User's Guide for the Interactive RadioEpidemiological Program (NIOSH-IREP)

Designed for use by the Department of Labor in adjudicating claims under the Energy Employees' Occupational Illness Compensation Program Act (EEOICPA)

v.6.0

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NIOSH National Institute for Occupational Safety and Health

OAK RIDGE CENTER for RISK ANALYSIS

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1.0 BACKGROUND

Under the Energy Employees' Occupational Illness Compensation Program Act (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 (NIH) working group in 1985. These radioepidemiological tables serve as a reference tool providing probability of causation (PC) estimates for individuals with cancer who were exposed to ionizing radiation.

A major technological change to the 1985 radioepidemiological tables represents a scientific as well as a practical improvement: the development of a computer program for calculating probability of causation. This software program, named the Interactive RadioEpidemiological Program (IREP), allows the user to apply the National Cancer Institute's (NCI) risk models directly to data about exposure for an individual employee. This makes it possible to calculate the 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 individualized exposure and to calculate the probability of causation.

Accounting for uncertainty is important because it can have a large effect on the probability of causation estimates for a specific individual. The Department of Veterans Affairs (VA), in their application of the 1985 radioepidemiological tables, uses the value at the upper 99 percent credibility limit of the probability of causation estimate. Similarly, as required by EEOICPA, the U.S. Department of Labor (DOL) uses the upper 99 percent credibility limit to determine whether the cancers of employees were 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 occupational radiation exposures.

A version of IREP was developed to specifically address the workforce covered by EEOIPCA. This version, called NIOSH-IREP, is tailored to the risks and radiation exposures characteristic of nuclear weapons employees. NIOSH-IREP is used by DOL to calculate the probability of causation for each claim.

2.0 INTRODUCTION

The NIOSH-IREP computer code is a web-based program that estimates the probability that an employee's cancer was caused by his or her individual radiation dose. Personal information (e.g., birth year, year of cancer diagnosis, gender) and exposure information (e.g., exposure year, dose) may be entered manually or through the use of an input file. For application by the U.S. Department of Labor (DOL), the input file option is used to preset all personal information, exposure information, and system variables. These input file(s) are created by NIOSH for each individual claim and transmitted to DOL for processing.

The purpose of this user's guide is to provide DOL with a concise step-by-step guide to the use of NIOSH-IREP in processing energy employee compensation claims.

A glossary containing definitions of radiation terms and other frequently used terms related to NIOSH-IREP is included in Section 8.0 of this user's guide. Readers interested in a more thorough discussion of the science behind NIOSH-IREP are encouraged to review the Technical Documentation and similar documents posted on NIOSH's Division of Compensation Analysis and Support (DCAS) web site at www.cdc.gov/niosh/ocas.

A set of example input files have been prepared to be used in conjunction with this user's guide to demonstrate the operation of NIOSH-IREP. These input files may be downloaded from the DCAS website (http://www.cdc.gov/niosh/ocas/nioshirep.html). Section 9.0 describes the input files and provides pre-calculated solutions for each case.

3.0 DETERMINING PROBABILITY OF CAUSATION

STEP 1: Log onto NIOSH-IREP

NIOSH-IREP can be accessed through NIOSH's Division of Compensation Analysis and Support (DCAS) website at:

https://www.cdc.gov/niosh/ocas/nioshirep.html

Please scroll down and click the link under "Online Access" section

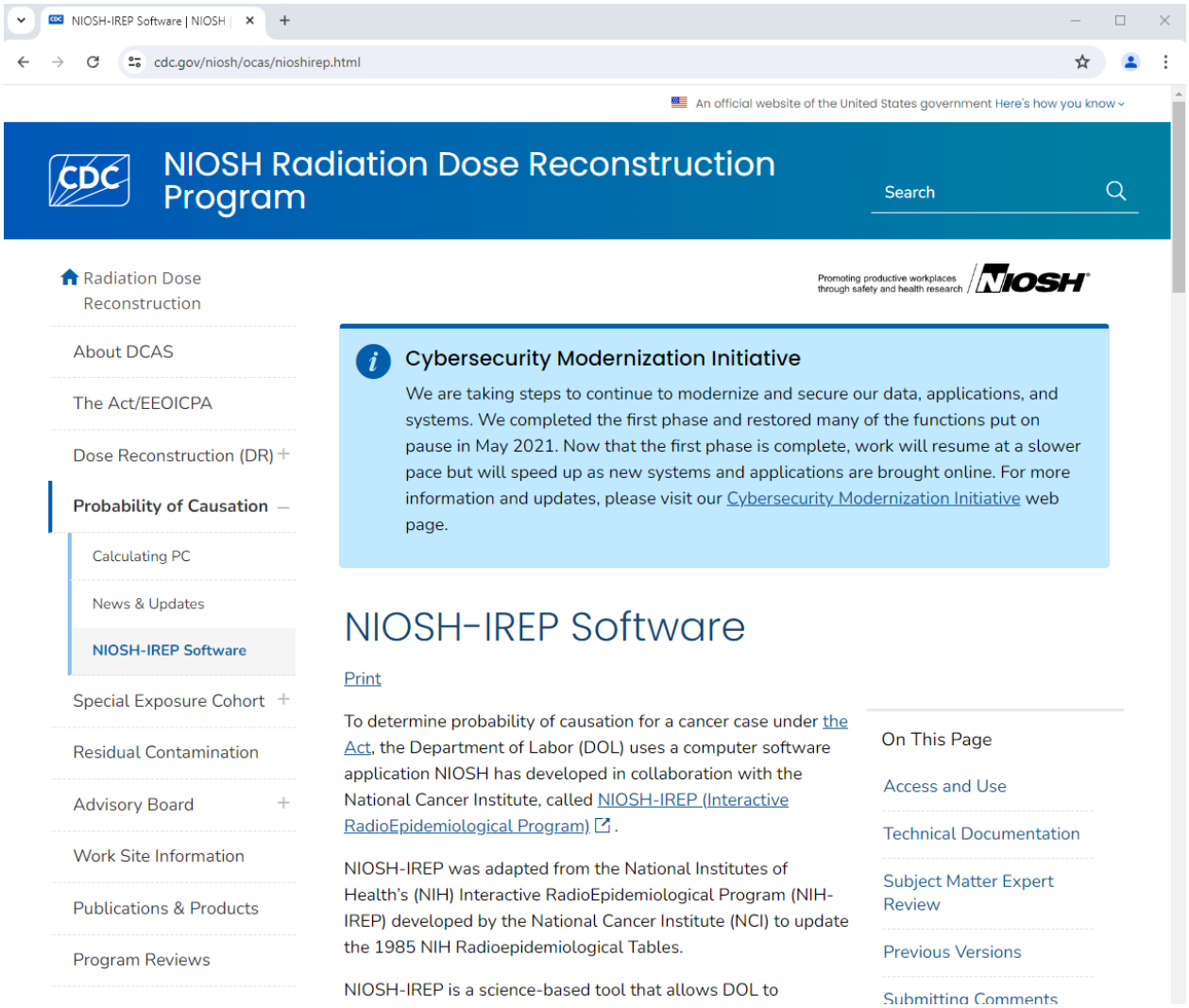


Figure 1. NIOSH web page containing the link to NIOSH-IREP Software

STEP 2: Start Program

On the initial log-in screen (Figure 2), select the option "To begin by using a NIOSH-provided input file" to start NIOSH-IREP.

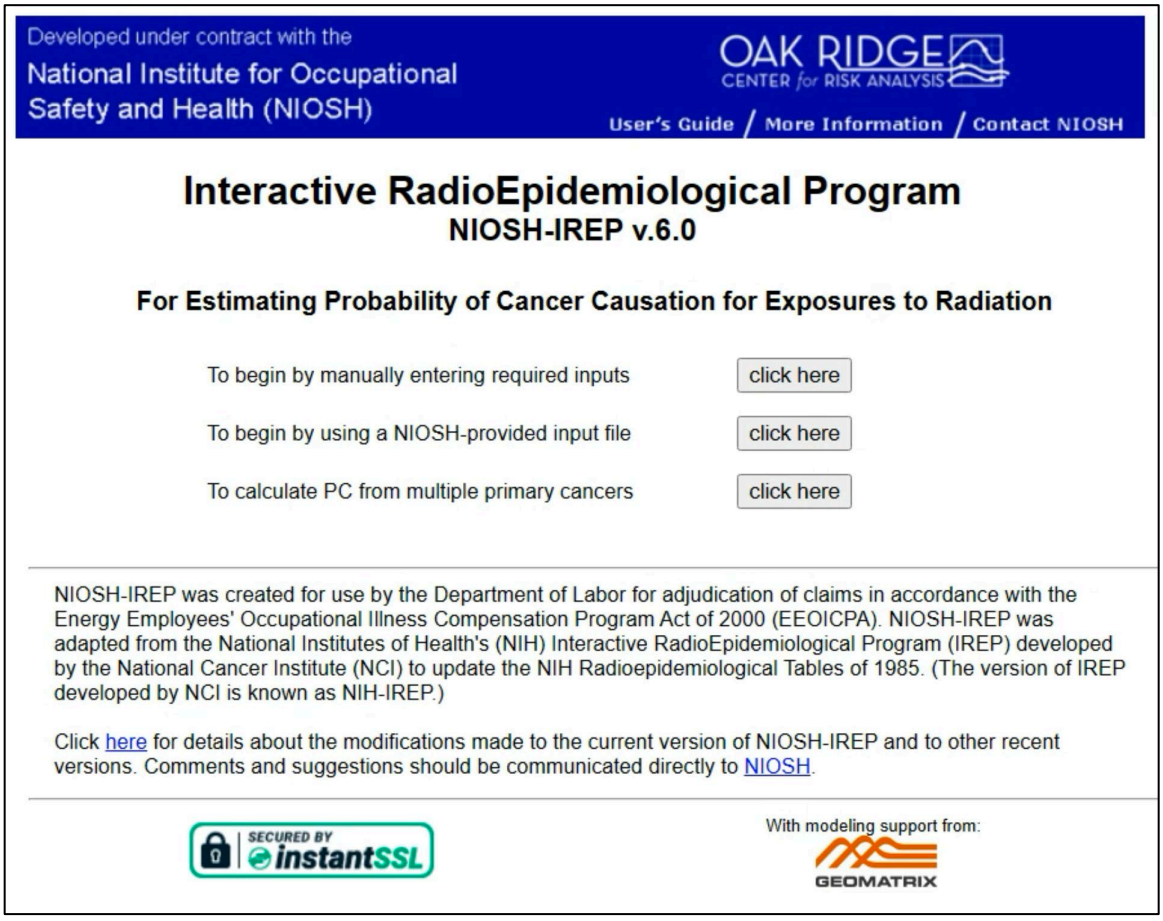


Figure 2. Initial log-in screen of the NIOSH-IREP computer program

NOTE: This screen allows a user to enter personal information (e.g., birth year, year of cancer diagnosis, gender) and exposure information (e.g., exposure year, dose) manually (click on top button) or through the use of an input file (middle button). The bottom button allows the user to access the multiple primary cancers calculator (Section 4.0).

As specified by 42 CFR Part 81 (Guidelines for Determining the Probability of Causation), DOL uses the data input file option to preset all personal information, exposure information, and system variables. This input file is created by NIOSH, as specified by 42 CFR Part 82 (Methods for Radiation Dose Reconstruction) and transmitted to DOL for processing.

STEP 3: Upload Claimant Input File

A. The first step of uploading a claimant input file is to identify where the file resides. Click the "Upload File" button on the screen shown in Figure 3.

B. Locate the input file in the "Choose file" dialog box (Figure 4). Once the input file is selected, click the "Open" button to upload it.

C. The file and path will appear on the screen (Figure 5). Click "Upload File."

D. A status message will appear, including the name of the uploaded file (Figure 6). Click "Continue" to populate the fields of the main input screen (as shown in Figure 7, next page) with the values saved in the input file.

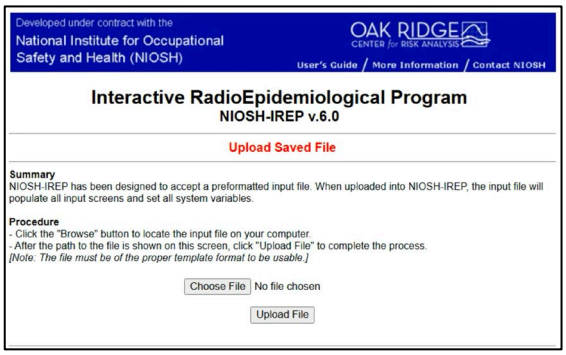


Figure 3. "Upload Saved File" screen

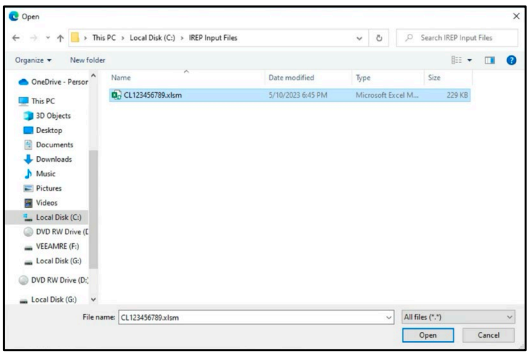


Figure 4. "Choose file" dialog box

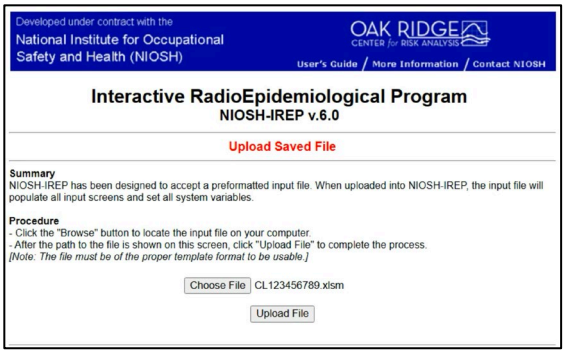


Figure 5. File appears in window

Figure 6. Success!

STEP 4: Perform Calculation

To calculate probability of causation, click the "Generate Results" button on the main input screen (Figure 7).

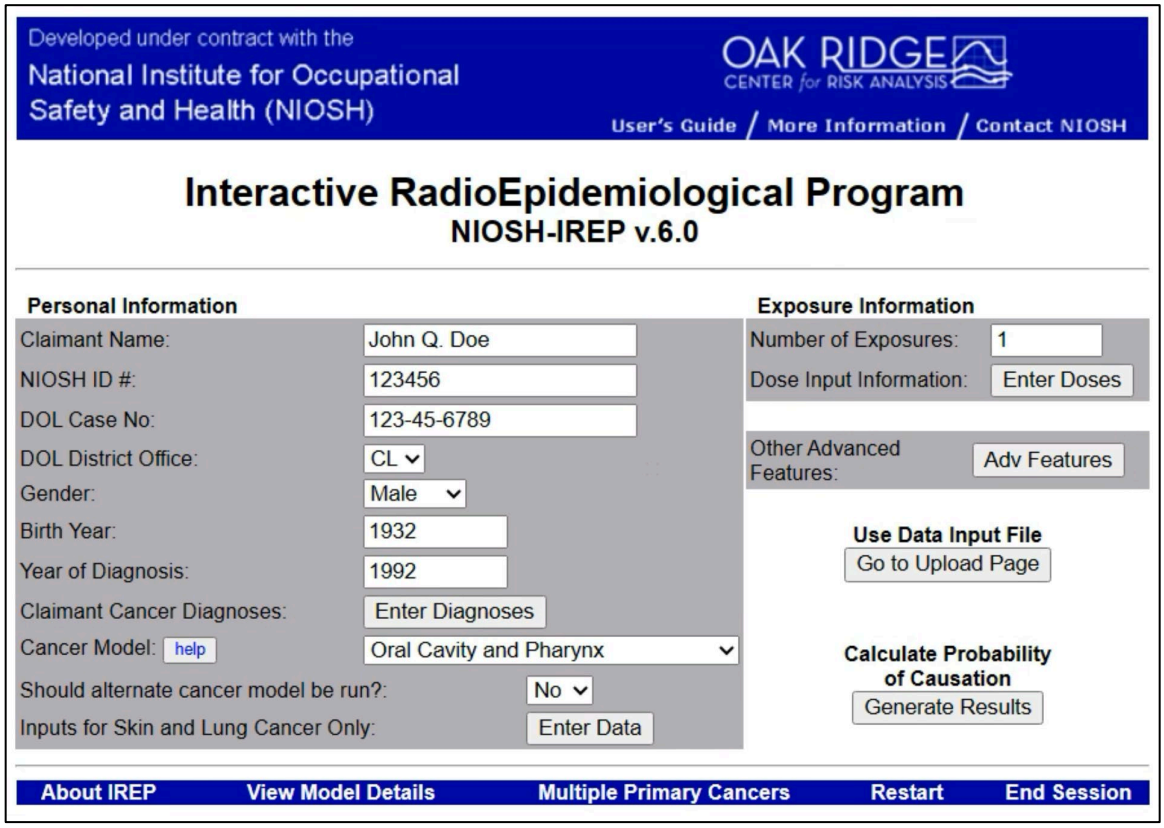


Figure 7. Main input screen

The claimant's information will be sent to the server that hosts NIOSH-IREP. The calculation will be performed in real-time, and the results will be returned in the form of a summary table suitable for printing and saving (Figure 8, next page).

Claimant Information Used In Probability of Causation Calculation:

Gender: Male
Race (skin cancer only): N/A
Birth Year: 1932
Year of Diagnosis: 1992
Cancer Model: Oral Cavity and Pharynx
Should alternate cancer model be run?: No
Smoking history (trachea, bronchus, or lung cancer only): N/A

NIOSH-IREP Assumptions and Settings:

User Defined Uncertainty Distribution: Lognormal(1,1)
Number of Iterations: 20000
Random Number Seed: 99

General Exposure Information:

#	Exp. Year	Organ Dose (cSv)	Exp. Rate	Radiation Type
1	1971	Lognormal (2, 2)	chronic	electrons E<15keV

Radon Exposure Information:

N/A (applies only to cases of Lung Cancer with Radon Exposures)

Probability of Causation (PC)

1st percentile	0.00 %
5th percentile	0.04 %
50th percentile	0.39 %
95th percentile	2.32 %
99th percentile	4.74 %

Figure 8. NIOSH-IREP Probability of Causation Results (Summary Report, truncated)

STEP 5: Print and Save Output Summary Report

To Print:

When the calculation is completed, the output summary report can be printed by right-clicking anywhere on the summary report and selecting the "Print" command in the pop-up menu.

To Save:

An electronic copy of the output summary report can be saved by right-clicking anywhere on the summary report and selecting the "Save As" command from the pop-up menu.

In the "Save Web Page" dialog window (Figure 9), enter the desired name of the file and select the location where the file is to be saved. Select "Webpage, complete (*,htm;*.html)" from the "Save as type" pull-down menu. Click "Save."

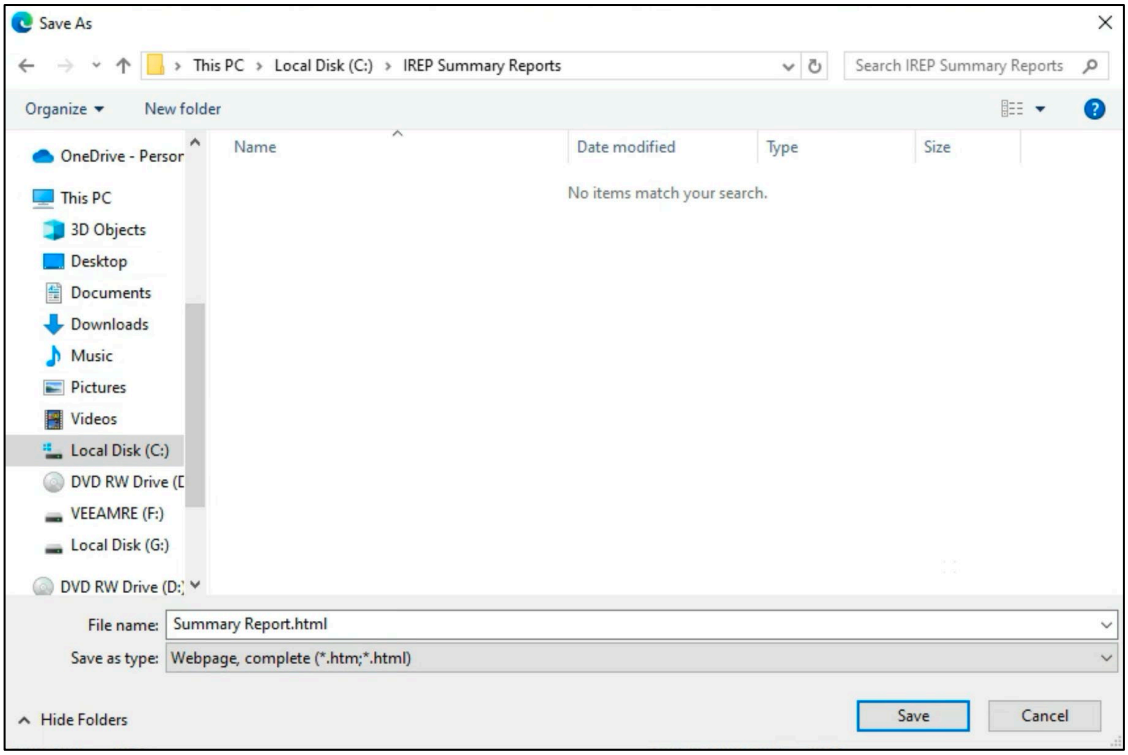


Figure 9. "Save Web Page" dialog window

4.0 MULTIPLE PRIMARY CANCERS

If a claimant is diagnosed with more than one primary cancer, NIOSH will provide an input file for each primary cancer. NIOSH-IREP should be run with each of the input files. Enter the results from each run into the "Multiple Primary Cancers" calculator. The Multiple Primary Cancers calculator is accessible from the initial log-in screen (Figure 10), by clicking the button located at the bottom of the main input screen (Figure 7), or by using the link at the bottom of the summary page.

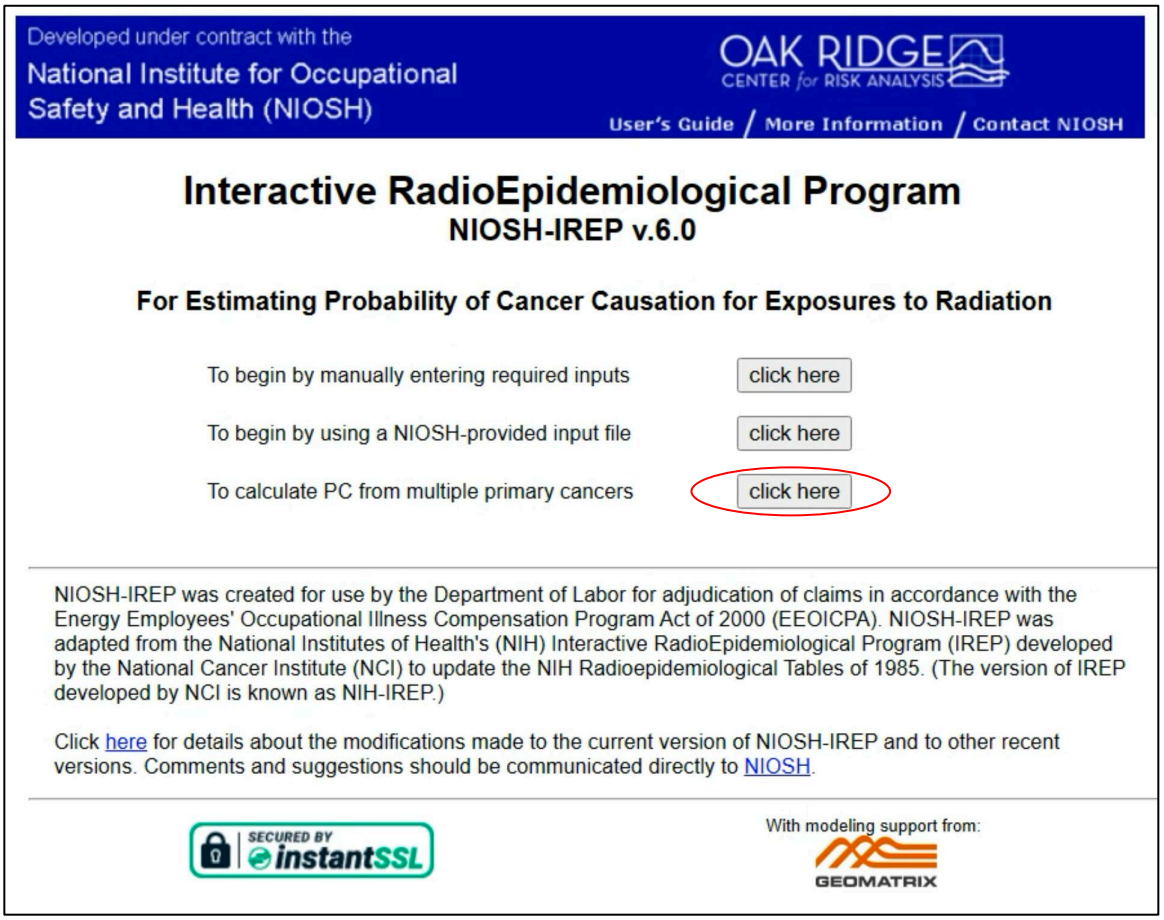


Figure 10. Initial Log-in Screen showing the "Multiple Primary Cancers" button

Multiple primary cancers (continued)

Follow the online instructions to estimate a claimant's total PC from two or more primary cancers (Figure 11).

[NOTE: As of June 2014, the capabilities of NIOSH-IREP were expanded to allow for the estimation of total PC from up to 240 primary cancers (previous limit was 120 primary cancers).]

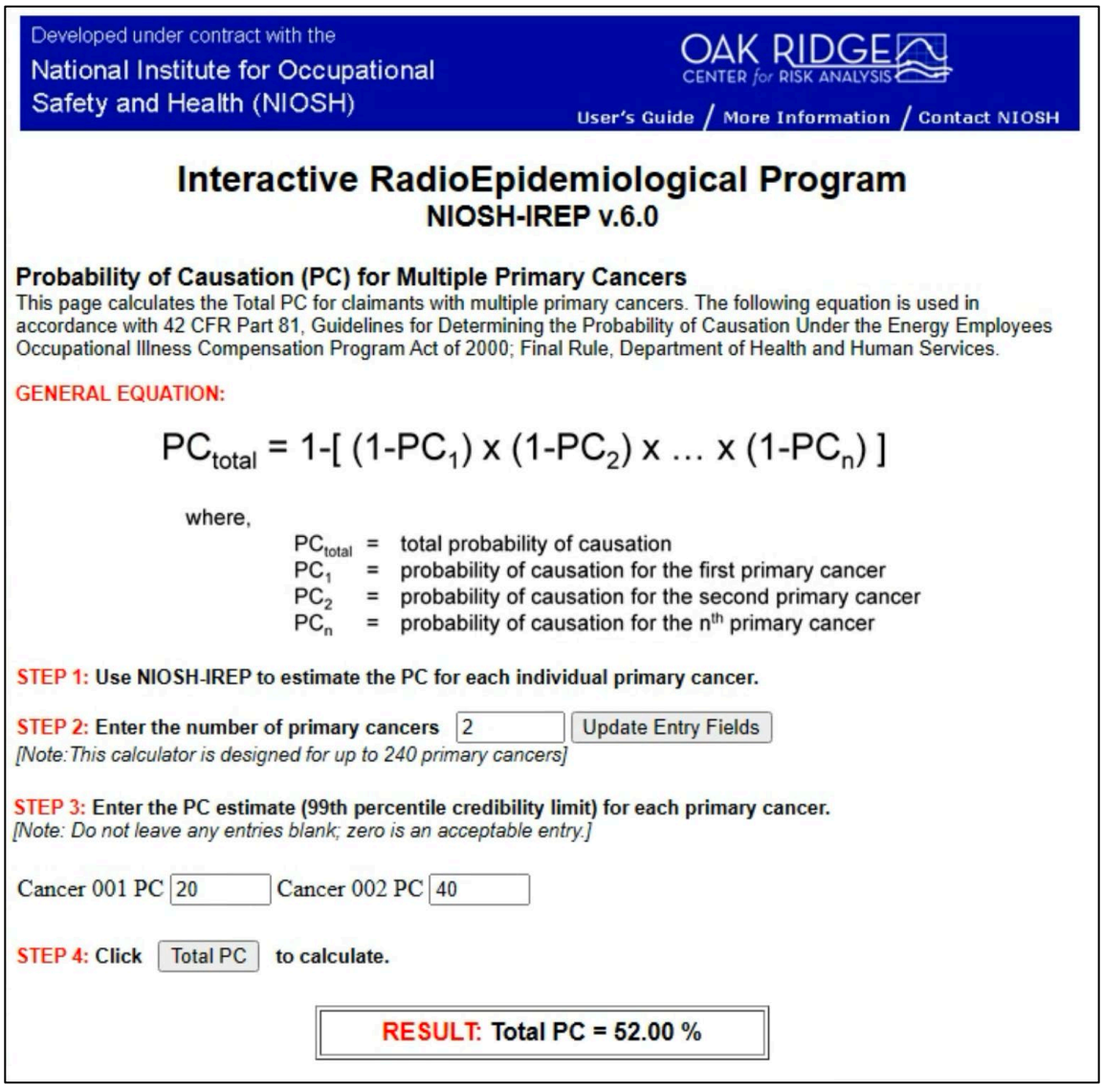


Figure 11. Multiple Primary Cancers screen

5.0 TECHNICAL ASSISTANCE

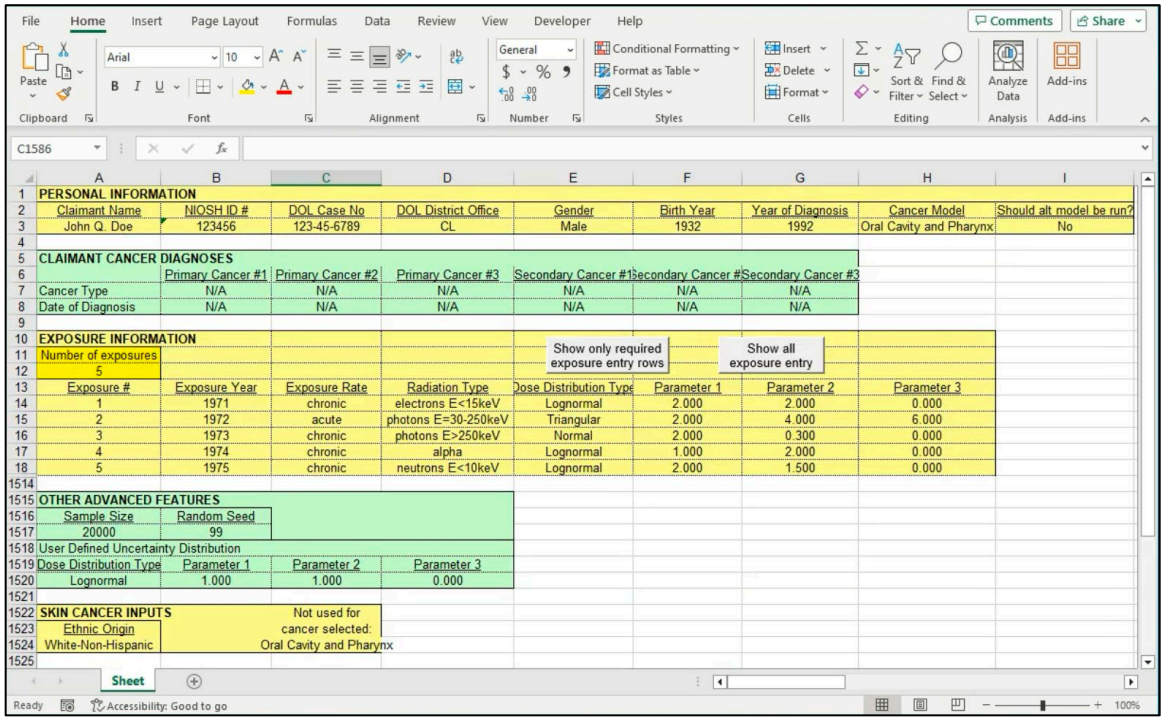
Technical information about NIOSH-IREP may be obtained, and comments about NIOSH-IREP may be made, by contacting the NIOSH Division of Compensation Analysis and Support (DCAS) by e-mail at dcas@cdc.gov, or by mail at:

National Institute for Occupational Safety and Health
Division of Compensation Analysis and Support
Robert A. Taft Laboratories, MS-C45
1090 Tusculum Avenue
Cincinnati, OH 45226

DOL staff requiring immediate technical assistance may call the DCAS office at (513) 533-6800.

6.0 INPUT FILE TEMPLATE

The input files produced by NIOSH are in Microsoft Excel format. These input files should not be modified by DOL. A screenshot of an example input file has been provided (Figure 12) for informational purposes.



	A	B	C	D	E	F	G	H	I
1	PERSONAL INFORMATION								
2	Claimant Name	NIOSH ID #	DOL Case No	DOL District Office	Gender	Birth Year	Year of Diagnosis	Cancer Model	Should alt model be run?
3	John Q. Doe	123456	123-45-6789	CL	Male	1932	1992	Oral Cavity and Pharynx	No
4									
5	CLAIMANT CANCER DIAGNOSES								
6		Primary Cancer #1	Primary Cancer #2	Primary Cancer #3	Secondary Cancer #1	Secondary Cancer #	Secondary Cancer #3		
7	Cancer Type	N/A	N/A	N/A	N/A	N/A	N/A		
8	Date of Diagnosis	N/A	N/A	N/A	N/A	N/A	N/A		
9									
10	EXPOSURE INFORMATION								
11	Number of exposures				Show only required exposure entry rows		Show all exposure entry		
12	5								
13	Exposure #	Exposure Year	Exposure Rate	Radiation Type	Dose Distribution Type	Parameter 1	Parameter 2	Parameter 3	
14	1	1971	chronic	electrons E<15keV	Lognormal	2.000	2.000	0.000	
15	2	1972	acute	photons E=30-250keV	Triangular	2.000	4.000	6.000	
16	3	1973	chronic	photons E>250keV	Normal	2.000	0.300	0.000	
17	4	1974	chronic	alpha	Lognormal	1.000	2.000	0.000	
18	5	1975	chronic	neutrons E<10keV	Lognormal	2.000	1.500	0.000	
1514									
1515	OTHER ADVANCED FEATURES								
1516	Sample Size	Random Seed							
1517	20000	99							
1518	User Defined Uncertainty Distribution								
1519	Dose Distribution Type	Parameter 1	Parameter 2	Parameter 3					
1520	Lognormal	1.000	1.000	0.000					
1521									
1522	SKIN CANCER INPUTS		Not used for						
1523	Ethnic Origin		cancer selected:						
1524	White-Non-Hispanic		Oral Cavity and Pharynx						
1525									

Figure 12. Screenshot of an example input file

7.0 PROCEDURE FOR CASES CLOSE TO 50%

When NIOSH-IREP was initially developed, claims in which the 99th percentile of probability of causation (PC_{99}) was equal to or greater than 45% but less than 50% using a default simulation sample size of 2,000 and a random seed value of 99 were resolved by increasing the sample size to 10,000 and rerunning the claim while choosing a new random seed value. The PC_{99} obtained from this run with a sample size of 10,000 determined the claim outcome, supplanting the initial PC value based on a sample size of 2,000.

To achieve greater statistical precision, a new procedure was developed and introduced on June 6, 2006 to replace the procedure described above. Each claim with a PC_{99} value falling between 45% and 52%, obtained using a sample size of 2,000, was processed by increasing the simulation sample size to 10,000, rerunning the claim in NIOSH-IREP 30 times with 30 new random seeds, and taking the average of the PC_{99} values from the 30 runs.

To further increase the statistical precision for claims very close to the compensation threshold of 50%, a new procedure (Figure 13) was developed and presented to the Advisory Board on Radiation and Worker Health on August 16, 2023. The new procedure was adopted and will replace the procedures described above.

New Methodology:

All claims are processed using a default sample size of 20,000 iterations. Claims in which the PC_{99} is greater than or equal to 45% and less than or equal to 52% when using a default sample size of 20,000 are processed by running NIOSH-IREP-EE 30 or 300 times with new random seed values. Sets of 300 runs will be used for enhanced precision when PC_{99} is greater than or equal to 49.5% and less than or equal to 50.5%.

NIOSH will provide DOL with dose reconstruction input files for claims with a single primary cancer or for claims with multiple primary cancers (see Section 4). DOL will process these files to adjudicate cases, which can be in one of the following categories.

A. Single Primary Cancer

(1) 30 additional IREP runs will be performed using a sample size of 20,000, and a new random seed value for each run. The average value (arithmetic mean) of the PC_{99} values from each of the 30 runs will determine the claim outcome, unless this average is between 49.5% and 50.5%.

(2) If the average of the PC_{99} values from 30 runs is between 49.5% and 50.5%, then the claim will be rerun 300 times, with a new set of random values. First, NIOSH will perform 300 IREP runs with 1,000 iterations; the IREP Predictive Tool will be used to determine and report the sample size needed to reach a precision of 0.1% for PC_{99} based on its 95% confidence interval. The claim will then be processed using 300 IREP runs (with the same set of 300 random seeds used in the previous step), and with the sample size suggested by the IREP Predictive Tool. If the sample size estimated by the IREP Predictive Tool is less than 20,000, then a minimum of 20,000 iterations will be used for the 300 IREP runs. The average of the PC_{99} values from the 300 runs will determine the claim outcome.

B. Multiple Primary Cancers

(1) For claims with more than one primary cancer in which the PC_{99} calculated from the "multiple primary" equation is equal to or greater than 45% but less than 52%, 30 runs will be performed for each primary cancer using a sample size of 20,000, and a new random seed value for each run. The arithmetic mean of the PC_{99} values from each of the 30 runs for each cancer will be entered into the multiple primary equation. The newly calculated combined PC_{99}, obtained based upon the arithmetic mean PC_{99} value of each cancer as entered into the multiple primary equation, will determine the claim outcome, unless the new combined PC_{99} is between 49.5% and 50.5%.

(2) If the combined PC_{99} from 30 runs is between 49.5% and 50.5%, the number of IREP runs will be increased to 300. The IREP Predictive Tool will be used by NIOSH to determine the sample size needed to reach a precision of 0.1% for the 95% confidence interval of PC_{99} of each cancer. The claim will be processed for each cancer using 300 additional IREP runs, with the sample size suggested by the IREP Predictive Tool. **The maximum value of all the sample sizes suggested by the IREP Predictive Tool for each cancer will be used as the new sample size for all cancers in the next rerun.** If this maximum value is less than 20,000, then 20,000 iterations will be used. The arithmetic mean of the PC_{99} values from the 300 runs for each cancer will then be entered into the multiple primary equation. The newly calculated PC_{99}, obtained based upon the arithmetic mean PC_{99} value of each cancer as entered into the multiple primary equation, will determine the claim outcome.

IREP Predictive Tool:

A predictive algorithm has been developed for determining the number of iterations required for claims where PC_{99} is very close to 50%. NIOSH will use this tool to determine an appropriate sample size which will be included in the dose reconstruction input file provided to DOL.

In a set of 300 IREP runs, the average of the PC_{99} values from the 300 runs has a 95% confidence interval with a length ($PC99_{upper}$ - $PC99_{lower}$) that decreases as a power function of the increasing number of iterations per run. That is, the precision of PC_{99} increases with increasing number of iterations per run.

Starting with results from 300 runs with 1,000 iterations and using the observed power function, the Predictive Tool estimates the number of iterations per run necessary to reach a 0.1% precision criterion for the 95% confidence interval of PC_{99} (i.e., $PC99_{upper}$ - $PC99_{lower} < 0.1\%$).

The IREP Predictive Tool is used only when a claim has a PC_{99} value that is between 49.5% and 50.5%.

If the number of iterations estimated by the IREP Predictive Tool is less than 20,000, then a minimum of 20,000 iterations will be used to run the 300 additional IREP runs, either for claims with a single primary cancer (A.2 above) or for claims with multiple primary cancers (B.2 above).

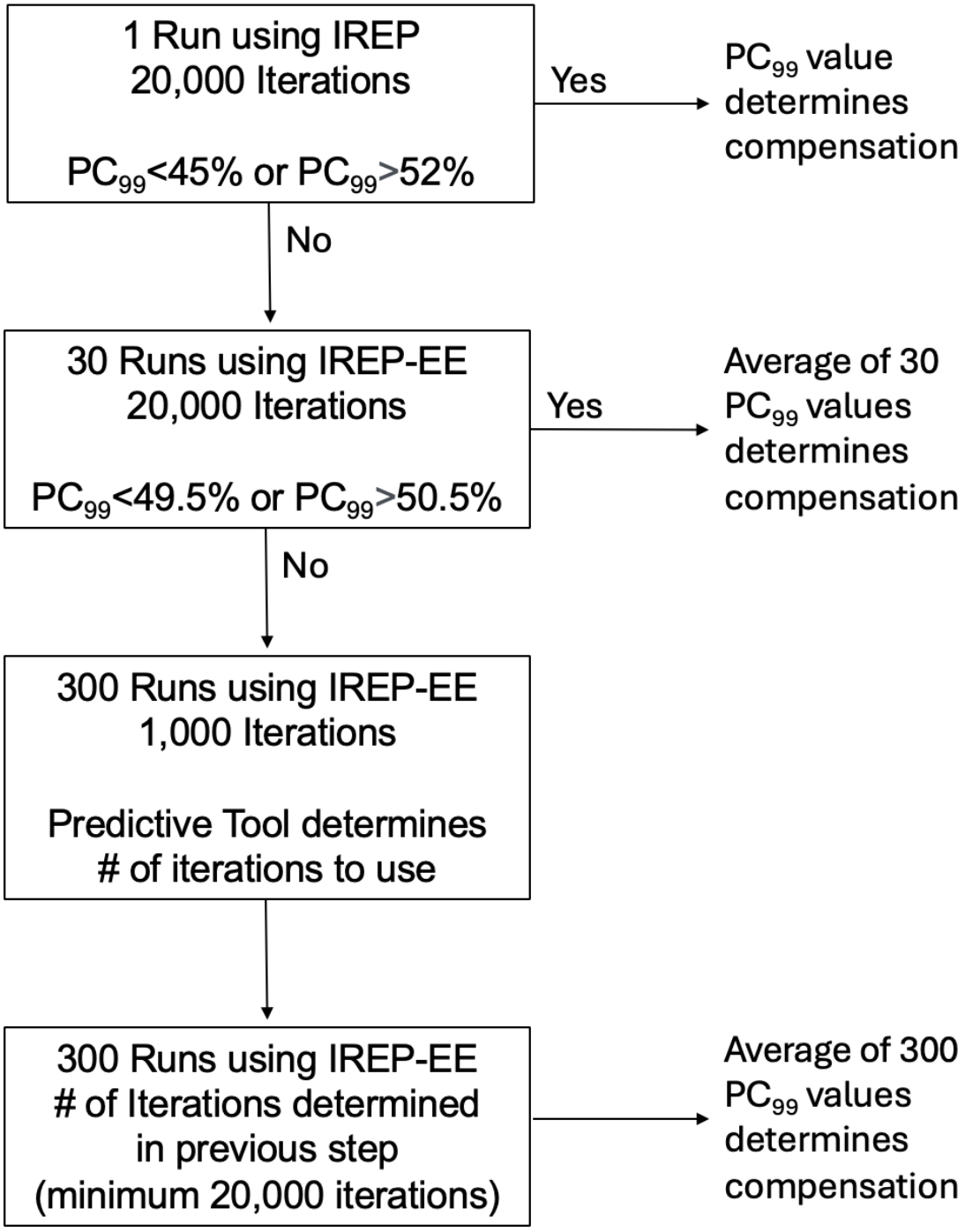


Figure 13. IREP calculation procedure

8.0 GLOSSARY[1]

Absorbed dose: The energy deposited by *ionizing radiation* per unit mass of tissue irradiated. It can be expressed in units of *gray (Gy)* or *rad*, where 1 Gy = 100 *rad*.

Activity: The rate of transformation (or disintegration or decay) of a radioactive material. It can be expressed in units of *becquerel (Bq)* or *curie (Ci)*.

Acute dose: A *radiation dose* received by a person over a short period of time (less than one day.) For purposes of cancer risk modeling, it has been suggested that a *dose* can be considered acute if it was delivered at a rate greater than 0.006 Gy per hour averaged over the first few hours.

Alpha particle: A particle emitted from a decay of certain heavy radionuclides. It has a short range and can be stopped by a sheet of paper or the outer dead layer of skin. Alpha particles constitute a health hazard only when alpha-emitting radionuclides are deposited in tissues following ingestion or inhalation.

Background radiation: Radiation emitted by natural sources such as cosmic radiation or radionuclides occurring naturally in soil, food, water or air.

Baseline cancer risk: The risk of cancer in the general population from causes other than exposure to the investigated agent (for example, the source of radiation.)

Becquerel (Bq): The unit of *activity* equal to one disintegration per second.

Beta particle: A particle emitted from a decay of certain radionuclides. It has a short range but can penetrate the dead layer of skin to produce a skin *dose*.

Carcinogen: Any substance or agent that can cause cancer.

Centi-sievert (cSv): An *equivalent dose* equal to 0.01 Sv or 1 *rem*.

Chronic dose: A *radiation dose* received by a person over a long period of time (more than one day.) For purposes of cancer risk modeling, it has been suggested that a *dose* can be considered chronic if it was delivered at a rate lower than 0.006 Gy per hour for more than one day.

Cohort: A group of individuals sharing one or more characteristics.

Confidence interval (CI): A range of values around a mean, proportion, or rate that serves as an estimate of *uncertainty*. The upper and lower values of a confidence interval are called the confidence limits.

Confounder (or confounding variable): In an epidemiologic study, a factor that is associated with both the exposure of interest (e.g., radiation) and the outcome of interest (e.g., cancer), and that distorts or masks the true effect of the exposure.

Covered employee: A current or former employee of DOE, a DOE contractor or subcontractor, or an atomic weapons employer, and for whom DOL has directed DCAS to perform a dose reconstruction.

Curie (Ci): A measure of the amount of *radioactivity* in a material. One curie is equal to 37 billion disintegrations per second.

DCAS: The Division of Compensation Analysis and Support, a division of *NIOSH* located in Cincinnati and created to fulfill *NIOSH's* responsibilities under *EEOICPA*.

[1] Words appearing in *italicized* text are also defined in the glossary.

Dose (or radiation dose): A general term representing either *absorbed dose* or *equivalent dose*.

Dose and dose-rate effectiveness factor (DDREF): A mathematical factor that takes into account that the response per unit *dose* at low *doses* and low *dose* rates may be different from the response per unit *dose* at high *doses* and high *dose* rates.

Dose reconstruction (DR): Research and analysis leading to a quantitative estimate of radiation exposure, particularly when radiation monitoring data are unavailable, incomplete, or unreliable.

Dose-response relationship: A relationship in which a change in the amount, intensity, or duration of an exposure is associated with either an increase or decrease in risk of a specified health outcome.

EEOICPA: The Energy Employees Occupational Illness Compensation Program Act of 2000, Public Law 106-398, as amended.

Electron volt (eV): The customary unit of energy for all *ionizing radiations*.

Epidemiology: The study of factors that affect health and disease in populations.

Equivalent dose: A measure of biological damage caused by exposure to radiation, expressed in units of *rem* or *sievert (Sv)*, where 1 Sv = 100 *rem*.

Excess relative risk (ERR): The risk due to exposure to radiation in excess of the baseline risk, divided by the baseline risk. ERR is the same as the *relative risk (RR)* minus one.

External dose: The *dose* from radiation sources located outside the body.

Gamma rays (or gamma radiation): Electromagnetic radiation emitted from a decay of certain radionuclides. It can be very penetrating, producing a *radiation dose* throughout the whole body.

Gray (Gy): The special name for the *SI* unit of *absorbed dose*. 1 Gy = 100 *rad*.

Health physics: The science of radiation protection to reduce or prevent radiation exposure. Health physicists at DCAS specialize in quantifying past radiation exposures (i.e., *dose reconstruction*) in order to evaluate their health effects.

Healthy worker effect: A phenomenon in which fewer deaths or illnesses (cancers, for example) are observed among workers in a given industry compared with the general population, even though the workers under study may be more exposed to hazardous substances (*ionizing radiation*, for example) than the general population. This counterintuitive effect is often attributed, in part, to the assumption that chronically ill or disabled persons are less likely to be employed than healthier persons. Thus, a *cohort* of workers – absent that less robust segment of the population – may be more resistant to disease than the population as a whole.

Internal dose: The *dose* from radioactive materials that have been absorbed, ingested, or inhaled into the body.

Inverse dose-rate effect: A phenomenon in which a given *dose* delivered chronically or in multiple fractions results in a greater biological response than the same *dose* delivered acutely.

Ionizing radiation: Particles or rays emitted from radioactive materials. If ionization is produced in a cell, the ions may damage the cell and the affected cells may become cancerous.

Milli-sievert (mSv): An *equivalent dose* equal to 0.001 *sievert (Sv)*. 1 *mSv* = 100 *mrem*

Missed dose: A *radiation dose* that was received by an individual, but that was not detected by monitoring methods nor recorded.

Monte Carlo simulation: A computerized method for estimating the statistical *uncertainty* of a *risk model*. Repeated samples are taken from special probability distribution functions and the *probability of causation (PC)* is calculated for each set of samples. The upper 99th percentile of the distribution of estimated PC values (*upper 99 percent credibility limit*) is used to determine eligibility for compensation under *EEOICPA*.

Neutron: An uncharged particle of radiation produced from certain nuclear reactions. It can be very penetrating, producing a *radiation dose* throughout the whole body.

NIOSH: The National Institute for Occupational Safety and Health, part of the Centers for Disease Control and Prevention, United States Department of Health and Human Services.

Odds ratio (OR): The ratio of the odds of disease among the exposed compared with the odds of disease among the unexposed. Under certain conditions, the odds ratio may be used as an estimate of the *relative risk*.

Organ dose: A general term representing either *absorbed dose* or *equivalent dose* received by a particular organ or tissue.

PC_{99}: 99th percentile of probability of causation.

Photon: Electromagnetic radiation emitted from one of several possible sources. Photons originating from radioactive decay are called gammas or *gamma rays*.

Predictive Tool: An algorithm developed to determine the number of iterations necessary to reach a 0.1% precision criterion for the 95% confidence interval of PC_{99}. This tool is used by NIOSH only for claims where the PC_{99} is very close to 50%.

Primary cancer: A cancer defined by the original organ site at which the cancer occurred, prior to any spread (metastasis) to other sites in the body.

Probability of causation (PC or PoC): The probability or likelihood that a cancer was caused by radiation exposure incurred by a *covered employee* while in the performance of duty. A PC of 50% or greater means that the claimant's cancer was, as least as likely as not, induced by occupational radiation exposure.

Rad: A unit of *absorbed dose*. 100 rad equals one *gray* (1 Gy).

Radiation dose: See *dose*.

Radiation effectiveness factor (REF): A mathematical factor, similar to *relative biological effectiveness (RBE)*, used to account for the fact that different types of radiation are more effective at producing an outcome (such as cancer) than others.

Radioactivity: The process or characteristic of an unstable atomic nucleus to spontaneously transform with the emission of energy in the form of radiation, such as *alpha particles*, *beta particles*, and *photons*. The term may also refer to radioactive materials.

Radioepidemiological Tables: Tables that allow computation of the *probability of causation (PC)* for various cancers associated with a defined exposure to radiation, after accounting for factors such as gender, age at exposure, age at diagnosis, and *time since exposure (TSE)*.

Radiogenic: Capable of being caused by exposure to *ionizing radiation*. Most types of cancers are considered to be radiogenic.

Radon: A radioactive noble-gas element. Radon constitutes a health hazard, primarily to the lungs, when it is released into the air and its decay products are inhaled.

Random seed value: The first number selected in a sequence of random numbers. A given seed value will produce the same sequence of random numbers every time a *Monte Carlo simulation* is run in *NIOSH*-IREP using the same *simulation sample size*.

Relative biological effectiveness (RBE): A mathematical factor used to account for the fact that different types of radiation are more effective at producing an outcome (such as cancer) than others.

Relative risk (RR): The ratio of disease incidence (or mortality) in an exposed population to that in an unexposed population. A relative risk of "1" means there is no association between exposure and disease.

Rem: A unit of measure for expressing *equivalent dose*. One rem is equal to 1 *centi-sievert (cSv)* or 0.01 *sievert (Sv)*.

Risk coefficient: A general term referring to the coefficient of the *dose-response relationship*. In particular, if the dose-response is linear, the risk coefficient is the slope of the dose-response, and it represents the risk of cancer per unit *dose* received by the exposed individual.

Risk model: A mathematical model based on the *dose-response relationship* determined for a given cancer type, used to estimate the *probability of causation (PC)* using information on *radiation dose* and personal data.

SEC: Special Exposure *Cohort*.

Secondary cancer: A cancer that has spread (metastasized) from its site of origin (the primary site) to another part of the body.

SI: The International System of Units

Sievert (Sv): A unit of measure for expressing *equivalent dose*. One sievert (1 Sv) is equal to 100 *rem*.

Simulation sample size: The number of *Monte Carlo simulations* used in each NIOSH-IREP run. The current default simulation sample size in NIOSH-IREP is 20,000.

Threshold dose: Radiation dose below which there is no measurable biological effect.

Time since exposure (TSE): The number of years between radiation exposure and diagnosis of cancer.

Uncertainty: A term used to describe the lack of precision and accuracy of a given estimate, the extent of which depends upon the amount and quality of the evidence or data available.

Uncertainty distribution: A range of discrete or continuous values arrayed to encompass, with high confidence, the true but unknown values of a given quantity or parameter.

Upper 99 percent credibility limit: The 99^{th} percentile of the range of values in an *uncertainty distribution*. The *uncertainty distribution* of the *probability of causation (PC)* is first estimated, and the upper 99^{th} percentile of this distribution is compared to the decision criterion (a PC of 50%) to determine eligibility for compensation.

Working Level: A unit of measure describing the level of exposure to radioactive *radon*.

Working Level Month (WLM): A unit of measure describing a cumulative exposure to one *working level* of *radon* for one working month (170 hours.)

X rays: A type of electromagnetic radiation (*photon*) similar to *gamma radiation* but generally less energetic.

9.0 DESCRIPTION OF EXAMPLE INPUT FILES

Example input files are available online to aid Department of Labor (DOL) staff in learning to use NIOSH-IREP. A description of each file is included below.

Example 1 is included to illustrate how PC is affected by the claimant's age at the time of exposure.

Example 1a

Filename:	irepug1a.xlsm
Gender:	Female
Age at exposure:	20
Age at diagnosis:	50
Cancer type:	Liver
No. of exposures:	1
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E=30-250 keV)
Dose:	10 cSv (constant)
Sample Size:	20,000 iterations
Random Seed:	99

Example 1a solution

Percentile	Probability of Causation (%)
1st	1.66
5th	3.10
50th	13.96
95th	42.41
99th	56.89

Example 1b

Filename:	irepug1b.xlsm
Gender:	Female
Age at exposure:	40
Age at diagnosis:	50
Cancer type:	Liver
No. of exposures:	1
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E=30-250 keV)
Dose:	10 cSv (constant)
Sample Size:	20,000 iterations
Random Seed:	99

Example 1b solution

Percentile	Probability of Causation (%)
1st	0.89
5th	1.70
50th	8.18
95th	29.26
99th	43.12

Example 2 is included to illustrate how PC is affected by smoking history.

Example 2a

Filename:	irepug2a.xlsm
Gender:	Male
Age at exposure:	20
Age at diagnosis:	50
Cancer type:	Lung
Smoking history:	Never smoked
No. of exposures:	1
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E=30-250 keV)
Dose:	Lognormal (geometric mean=15 cSv; geometric sd=2.0)
Sample Size:	20,000 iterations
Random Seed:	99

Example 2a solution

Percentile	Probability of Causation (%)
1st	0.59
5th	1.42
50th	9.24
95th	40.85
99th	59.94

Example 2b

Filename:	irepug2b.xlsm
Gender:	Male
Age at exposure:	20
Age at diagnosis:	50
Cancer type:	Lung
Smoking history:	Smoker (20-39 cigarettes/day)
No. of exposures:	1
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E=30-250 keV)
Dose:	Lognormal (geometric mean=15 cSv; geometric sd=2.0)
Sample Size:	20,000 iterations
Random Seed:	99

Example 2b solution

Percentile	Probability of Causation (%)
1st	0.07
5th	0.15
50th	1.93
95th	22.02
99th	39.42

Example 3 is included to show how multiple exposures are handled in NIOSH-IREP.

Example 3

Filename:	irepug3.xlsm
Gender:	Male
Age at exposure:	25, 26, 27, 28, 29
Age at diagnosis:	60
Cancer type:	Colon
No. of exposures:	5
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E=30-250 keV)
Dose:	Lognormal (geometric mean=5 cSv, geometric sd=1.7)
Sample Size:	20,000 iterations
Random Seed:	99

Example 3 solution

Percentile	Probability of Causation (%)
1st	1.06
5th	3.20
50th	14.13
95th	40.17
99th	53.17

Example 4 demonstrates a calculation for a claimant with 3 radon and 3 other radiation exposures.

Example 4

Filename:	irepug4.xlsm
Gender:	Male
Age at exposure:	20, 21, 22
Age at diagnosis:	50
Cancer type:	Lung
Smoking history:	Never smoked
No. of exposures:	3
Exposure rate:	chronic
Radiation type:	high-energy gamma rays (photons; E>250 keV)
Dose:	Triangular (min=2, mode=4, max=8)
Radon exposure:	Lognormal (geometric mean=0.4 WLM, geometric sd=2)
Sample Size:	20,000 iterations
Random Seed:	99

Example 4 solution

Percentile	Probability of Causation (%)
1st	3.90
5th	6.14
50th	16.79
95th	42.88
99th	57.78