 99th percentile credibility limit falls at 50 percent probability of causation or higher, the claim is deemed compensable.

Discussion

There are two different versions of IREP: NIOSH-IREP, the version maintained by NIOSH, and a separate version maintained by the National Cancer Institute (NCI) known as "NIH-IREP." 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. The cancer risk models in NIOSH-IREP, on the other hand, are intended to fit the characteristics and radiation exposures incurred by

civilian nuclear weapons workers. Most of the computerized risk models in both NIOSH-IREP and NIH-IREP are derived from a set of Radio-Epidemiological Tables created in 1985 by the National Institutes of Health (NIH) and periodically updated by NCI. The primary source of data for the Radio-Epidemiological Tables is the excess cancer incidence among Japanese atomic bomb survivors from World War II.

Although NIOSH-IREP and NIH-IREP are similar in many ways, there are important differences in some risk models. Perhaps the most significant difference lies in the respective risk models for lung cancer (includes cancer of the trachea and bronchus) for exposure to radiation other than radon. Initially, the lung cancer models were identical in the two versions of IREP. However, NCI substantially revised the NIH-IREP lung cancer model in late 2003 to reflect a more recent analysis of lung cancer incidence among the Japanese atomic bomb survivors. The revision was based on published data (Pierce, et. al., 2003) and unpublished data (Land and Pierce, 2004.) NCI made a second revision to the NIH-IREP lung model in mid-2004 which affected only exposures to alpha radiation. This later revision was made in order to ensure consistency with the NIH-IREP documentation published by NCI in 2003. ("Report of the NCI-CDC Working Group to Revise the 1985 NIH Radioepidemiological Tables," available via the NIOSH/OCAS Web site. See access instructions under "Online References.")

In the revised NIH-IREP lung model, ERR per unit dose is adjusted for age at exposure and age at diagnosis, whereas the NIOSH-IREP lung model does not adjust for these age-dependent factors. Further, the NIH-IREP lung model is less heavily weighted toward a multiplicative interaction than is 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 significantly different probabilities of causation for some exposure profiles. In terms of potential claim compensability, the main effect of the NCI revision is that NIH-IREP is generally more favorable to smokers and NIOSH-IREP is generally more favorable to non-smokers. Other effects (gender-related, for example) are more difficult to generalize.

A detailed analysis of the differences between the two IREP lung models can be found in the attached report (Apostoaei and Trabalka, 2004) commissioned by NIOSH from SENES Oak Ridge, Inc., the company that, under separate contracts with NIOSH and NCI, designed and programmed the IREP software packages according to the specifications of the two agencies. As noted in their report, SENES recommends that NIOSH adopt the NIH-IREP lung model for use in NIOSH-IREP. In SENES' judgment, this change is warranted because the revised NIH-IREP model is based on four additional years of follow-up of the Japanese atomic bomb survivor cohort and, therefore, represents a more advanced state of scientific knowledge. As an alternative, SENES notes that NIOSH-IREP could be reprogrammed to run both IREP lung models and to output only the higher of the two probabilities of causation, thereby resolving differences in uncertainty by always erring on the side of the claimant.

As noted earlier, NIOSH is charged with updating, as warranted, the scientific guidelines for assessing eligibility for compensation under EEOICPA. Potential modifications to

NIOSH-IREP cancer risk models must be evaluated by NIOSH for scientific merit and for their relevance and applicability to compensation claims. To help resolve this current issue, NIOSH is seeking input from outside experts.

Question

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 output only the higher probability of causation? Please provide the rationale for your conclusion.

Report and remuneration

Please submit your conclusion no later than February 14, 2005. To facilitate prompt reimbursement for your efforts, please include your SSN and postal mailing address and indicate the total number of days spent working on this project. NIOSH is authorized to provide $250.00 per day for time spent reviewing materials and preparing your report, not to exceed 10 days (maximum payment = $2500.00.) E-mail is an acceptable mode of transmission for your response and for your invoice for payment.

Your report and invoice, as well as questions regarding any aspect of this project should be directed to:

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Acronyms

EEOICPA: Energy Employees Occupational Illness Compensation Program Act of 2000, as amended
HHS: Department of Health and Human Services
NCI: National Cancer Institute
NIH: National Institutes of Health
NIOSH: National Institute for Occupational Safety and Health
OCAS: Office of Compensation Analysis and Support (an office of NIOSH created to carry out HHS responsibilities under EEOICPA)

Suggested References for Lung Model Evaluation (Attached)

Apostoaei AI, Trabalka JR. Differences in the estimation of lung cancer risk between NIOSH-IREP and NIH-IREP. SENES Oak Ridge, Inc., 2004 (unpublished report commissioned by NIOSH, 27 pages, PDF file) **Note: Questions related to the SENES report may be addressed directly to Dr. F. Owen Hoffman, Director, SENES Oak Ridge, Inc. (phone: 865-483-6111; e-mail: sensor@senes.com)**

Land CE, et.al. Draft Report of the NCI-CDC Working Group to Revise the 1985 NIH Radioepidemiological Tables, May 17, 2002, excerpts. (Note: This is an unpublished early draft of the report published in 2003 [see "Online References"] that formed the basis for the lung cancer model used in NIOSH-IREP; relevant pages are excerpted here. 51 total pages, PDF file)

Land CE, Pierce DA. Likelihood profile for parameter alpha used in computation of statistical uncertainty for ERR/Sv in NIH-IREP lung cancer model; re: Table IV.D.3, page 50, Report of the NCI-CDC Working Group to Revise the 1985 NIH Radioepidemiological Tables (Personal communication from Dr. Charles Land, 2004, titled by NIOSH for this reference. 5 pages, MS Word file)

Pierce DA, Sharp GB, Mabuchi K. Joint effects of radiation and smoking on lung cancer risk among atomic bomb survivors. Radiation Research 159: 511-520, 2003 (10 pages, PDF file)

Suggested Online References (Available via NIOSH/OCAS Web Page)

The NIOSH-IREP software program is posted on the Web and is freely available to the public; no password is required. To access the software, navigate to the NIOSH/OCAS Web site at http://www.cdc.gov/niosh/ocas/default.html and then click on the link to the "Probability of Causation (NIOSH-IREP)" page, located in the "OCAS Directory" menu. A link to NIOSH-IREP can be found on that page. Direct links to documentation and help files are embedded throughout the series of NIOSH-IREP user screens.

Additionally, a variety of technical references useful in evaluating the NIH-IREP and NIOSH-IREP lung models are accessible directly from the "Probability of Causation (NIOSH-IREP)" Web page. In particular, please note the following links:

(1) Final Rule: Guidelines for Determining the Probability of Causation – 42 CFR 81

(2) User's Guide for the Interactive Radio-Epidemiological Program (NIOSH-IREP)

(3) NIOSH-IREP Technical Documentation (In particular, see pages 32-33 and 57)

(4) Report of the NCI-CDC Working Group to Revise the 1985 NIH Radioepidemiological Tables (i.e., the technical documentation for NIH-IREP, published in September 2003. In particular, see pages 26, 40-41, 50, and 69)