NIOSH-Interactive RadioEpidemiological Program (NIOSH-IREP) Technical Documentation

Final Report

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I. Background

Under the Energy Employees' Occupational Illness Compensation Program Act of 2000

(EEOICPA), the National Institute for Occupational Safety and Health (NIOSH) is charged with the

development of guidelines to determine whether a claimant's cancer meets the criterion for causation by

workplace exposure to ionizing radiation (i.e., a 50% or greater probability of causation).

The basis for this determination, as specified in EEOICPA, is the set of radioepidemiological

tables developed by a National Institutes of Health Ad Hoc working group in 1985 (NIH 1985), as

they are updated periodically. These radioepidemiological 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 of 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 line of duty

to radiation from atomic weapon detonations. The primary source of data for the 1985 tables is

research on the occurrence of cancer-related deaths among Japanese atomic bomb survivors from

World War II.

The 1985 tables have recently been updated by the National Cancer Institute (NCI) and the

Centers for Disease Control and Prevention (CDC) to incorporate progress in research on the

relationship between radiation and cancer risk, including the assessment of associated uncertainties.

The draft update (NCI 2000) has been reviewed by the National Research Council (NAS/NRC

2000). The finalized update (NCI 2002) will be available soon for public release. HHS/NIOSH has

employed the finalized version of the NCI update, with certain modifications important to claims under

EEOICPA, as a basis for determining probability of causation for employees covered under

EEOICPA.

A scientific change achieved by the NCI 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 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 as well

as practical improvement, is the development of a computer software program for calculating assigned

share. The assigned share is a term recommended in the NCI update of the radioepidemiological

tables, instead of probability of causation, to properly reflect that these estimates are properties of

groups of similar people, not of the individual. In other words, it is not possible to determine, for a

given individual, whether his or her cancer resulted from a workplace exposure to ionizing radiation.

The assigned share is used to estimate the probability of causation needed for determining eligibility for

an award under EEOICPA, and these terms are used interchangeably in this document. It should also

be noted that this software does not predict an individual's chances of getting cancer from workplace

radiation exposure. Rather, it estimates (from epidemiological models combined with information on

the individual's past exposure) the likelihood that an existing cancer resulted from that exposure.

The software program, named the Interactive RadioEpidemiological Program (IREP), allows the user to apply the NCI risk models directly to data on an individual claimant. This makes it possible to calculate 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 calculate probability of causation. There typically is uncertainty about the radiation dose levels to which a person has been exposed, as well as uncertainty in the science 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 its use of the 1985 radioepidemiological tables, employs the value found in the tables at the upper 99 percentile of the probability of causation estimate. Similarly, as required by EEOICPA, the U.S. Department of Labor (DOL) 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 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 radiation exposures.

The risk models developed by NCI and CDC for IREP (NCI 2002) provide the primary basis for developing guidelines for estimating probability of causation under EEOICPA. They directly address most 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. The risk model

for lung cancer takes into account smoking history as well. 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.

As stated above, the final draft of the National Cancer Institute's IREP software (NCI 2002)

has formed the basis of the NIOSH-IREP software. The NCI's final draft has been updated from the

version reviewed by the National Research Council in several ways. The updated draft includes a

model for lung cancer resulting from radon exposure, developed from an analysis of U.S. uranium miner

cohorts (RECA Committee, 1996), the development of models for non-melanoma skin cancer, the

incorporation of a "miscellaneous cancer model", which they suggest should be used for bone cancer

and male breast cancer, and the inclusion of models for non-melanoma skin cancer (squamous cell and

basal cell carcinoma). Other changes include the incorporation of an uncertainty distribution for the

latency of solid cancers, and the development of statistical distributions for the radiation effectiveness

factors (REF) and dose and dose-rate effectiveness factor (DDREF) of different energies of photons,

neutrons, and alpha particles (Kocher et al. 2002).

One important change in the NCI's methodology (which also constitutes the basis of NIOSH-

IREP) is in the method of modeling solid cancer risk from the Japanese atomic bomb survivor study

(NCI 2002, pp 27-31). Effects of gender, age at exposure and attained age were modeled for all

solid cancers as a group. The risk modifications from these general models were then applied to the

site-specific models, unless there was a statistically-significant difference between these risk modifiers for the site-specific and general model. This approach has been recommended by an international expert committee (Pierce and Preston 1993; UNSCEAR 2000b, p. 208). The models show higher sensitivity (in general) for females compared to males. The general coefficients also show reductions in risk per unit dose between ages-at-exposure of 15 and 30 (if attained age is held constant). The ERR per Sv estimates do not change after age-at-exposure of 30. Thus, for most cancers NIOSH-IREP relies on direct evidence from the A-bomb survivors exposed as adults rather than as young children. This modulates the strong decline in risk with increasing age that is observed among those exposed as children in that study, and thus is more appropriate for modeling risks among those exposed as adults.

The modeling of risk from exposures as young as age 15 is a result of the Poisson regression procedure used to analyze the atomic bomb survivor cohort. This is a grouped data method; data are available for modeling within 5-year age-at-exposure categories; therefore, the modeled exposure classes for adults must begin at either age 15 or age 20. Because DOE employees may have begun working and accrued workplace radiation exposures before age 20, for EEOICPA it is necessary to model exposure categories beginning at age 15.

No age-at-exposure effect has been incorporated for acute myeloid leukemia, chronic myeloid leukemia, lung cancer (non-radon exposures), and female genital cancers other than ovary. The NCI models incorporate a trend of decreasing risk per unit dose with increasing age at exposure for acute lymphocytic leukemia, all leukemia other than chronic lymphocytic, basal cell carcinoma, and cancers of thyroid. For thyroid and non-melanoma skin cancer models, the age at exposure effects were modeled

using site-specific estimates, and generally decrease with increasing age at exposure. For the skin cancer model, a log-linear term is used to decrease risks for increasing ages at exposure between 10 and 40. Ideally, this model would include only adult exposures (as for other solid cancers); however, the data were not modeled in this way for NCI-IREP, and the data were not available to NIOSH researchers. Data were modeled categorically for a given age at exposure, and risk coefficients for intermediate ages at exposure were obtained through interpolation from values at surrounding age categories (Table IV.D.9 of NCI 2002).

For radon exposures and lung cancer, there is no direct adjustment for exposure age; risks are dependent on time since last exposure and on age at diagnosis. The effect of this adjustment is that, at a constant "time since last exposure", the risk decreases for increasing age at last exposure; however, for constant "age at diagnosis", the risk increases for increasing age at last exposure. For all other cancers, the NCI models incorporate a trend of decreasing risk per unit dose for exposure ages between 15 and 30, and assumes constancy thereafter.

These changes are detailed in the NCI IREP documentation being finalized by the NCI (NCI 2002). [It must be noted, however, that the NCI IREP is not finalized at the time of this writing. (May 2002) Any changes or modifications which occur as part of the finalization of the NCI-IREP which are not notes here must be evaluated for scientific merit and applicability under EEIOCPA.] Changes in the NCI IREP that are relevant to the evaluation of compensation claims under EEOICPA may be incorporated into future versions of NIOSH-IREP.

II. NIOSH-IREP and its implementation under EEOICPA

A. Dosimetry Issues

NIOSH-IREP includes twelve types of radiation exposure. For this purpose, radon is

considered an exposure that may contribute to risk of lung cancer only, and the remaining eleven types

of exposure, considered for any cancer type, are described in Table 1. These types of exposures are

differentiated by the assumed radiation weighting factor (termed here the radiation effectiveness factors

or REF) and in some cases, a factor accounting for reduced or enhanced effectiveness in producing

cancers resulting from dose protraction (dose and dose rate effectiveness factor, or DDREF). The

distributions assumed for these factors are described in Section II.D below. There are two classes of

electron (beta particle) exposure within NIOSH-IREP: one class associated with exposure to tritium,

and a second class for all other electrons. Three different photon energy classes exist within NIOSH-

IREP: photons of energy greater than 250 keV (exemplified by high-energy gamma radiation that was

the primary exposure of the Japanese atomic bomb survivors), photons of energy between 30 and 250

keV, which includes photofluorographic x rays used during the 1940s and 1950s at some Department

of Energy (DOE) facilities (Cardarelli 2000), and photons of energy less than 30 keV, which includes

photons emitted by certain transuranic radionuclides. There are five classes of neutrons differentiated

by energy type. The most commonly encountered type of neutron exposure within the DOE workforce

is fission neutrons, composed primarily of neutrons with energy between 100 keV and 2 MeV.

However, neutrons of higher and lower energy are included because these exposures are relevant for

certain DOE workers. Finally, a single class of radiation exposure is included for non-radon alpha

particles. The exposure units used in NIOSH-IREP are working level months (WLM) for radon, and cSv (rem) for all other radiation types.

For each type of exposure, the dose used in NIOSH-IREP will be based on the individual organ or tissue in which the primary cancer occurred, or, if unavailable, in the nearest relevant organ or tissue. For bone cancer, dose to the endosteal cells (the cells of the outer bone surface) will be calculated. For skin cancer, a more site-specific approach will be used. Because studies of medically-exposed persons have shown that radiation-induced skin cancers tend to occur within the field of radiation exposure (van Daal et al. 1983, Shore et al. 1984, Hildreth et al. 1985, Lichter et al. 2000), skin dose will be calculated only for the location where the cancer occurred, as reflected in the 9th Revision of the International Classification of Diseases (ICD-9) 4-digit nosology code (i.e., lip, eyelid, ear, other parts of face, scalp and neck, trunk, upper limb, lower limb). If the body location is unspecified, the maximum skin dose at any location will be calculated as input to NIOSH-IREP.

In determining the dose rate (i.e., acute or chronic) that should be assumed for use in NCI-IREP, the NCI working group referenced the definition used by the UNSCEAR (UNSCEAR 1993), which is that an acute dose is delivered at a dose rate of 6 mGy per hour or greater (NCI 2002, p. 37), averaged over several hours. This is equivalent to a dose rate of 0.1 mGy (10 mrem) per minute. Lower exposure rates should be considered chronic, according to this definition.

Work-related medical x-ray exposures are clearly acute, by this definition. Although likely to have been chronic, the true dose rate of these gamma and neutron exposures is unknown for any given worker within the badging period. *Therefore, the approach used in the NIOSH Dose*

Reconstruction methods and NIOSH-IREP is to make an assumption about duration of exposure that is most favorable to the claimant. This is consistent with the approach used elsewhere in NIOSH-IREP, of providing the benefit of doubt to the claimant where two or more plausible alternatives for input exist. This approach was, additionally, recommended by the NAS panel reviewing NCI-IREP: "... the officials responsible for adjudicating claims might routinely assume that the exposure aggregated over the smallest unit of time available (such as a quarter-year) was received as a single acute dose to provide a liberal estimate of risk" (NAS/NRC 2000, p. 13). In the case of gamma exposures, such a liberal assumption would be that the dose was acute. For neutron exposures, an assumption of chronic dose rate would produce the most liberal estimate of risk.

For these reasons, in the dose reconstruction process, gamma and x ray doses will be considered acute over the smallest period of time during which the exposure measurement occurred. As a practical matter, this means that the exposure rate will be categorized as acute for each badge reading, and each will be specified separately within a given year in NIOSH-IREP. For example, if a claimant's dosimetry badges were exchanged and read on a quarterly basis, each of the four badge results would be entered as a separate <u>acute</u> dose (or dose distribution) in NIOSH-IREP. In contrast, photon exposures resulting from the intake of an internal emitter will be assumed to be chronic, as the decay path of the alpha particle (which is a known physical quantity) produces a chronic exposure. For reasons outlined above, neutron doses will be assumed to be chronic over the badge reading period. This assumption will have the effect of increasing the probability of causation for neutron exposures, because of the use of a protraction enhancement factor (e.g., see Section II.D and Kocher et al. 2002).

B. Cancers added to NIOSH-IREP

The final NCI-IREP program (NCI 2002) includes more cancer models than the draft NCI-IREP program reviewed by the NAS panel (NCI 2000). Cancer models for squamous cell carcinoma of skin and basal cell carcinoma of skin have been added, based on new analyses conducted by researchers at the Radiation Effects Research Foundation (RERF), in Japan (see discussion of "skin cancer models" in Sec. II.B.2, below). Certain cancer models have been added to NIOSH-IREP. These include malignant melanoma of skin, and cancers of the male breast, bone, connective tissue, eye, and endocrine glands other than thyroid. The NCI version of IREP includes the last four of these in a general "miscellaneous" cancer model, but they are explicitly separated in NIOSH-IREP. The scientific basis of these models and their implementation in NIOSH-IREP are described below.

In summary, NIOSH-IREP incorporates three different models for skin cancer. For non-melanoma skin cancer, basal cell and squamous cell carcinoma models are based on different sets of risk coefficients. In claims for which the non-melanoma skin cancer type is indeterminate, the model for basal cell carcinoma is to be used in estimating the probability of causation. Both basal cell and non-basal cell carcinoma models are modified by race-specific background incidence rates for combined non-melanoma skin cancers. A third skin cancer model, for malignant melanoma, uses basal cell carcinoma risk coefficients, modified by background incidence rates for malignant melanoma. All three skin cancer models use the "general" risk transfer uncertainty distribution (developed for all solid cancers save breast and thyroid). For other cancer types, the sites used to produce excess relative risk

(ERR) per Sv estimates for each risk model, and the cancer groupings to which these models were applied, are given in Table 2.

1. Bone cancer:

Exposure to plutonium has been found in numerous animal studies to cause bone cancer (NAS 1988). There is also a large body of literature regarding the induction of bone cancer from occupational exposure to radium, in the form of Thorotrast (see NAS/NRC 1988 and IARC 2001, for summary). Most U.S. worker studies are based on relatively low exposures and small numbers of workers exposed to plutonium, and have thus been inconclusive with respect to bone cancer induction. However, a recent study of the Russian Mayak facility (Koshurnikova et al. 2000) found elevated rates of bone cancer among workers with positive plutonium body burdens, after adjusting for cumulative external dose (RR = 7.9; 95% confidence interval = 1.6-32). Unfortunately, this study cannot be used for quantitative assessment of risk, because of serious limitations in the plutonium dosimetry for these workers (Koshurnikova et al. 2000); however, it does provide strong qualitative evidence for an association between plutonium exposure and bone cancer in humans.

For the purposes of NIOSH-IREP, two sources of risk coefficients were considered: data from the risk analysis conducted for plutonium exposures among Rocky Flats workers (Grogan et al. 2000, 2001), and the miscellaneous cancer model used in NCI-IREP. The risk coefficients from Grogan and colleagues' analysis are based on three sources: mortality data from the Japanese atomic bomb survivors studies (modified by the uncertain radiation

effectiveness factors for alpha particles as compared to low-energy photons and by the dose-and-dose rate effectiveness factor); studies of humans exposed to other alpha-emitters; and studies of animals exposed to plutonium. A subjectively weighted combination of these risk estimates for plutonium exposure was then used to produce estimates of lifetime risk per unit dose and per unit intake of plutonium.

The approach of Grogan and colleagues is quite difficult to incorporate into IREP, however, because of the need of IREP to incorporate risks from many types of radiation exposure, not just plutonium and other alpha-emitting radionuclides. The problem with using human and animal studies of alpha-exposed groups as a source of risk coefficients in IREP is that, in the former, the risk per unit dose is expressed as a function of the initial (rather than the committed dose), while in the latter, the risk per unit dose is expressed on an incremental basis as dose is received by the target organ. In other words, in the studies upon which the risk models are based, the radionuclide is deposited in the target organ (e.g., the bone surfaces), and the dose to bone surfaces is delivered throughout the life of the individual. The expression of risk in these studies is based on the initial exposure to the bone surface, which is an underestimate of the total dose received by the organ. While this is not an inconsistent approach for evaluating the risks of plutonium or other transuranic radionuclides, it is incompatible with the approach used throughout IREP, which is concerned with both these radionuclides and external ionizing radiation exposures. The model implemented by Grogan and colleagues that is most compatible with the approach of IREP is the bone cancer model

obtained from Japanese atomic bomb survivors, modified by relevant distributions of REF and DDREF for different types of radiation. Use of this approach is also consistent with that adopted by NCI for other tissues in which transuranic radionuclides tend to accumulate (e.g., liver).

The study of cancer incidence among atomic bomb survivors (Thompson et al. 1994) does not quantify bone cancer risks; however, the Grogan model uses excess risk estimates from the latest mortality study (Pierce et al. 1996) for its cancer incidence model. This model was not deemed appropriate by NCI for IREP because the extreme rarity of this cancer, particularly in the exposed group, would have resulted in a model that was inconsistent with the methods used for other cancers (which were based on risk coefficients for groups of similar cancers that numbered at least 50 in the population exposed to 0.5 cSv or greater).

The final NCI-IREP program includes bone cancer among the grouping of miscellaneous cancers includes bone cancer (NCI 2002). The primary argument against the use of the miscellaneous cancer risk coefficients for bone cancer claims is that the model includes many disparate types of cancers, including those of bone, connective tissue, eye, male breast cancer, non-thyroid endocrine glands, and ill-defined sites. The alternative, however, of using highly uncertain risk coefficients (from the bone cancer mortality series) without modification from other information sources, seems less defensible, and inconsistent with the approach used for other cancers in this class. The point estimates for the two models are quite similar. Therefore, we concur with the NCI that the most appropriate source of risk coefficients

for use at this time in the bone cancer models is the miscellaneous cancer model from NCI-

IREP. As is the case for other cancers in this category, the risk coefficients are modified by the

background incidence rates for the specific cancer.

2. Non-melanoma skin cancer:

Some expert groups consider skin cancer risk in establishing low-level skin radiation

exposure limits (ICRP 1991a), as several studies have provided evidence that non-melanoma

skin cancers, particularly basal cell carcinoma (BCC), are related to exposure to ionizing

radiation (Shore 2001). These include studies of radiologists, uranium miners, and patients

exposed during treatment for medical conditions, as well as the Japanese atomic bomb

survivors (Sevcova et al. 1978, van Daal et al. 1983, Hildreth et al. 1985, Thompson et al.

1994, Ron et al 1998). Many studies suggest that, of the two types comprising non-melanoma

skin cancer, BCC is much more radiosensitive than squamous cell carcinoma and other non-

melanoma skin cancers (SCC; van Daal et al. 1983, Ron et al. 1998, Shore 2001); however,

others do not specify the relative radiosensitivity of these two skin cancer types (Hildreth et al.

1985), or found similar radiosensitivity of the two types (Lichter et al. 2000).

Within NIOSH-IREP, only skin cancer has an adjustment for race and/or ethnicity in

determining the probability of causation. Unlike other cancers, the biological justification for

this adjustment is very strong: skin cancer incidence rates vary by a factor of 20 or more for

individuals of different racial or ethnic groups, while most other cancers that show racial

variation in incidence differ by a factor of two or less (Fig. 1). For malignant melanoma,

incidence rates are 18-20 times greater among non-Hispanic U.S. whites than among African-

Americans. Skin cancer incidence rates for Asian-Americans and Native Americans are similar

to African-Americans (Miller and Gaudette 1996), and rates for Hispanic whites are

intermediate between those of African-Americans and whites (Scotto et al. 1996). For most

cancers, the reasons for disparity in incidence by race are not known, but probably include

factors such as differences in tobacco use, dietary factors, and access to health care. In

contrast, the reasons for racial and ethnic differences in skin cancer incidence rates appear

strongly related to the damage produced by exposure to ultraviolet radiation (UV) in

susceptible individuals. Non-whites are thought to be at less risk of cancer from exposure to

UV through the protective effect of melanin, which absorbs harmful UV radiation in the skin

(Kaidbey et al. 1979, Altman et al. 1987, Kollias et al. 1991). The net effect of incorporating

the background incidence rate of skin cancer is to properly reflect the increased probability of

causation for radiation-induced skin cancer for non-white claimants, compared to whites

exposed to the same doses under the same conditions, if a sub-multiplicative relationship exists

between radiation exposure and sensitivity to UV radiation exposure. Not incorporating the

ethnic differences in background risk would have the effect of underestimating the probability of

causation of radiation-induced skin cancers among non-whites.

The true form of the interaction between ionizing and UV radiation exposure is unclear.

On theoretical grounds, ionizing radiation might be expected to interact additively with

background risk (caused primarily by exposure of susceptible skin to UV radiation; UNSCEAR 2000b, p. 200), if melanin is not similarly protective of its effects. However, some studies have suggested that melanin provides protection from radiation-induced skin cancer as well (Harley et al. 1983, Shore et al. 1984, Davis et al. 1989). Unfortunately, few studies have evaluated formally the interaction of ionizing radiation exposure with skin pigmentation. A meta-analysis of twelve epidemiologic studies of UV and ionizing radiation exposed individuals could not distinguish between an additive and multiplicative interaction, due to the lack of controls with ionizing radiation exposure alone (Shore 1990; UNSCEAR 2000b). Without the capability to formally test for the form of interaction within a study, the United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) recommends careful comparison of the relative risks among different populations in comparable studies (UNSCEAR 2000c, p. 310). The ICRP evaluated existing studies, and, given the findings of several studies that excess absolute risk from ionizing radiation exposure is greatest among white populations (and is still higher in areas of the skin usually exposed to greater UV radiation), suggested an interaction that is more than additive (Harley et al. 1983, Shore et al. 1984; ICRP 1991a, pp. 75-78). However, a recent analysis of non-melanoma skin cancer among the Japanese atomic bomb survivors found excess relative risks per unit dose nearly ten times higher for areas of the body unexposed to UV radiation (Ron et al. 1998). This finding strongly suggests a submultiplicative interaction between ionizing and UV radiation exposures. An authoritative

UNSCEAR report (UNSCEAR 2000b) suggests that a sub-multiplicative model should be employed for risk modeling, based on the totality of evidence.

The uncertainty in the appropriate form of interaction between UV and ionizing radiation exposure is expected to be most critical in determining the role of race or ethnicity in modifying the excess relative risk estimates produced from the Japanese atomic bomb survivor study. Because of this large uncertainty, the method of risk transfer from the Japanese to the U.S. racial/ethnic groups, built into the NIOSH-IREP program, should incorporate the possibility of an additive or multiplicative interaction (or a mixture of these). Given the conflicting evidence regarding the appropriateness of any specific interaction model between UV and ionizing radiation exposure, the IREP program uses the same uncertainty distribution for risk transfer as was used for all other solid cancers (except breast and stomach cancer). This distribution is trapezoidal, equally weighting the probabilities for an additive and multiplicative interaction, with slight probabilities of sub-additive or super-multiplicative interactions.

In order to apply the risk transfer function referenced above, background cancer incidence rates in Japan and the U.S. (by race/ethnicity categories) are required. Incidence rates for non-melanoma skin cancer are available for Japan, but not for the U.S., as this is not a reportable cancer among U.S. registries. However, a survey of non-melanoma skin cancer rates was carried out by researchers at the National Cancer Institute in the early 1980s, reflecting rates across a wide area within the U.S. for 1977-1980 (Scotto et al. 1983). In

Japan, non-melanoma skin cancers are reportable, and incidence rates are available both for

1990 (Parkin et al. 1977) and for 1978-1982 (Muir et al. 1987). Therefore, to more

accurately reflect comparative rates in both countries, incidence rates for the late 1970s (age-

adjusted to the 1970 U.S. standard population) were used from both countries for NIOSH-

IREP. For the U.S. population of non-Hispanic whites, these data were obtained from Tables

5 (males) and 6 (females) of Scotto et al. (1983). For Hispanic whites and African-Americans

(Hispanic and non-Hispanic), these data were obtained from Scotto et al. (1996). The age-

adjusted background incidence rates used in NIOSH-IREP are shown here in Table 3.

Incidence rates for Asian or Native Americans have not been estimated in the special surveys

of non-melanoma skin cancer incidence (Scotto et al. 1983, 1996). Based on literature

reporting low rates of non-melanoma skin cancer risk among these groups (Miller and Gaudette

1996), as well as the similarity in malignant melanoma incidence among Native Americans,

Asian-Americans and African-Americans (Table 3), the non-melanoma skin cancer incidence

for the former two ethnic groups is assumed to be the same as for African-Americans, for

purposes of NIOSH-IREP. While the background incidence rates for most cancers are based

on relatively current rates (i.e., circa 1990), the rates for non-melanoma skin cancer for both

the Japanese and U.S. populations are based on data from the late 1970s. More recent studies

show that incidence rates have likely increased since that time (Miller and Weinstock 1994).

This is not likely to be an unacceptable source of error for calculation of probability of

causation within the DOE workforce, since claims are to be considered for any cancer

occurring since the worker began employment at a facility (i.e., a time period extending from the 1940s through the present day).

While many studies have found an association between ionizing radiation exposure and skin cancer, the appropriate form of dose-response model for skin cancer is highly uncertain (ICRP 1991a, p. 52). Some researchers advocate the use of a threshold model, on the basis of observations about dose-response relationships for such deterministic endpoints as skin dermatitis, desquamation and erythema, and upon evidence for a nonlinear dose-response relationship observed in some animal studies (reviewed in ICRP 1991a, pp 52-55). However, no evidence of a dose threshold was observed in a meta-analysis of twelve UV and ionizing radiation-exposed groups (Shore 1990, UNSCEAR 2000b). A recent study evaluated various forms of the dose-response relationship for the atomic bomb survivors, and concluded that the best-fitting model for non-melanoma skin cancer is proportional to the fourth power of dose (Little and Charles 1997). However, a more recent analysis found no significant model improvement (over linearity) using a linear-quadratic model (Ron et al. 1998). A linear dose-response relationship for non-melanoma skin cancer has been advocated by others as well (e.g., Scotto et al. 1996). The mechanisms in skin carcinogenesis that might lead to a threshold, not observed for most other organs in these studies, are unclear (ICRP 1991a, pp. 54-55).

Skin doses are poorly estimated in most studies of risks associated with ionizing radiation exposure, making quantitative dose-response analysis difficult. As for other cancer sites, an exception is the Japanese atomic bomb survivors study. The final version of NCI-

IREP includes separate risk coefficients for BCC and other non-melanoma skin cancers (mainly

SCC), based on new analyses of skin cancer incidence among atomic bomb survivors

conducted by researchers at the Radiation Effects Research Foundation in Japan (NCI 2002,

p. 34). The method used to develop risk coefficients for these separate models is quite

consistent with that for other cancers. The results of this modeling effort support the use of

substantially different risk coefficients for the two non-melanoma skin cancer types. However,

it should be noted that ICD-9 (and its revision, ICD-10) does not distinguish between SCC

and BCC within the non-melanoma skin cancer category. In cases where it is not possible to

determine which cancer cell type applies to a given claimant, DOL is instructed to use the risk

models for basal cell carcinoma.

The risk coefficients developed for non-melanoma skin cancer in the finalized NCI-

IREP were incorporated into the final NIOSH-IREP. The excess relative risk coefficients for

BCC vary by age at exposure but not by gender or attained age, and are linear in dose. The

coefficients for SCC do not vary by gender, age at exposure, or attained age. No adjustment is

made for time since exposure (except the latency adjustment used for all other cancers between

0 and 5 years after exposure). This is supported by evidence from several studies which

indicate that radiation-related skin cancer risks remain elevated for many years following

exposure (van Daal et al. 1983; Ron et al. 1998).