11 Appendix: *Guidelines for Determining the Probability of Causation and Methods for Radiation Dose Reconstruction Under the Employees Occupational Illness Compensation Program Act of 2000*

SUMMARY: This rule implements select provisions of the Energy Employees Occupational Illness Compensation Program Act of 2000 ("EEOICPA" or "Act"). The Act requires the promulgation of guidelines, in the form of regulations, for determining whether an individual with cancer shall be found, "at least as likely as not," to have sustained that cancer from exposure to ionizing radiation in the performance of duty for nuclear weapons production programs of the Department of Energy and its predecessor agencies. The guidelines will be applied by the U.S. Department of Labor, which is responsible for determining whether to award compensation to individuals seeking federal compensation under the Act.

B. Purpose of Probability of Causation Guidelines

Under EEOICPA, a covered employee seeking compensation for cancer, other than as a member of the Special Exposure Cohort seeking compensation for a specified cancer, is eligible for compensation only if DOL determines that the cancer was "at least as likely as not" (a 50% or greater probability) caused by radiation doses incurred in the performance of duty while working for DOE and/or an atomic weapons employer (AWE) facility. These guidelines provide DOL with the procedure to make these determinations, and specify the information DOL will use.

D. Understanding Probability of Causation

Probability of Causation is a technical term generally meaning an estimate of the percentage of cases of illness caused by a health hazard among a group of persons exposed to the hazard. This estimate is used in compensation programs as an estimate of the probability or likelihood that the illness of an individual member of that group was caused by exposure to the health hazard. Other terms for this concept include "assigned share" and "attributable risk percent".

In this rule, the potential hazard is ionizing radiation to which U.S. nuclear weapons workers were exposed in the performance of duty; the illnesses are specific types of cancer. The probability of causation (PC) is calculated as the risk of cancer attributable to radiation exposure (RadRisk) divided by the sum of the baseline risk of cancer to the general population (BasRisk) plus the risk attributable to the radiation exposure, then multiplied by 100 percent, as follows:

$$\text{PC} = \frac{\text{RadRisk}}{\text{RadRisk} + \text{BasRisk}} \times 100\%$$

This calculation provides a percentage estimate between 0 and 100 percent, where 0 would mean 0 likelihood that radiation caused the cancer and 100 would mean 100 percent certainty that radiation caused the cancer.[18]

Scientists evaluate the likelihood that radiation caused cancer in a worker by using medical and scientific knowledge about the relationship between specific types and levels of radiation dose and the frequency of cancers in exposed populations. Simply explained, if research determines that a specific type of cancer occurs more frequently among a population exposed to a higher level of radiation than a comparable population (a population with less radiation exposure but similar in age, gender, and other factors that have a role in health), and if the radiation exposure levels are known in the two populations, then it is possible to estimate the proportion of cancers in the exposed population that may have been caused by a given level of radiation.

If scientists consider this research sufficient and of reasonable quality, they can then translate the findings into a series of mathematical equations that estimate how much the risk of cancer in a population would increase as the dose of radiation incurred by that population increases. The series of equations, known as a dose-response or quantitative risk assessment model, may also take into account other health factors potentially related to cancer risk, such as gender, smoking history, age at exposure (to radiation), and time since exposure. The risk models can then be applied as an imperfect but reasonable approach to determine the likelihood that the cancer of an individual worker was caused by his or her radiation dose.

[18] To regenerate our previous formula for Attributable Risk, define RadRisk to be $p_E - p_{NE}$.

E. Development and Use of the RadioEpidemiological Tables and Interactive RadioEpidemiological Program

In 1985, in response to a congressional mandate in the Orphan Drug Act, a panel established by the National Institutes of Health developed a set of Radioepidemiological Tables. The tables serve as a reference tool providing probability of causation estimates for individuals with cancer who were exposed to ionizing radiation. Use of the tables requires information about the person's dose, gender, age at exposure, date of cancer diagnosis and other relevant factors. The tables are used by the Department of Veterans Affairs (DVA) to make compensation decisions for veterans with cancer who were exposed in the performance of duty to radiation from atomic weapon detonations.

The primary source of data for the 1985 tables is research on cancer-related deaths occurring among Japanese atomic bomb survivors from World War II.

The 1985 tables are presently being updated by the National Cancer Institute (NCI) and the Centers for Disease Control and Prevention to incorporate progress in research on the relationship between radiation and cancer risk. The draft update has been reviewed by the National Research Council and by NIOSH. DOL will employ the updated version of the tables, with modifications important to claims under EEOICPA, as a basis for determining probability of causation for employees covered under EEOICPA.

A major scientific change achieved by this update is the use of risk models developed from data on the occurrence of cancers (cases of illness) rather than the occurrence of cancer deaths among Japanese atomic bomb survivors. The risk models are further improved by being based on more current data as well. Many more cancers have been modeled in the revised report. The new risk models also take into account factors that modify the effect of radiation on cancer, related to the type of radiation dose, the amount of dose, and the timing of the dose.

A major technological change accompanying this update, which represents a scientific improvement, is the production of a computer software program for calculating probability of causation. This software program, named the Interactive RadioEpidemiological Program (IREP), allows the user to apply the NCI risk models directly to data on an individual employee. This makes it possible to estimate probability of causation using better quantitative methods than could be incorporated into printed tables. In particular, IREP allows the user to take into account uncertainty concerning the information being used to estimate probability of causation. There typically is uncertainty about the radiation dose levels to which a person has been exposed, as well as uncertainty relating levels of dose received to levels of cancer risk observed in study populations.

Accounting for uncertainty is important because it can have a large effect on the probability of causation estimates. DVA, in their use of the 1985 Radioepidemiological Tables, uses the probability of causation estimates found in the tables at the upper 99 percent credibility limit. This means when DVA determines whether the cancer of a veteran was more likely than not caused by radiation, they use the estimate that is 99 percent certain to be greater than the probability that would be calculated if the information on dose and the risk model were perfectly accurate. Similarly, these HHS guidelines, as required by EEOICPA, will use the upper 99 percent credibility limit to determine whether the cancers of employees are at least as likely as not caused by their occupational radiation doses. This will help minimize the possibility of denying compensation to claimants under EEOICPA for those employees with cancers likely to have been caused by occupational radiation exposures.

F. Use of IREP for Energy Employees

The risk models developed by NCI and CDC for IREP provide the primary basis for developing guidelines for estimating probability of causation under EEOICPA. They directly address 33 cancers and most types of radiation exposure relevant to employees covered by EEOICPA. These models take into account the employee's cancer type, year of birth, year of cancer diagnosis, and exposure information such as years of exposure, as well as the dose received from gamma radiation, x-rays, alpha radiation, beta radiation, and neutrons during each year. Also, the risk model for lung cancer takes into account smoking history and the risk model for skin cancer takes into account race/ethnicity. None of the risk models explicitly accounts for exposure to other occupational, environmental, or dietary carcinogens. Models accounting for these factors have not been developed and may not be possible to develop based on existing research. Moreover, DOL could not consistently or efficiently obtain the data required to make use of such models.

IREP models do not specifically include cancers as defined in their early stages: *carcinoma in situ* (CIS). These lesions are becoming more frequently diagnosed, as the use of cancer screening tools, such as mammography, have increased in the general population. The risk factors and treatment for CIS are frequently similar to those for malignant neoplasms, and, while controversial, there is growing evidence that CIS represents the earliest detectable phase of malignancy. Therefore, for determining compensation under EEOICPA, HHS requires that CIS be treated as a malignant neoplasm of the specified site.

Cancers identified by their secondary sites (sites to which a malignant cancer has spread), when the primary site is unknown, raise another issue for the application of IREP. This situation will most commonly arise when death certificate information is the primary source of a cancer diagnosis. It is accepted in medicine that cancer causing agents such as ionizing radiation produce primary cancers. This means, in a case in which the primary site of cancer is unknown, the primary site must be established by inference to estimate probability of causation.

HHS establishes such assignments in these guidelines, based on an evaluation of the relationship between primary and secondary cancer sites using the National Center for Health Statistics (NCHS) Mortality Database for years 1995–1997. Because national cancer incidence databases (e.g., the National Cancer Institute's Surveillance, Epidemiology and End Results program) do not contain information about sites of metastasis, the NCHS database is the best available data source at this time to assign the primary site(s) most likely to have caused the spread of cancer to a known secondary site. For each secondary cancer, HHS identified the set of primary cancers producing approximately 75% of that secondary cancer among the U.S. population (males and females were considered separately). The sets are tabulated in this rule. DOL will determine the final assignment of a primary cancer site for an individual claim on a case-by-case basis, as the site among possible primary sites which results in the highest probability of causation estimate.

Employees diagnosed with two or more primary cancers also raise a special issue for determining probability of causation. Even under the assumption that the biological mechanisms by which each cancer is caused are unrelated, uncertainty estimates about the level of radiation delivered to each cancer site will be related. While fully understanding this situation requires statistical training, the consequence has simple but important implications. Under this rule, instead of determining the probability that each cancer was caused by radiation independently, DOL will perform an additional statistical procedure following the use of IREP to determine the probability that at least one of the cancers was caused by the radiation. This approach is important to the claimant because it would determine a higher probability of causation than would be determined for either cancer individually.