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**COMMENTS FOR THE MEETING OF THE
VETERANS ADVISORY BOARD ON DOSE RECONSTRUCTION (VBDR)
March 7, 2007
Las Vegas NV**

**Briefing on:
The Use of the Interactive Radioepidemiological Program (IREP)
by the
Department of Veterans Affairs (VA)**

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Introduction

As some of the VBDR members know, I am a physician in the Office of Public Health and Environmental Hazards (OPHEH), the office within the Veterans Health Administration (VHA) of the Department of Veterans Affairs (VA) which is responsible for providing medical opinions to assist in the adjudication of some radiation compensation claims, when requested.

-- **SLIDE 1** is an organizational diagram of the VA and where our office is located administratively.

Our office does not make actual adjudication decisions, which are the responsibility of the Veterans Benefits Administration (VBA).

-- **SLIDE 2** is a diagram of how a non-presumptive radiation claim from an Atomic Veteran is adjudicated by the VA including the role of our office.

I should mention that our office provides medical opinions for compensation claims related to other types of radiation exposure in addition to claims from Atomic Veterans. These include claims relating to "occupational" exposures, (such as service in the nuclear navy, duties involving nuclear weapons, doses received as military X-ray and dental techs, etc.), "medical" exposures (such as veterans who received X-ray treatments for acne in service, and those receiving nasopharyngeal (NP) radium treatments for aero-otitis) and "environmental" exposures (such as veterans stationed in Germany at the time of the Chernobyl nuclear accident or performing duties near Hanford).

Our office also is involved in other activities relating to radiation including the VA's Ionizing Radiation Registry (IRR) examination program, the Depleted Uranium (DU) screening and surveillance programs, and emergency preparedness.

Role of the VA in development of the IREP

Prior to the development of the Interactive Radioepidemiological Program (IREP), the VA utilized screening doses developed by the Committee on Interagency Radiation Research and Policy Coordination (CIRRPC) to evaluate radiation compensation claims, when applicable. The CIRRPC screening doses were published in 1988 and were based on the original 1985 National Institutes of Health (NIH) Radioepidemiological Tables.

When I became involved with VA radiation compensation claims around 1994, our office submitted a request to CIRRPC to update and expand the screening doses to reflect more current scientific information and address additional diseases that the VA recognized as potentially radiogenic. We were informed by CIRRPC that new screening doses could not be provided until the radioepidemiological tables themselves were updated. A request therefore was submitted to the Director of the NIH referencing the requirement in the Orphan Drug Act for updating the tables. Subsequently CIRRPC was dissolved.

In follow-up to a recommendation in the 1995 final report of the presidential Advisory Committee on Human Radiation Experiments (ACHRE), the VA and HHS agreed to jointly fund a project to revise the original radioepidemiological tables with HHS being responsible for the scientific content. This project resulted in development of the original National Cancer Institute (NCI) version of the IREP.

Subsequently a slightly modified version of the IREP was developed for use by the National Institute for Occupational Safety and Health (NIOSH) to evaluate compensation claims from some workers at nuclear weapons facilities.

After a period of using the IREP in parallel with the CIRRPC screening doses, the VA began using the IREP exclusively in April 2005 as recommended by the Veterans Advisory Committee on Environmental Hazards (VACEH).

Use of the IREP by the VA

General

Our office currently uses the NIOSH version of the IREP computer software, available on the Internet at http://198.144.166.6/irep_niosh/, for most radiation medical opinions. In general, our office has followed NIOSH guidance as contained in its on-line "help" screens, User's Guide, and Technical Documentation report, with a few differences. Our office utilizes the 99th

percentile value for the probability of causation calculated by the NIOSH IREP software.

Multiple malignancies and/or other diseases

For claims involving multiple malignancies and/or other disorders, each disease is considered individually, and the NIOSH IREP Multiple Primary Cancers calculator has not been used for medical opinions.

Cancer models used

For chronic lymphocytic leukemia (CLL) [ICD-9 code 204.1] the NIOSH IREP cancer model for lymphoma and myeloma is used since this disease is not included with other forms of lymphoid leukemia in the NIOSH IREP and since CLL may be considered to be a form of non-Hodgkin's lymphoma (e.g., in the NCI PDQ system).

Since the term myelodysplastic syndrome may be used to include some leukemic conditions as well as preleukemic disorders, our office has used NIOSH IREP cancer models for leukemia in addition to using the cancer model for lymphoma and myeloma in accordance with the NIOSH IREP guidance.

Similarly, for myelofibrosis with myeloid metaplasia, our office has used NIOSH IREP leukemia cancer models in addition to using the NIOSH IREP cancer model for lymphoma and myeloma.

For cases of hairy cell leukemia, our office has used the NIOSH IREP cancer models both for leukemia and lymphoma and myeloma, since this disorder sometimes is included with both groups of disorders.

In some other cases more than one cancer model also may be used such as a malignant schwannoma, a neoplasm of connective-tissue origin, involving the central nervous system.

For carcinoma in situ of the skin, our office has used the cancer model corresponding to the specific pathology of the veteran's neoplasm.

Entry of radiation doses

According to VA regulations relating to ionizing radiation claims, when a range of dose estimates are provided, exposure at the highest level of the dose range will be presumed [3.311 (a)].

Therefore upper-bounds or "worse-case" doses reported by the Defense Threat Reduction Agency (DTRA) are utilized for cases involving Atomic Veterans.

Radiation doses are entered into the NIOSH IREP as "constant values" [rather than as probability distributions].

-- **SLIDE 3** shows the NIOSH IREP settings that our office currently uses for most Atomic Veteran cases.

External doses

External gamma doses are entered as acute photon of $E > 250$ keV

External neutron doses are entered as chronic neutron of $E = 0.1-2$ MeV

External beta doses are entered as acute electron of $E > 15$ keV

Combined external beta/gamma doses (e.g., skin doses) are entered as external gamma or external beta depending on the predominant emitter.

Internal doses

Internal gamma doses are entered as chronic photon of $E > 250$ keV

Internal beta doses are entered as chronic electron of $E > 15$ keV

Internal alpha doses are entered as chronic alpha

Combined internal beta/gamma dose are entered as chronic photon $E > 250$ keV or chronic electron $E > 15$ keV

Internal doses with radiation types not specified by DTRA have been entered as chronic photon of $E > 250$ keV

Combined external-internal doses (e.g., some prostate cancer cases)

In such cases, the IREP were run twice entering dose as all external and all internal

Doses received in more than one year of exposure (e.g., total doses reported for tests involving more than one calendar year or participation in more than 1 test series) –Total doses are entered in the earliest year of exposure or multiple computer runs are performed entering the total doses for each exposure year.

Year of diagnosis: If there are inconsistencies in the medical record regarding year of diagnosis, the NIOSH IREP software is run for each year.

Additional calculations: If the initial probability of causation (PC) value is 45 % or more but less than 50%, 30 additional computer runs are performed. It is then determined whether the average PC value of these additional runs is at least 50% or not.

--**SLIDES 4 thru 7** show a sample NIOSH IREP computer run for an imaginary veteran born in 1926, who participated in the CROSSROADS test in 1946, and was diagnosed with prostate cancer in 1966, using DTRA “worse case” doses.

Estimating the likelihood that ionizing radiation was responsible for the claimed condition

VA regulations mandate consideration of a number of factors in determining whether a veteran’s disease resulted from exposure to ionizing radiation in service [3.311(e)].

These include:

- Probable dose

- Relative sensitivity of the involved tissue to radiation induction of the specific pathology

- Gender and pertinent family history

- Age at exposure

- Time lapse between exposure and onset of the disease, and

- Extent to which exposure to radiation or other carcinogens outside of service may have contributed to the development of the disease

Some of these factors are incorporated into the NIOSH IREP software.

As I mentioned previously, upper 99th percentile values for the probability of causation calculated by the NIOSH IREP are utilized.

When multiple cancer models are used in accordance with the NIOSH IREP guidance (such as when the primary site of the cancer was unknown), the specific pathology of the veteran’s neoplasm is considered to determine which probability of causation values are relevant.

Other factors are considered, as appropriate, along with the NIOSH IREP probability of causation results when formulating the medical opinion.

Documentation and Communication of IREP results

Hard copies of the NIOSH IREP Summary Reports are returned with our office’s medical opinions.

Summaries of our office's radiation medical opinions including the NIOSH IREP 50th and 99th percentile values for the probability of causation are provided to the Veterans Advisory Committee on Environmental Hazards (VACEH).

Copies of summaries also have been provided to a member of the VBDR, Dr. John Lathrop.

Conditions not included in IREP

It should be noted that not all conditions are included in the IREP. For instance, benign neoplasms, and deterministic effects of radiation are not addressed.

For compensation cases claiming disorders not covered by IREP, our office uses sources such as the National Research Council (NRC) BEIR (Biological Effects of Ionizing Radiation) reports, the Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profile for Ionizing Radiation, major textbooks, and key scientific papers to formulate medical opinions.

Summary of medical opinions

In the summary covering the period 6/14/06-10/13/06 submitted to the VACEH prior to its November 2006 meeting, our office provided medical opinions on 162 radiation cases, 111 of which involved Atomic Veterans.

The NIOSH IREP was applicable to 104 of the 111 cases (94 %) involving Atomic Veterans. Examples of disorders of Atomic Veterans for which the IREP could not be used included cataracts and non-malignant thyroid nodular disease.

Favorable medical opinions were provided on 20 cases involving Atomic Veterans all for skin cancer.

This represents 18 % favorable opinions based on all 111 cases from Atomic Veterans and 41 % favorable opinions based on 49 cases involving Atomic Veterans involving skin cancers.

Use of screening doses for "expedited" skin and prostate cancer cases

Beginning last year, the DTRA has reported "expedited" "worse-case" "generic" doses for hundreds of skin and prostate cancer claims cases from Atomic Veterans.

To facilitate review, screening doses based on the NIOSH IREP have been used by our office to evaluate some of these cases. Also, to permit more timely adjudication, our office has provided instructions so that VBA staff can utilize these screening doses.

Our office will continue to use the NIOSH IREP software to evaluate individual cases when necessary.

Acknowledgements

I would like to acknowledge staff at SENES [Specialists in Energy, Nuclear, and Environmental Sciences] Oak Ridge, Inc., the contractor that developed the IREP software, as well as staff at the NCI, DTRA, and NIOSH who have assisted our office in using the IREP software.

Questions and recommendations

I would be happy to try to answer any questions regarding our office's use of the IREP.

Our office would appreciate feedback and recommendations from the VBDR regarding use of the IREP or on other issues.

Thank you.

References

Committee on Interagency Radiation Research and Policy Coordination [CIRRPC], Science Panel Report Number 6, Use of Probability of Causation by the Veterans Administration in the Adjudication of Claims of Injury Due to Exposure to Ionizing Radiation, 1988

Defense Threat Reduction Agency [DTRA], Expedited Process for Radiation Dose Assessment for Skin Cancer in Veterans' Compensation Claims, November 27, 2006, (Document for official use only)

Kocher, D.C., and Apostoaei, A.I., Screening Doses for Induction of Cancers Calculated with Interactive Radioepidemiological Program (IREP), Report to Defense Threat Reduction Agency, Revision 2, May 2006 (Document for official use only)

National Institute for Occupational Safety and Health [NIOSH] Office of Compensation Analysis and Support, NIOSH-Interactive RadioEpidemiological Program (NIOSH-IREP) Technical Documentation Final Report, June 18, 2002

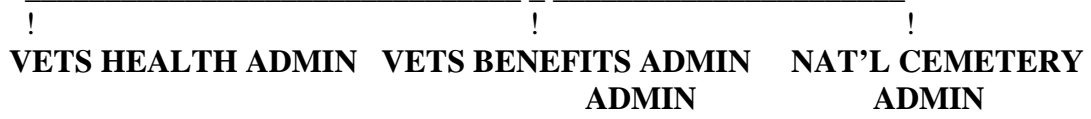
Report of the National Institute of Health Ad Hoc Working Group to Develop Radioepidemiological Tables, 1985, NIH Publication No. 85-2748

Report of the NCI-CDC Working Group to Revise the 1985 NIH Radioepidemiological Tables, 2003, NIH Publication No. 03-5387

SLIDE 1

VA SECRETARY

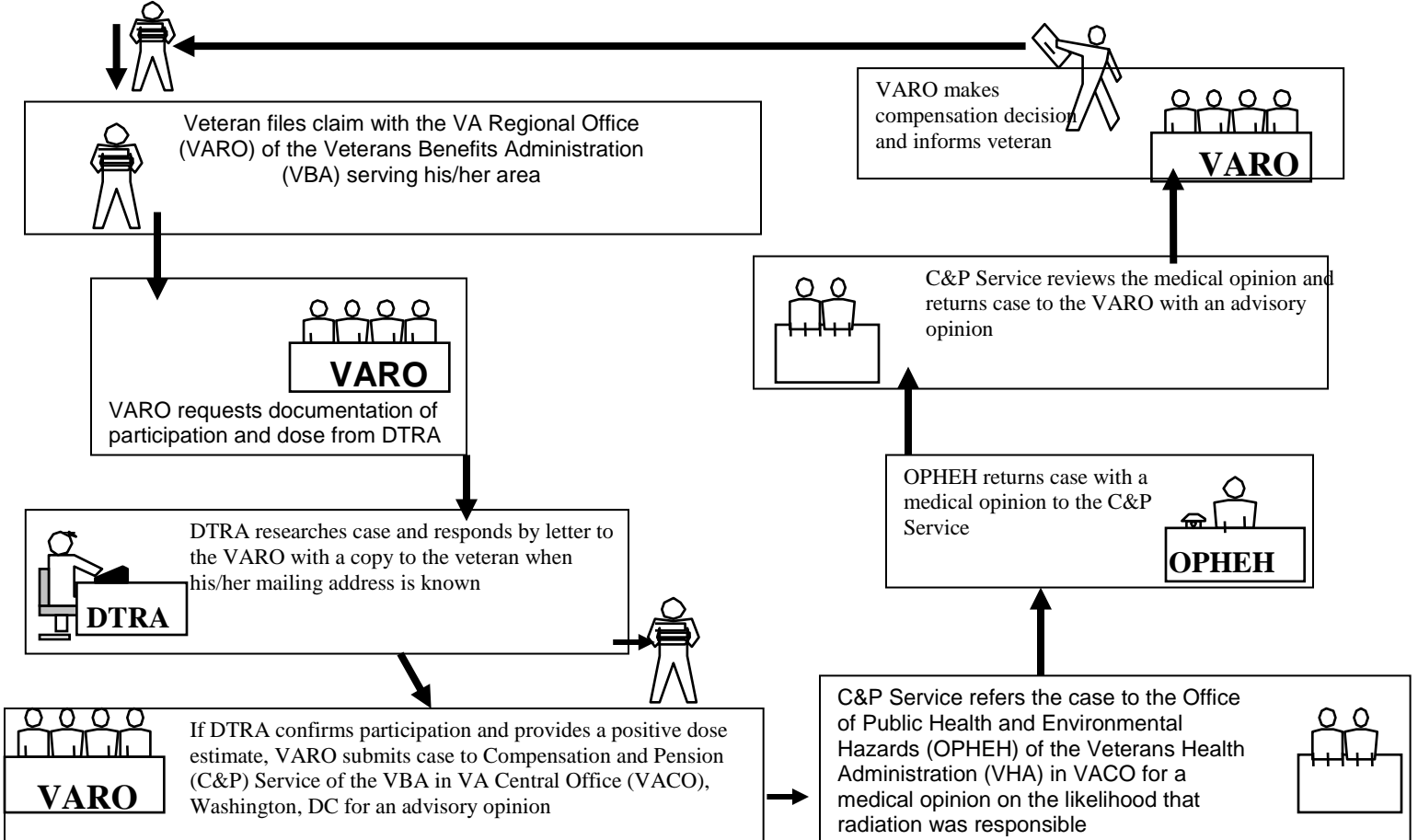
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SLIDE 2

FLOW DIAGRAM FOR ADJUDICATION OF A VA RADIATION CLAIM FROM AN "ATOMIC VETERAN" FOR A "NON-PRESUMPTIVE" DISORDER



SLIDE 3

**NIOSH IREP SETTINGS CURRENTLY USED FOR MOST ATOMIC VETERAN
CASES****DTRA Upper-bounds
Doses reported****NIOSH IREP Settings Used
(all doses entered as "constant values")**

External gamma

Acute photon E > 250 keV

External neutron

Chronic neutron E 0.1-2 MeV

External beta/gamma
(e.g., for skin)Acute electrons E > 15 keV or
Acute photon E > 250 keV

Internal alpha

Chronic alpha

Internal beta/gamma

Chronic photon E > 250 keV or
Chronic electron E > 15 keV**Sources: NIOSH IREP Technical Documentation Final Report, 6/18/02 and
"on-line" help screens**

SLIDE 4

Developed under contract with the
National Institute for Occupational
Safety and Health (NIOSH)



User's Guide / More Information / Contact NIOSH

Interactive RadioEpidemiological Program NIOSH-IREP v.5.5.1

Personal Information

Claimant Name:	<input type="text" value="John Q. Doe"/>
NIOSH ID #:	<input type="text" value="123456"/>
Claimant SSN:	<input type="text" value="123-45-6789"/>
DOL District Office:	<input type="text" value="CL"/> ▼
Gender:	<input type="text" value="Male"/> ▼
Birth Year:	<input type="text" value="1926"/>
Year of Diagnosis:	<input type="text" value="1966"/>
Claimant Cancer Diagnoses:	<input type="text" value="Enter Diagnoses"/>
Cancer Model* (ICD-9 code):	<input type="text" value="All Male Genitalia (185-187)"/> ▼
Should alternate cancer model be run?:	<input type="text" value="No"/> ▼
Inputs for Skin and Lung Cancer Only:	<input type="text" value="Enter Data"/>

Exposure Information

Number of Exposures:	<input type="text" value="4"/>
Dose Input Information:	<input type="text" value="Enter Doses"/>
Other Advanced Features:	<input type="text" value="Adv Features"/>

Use Data Input File

Calculate Probability of Causation

[About IREP](#)

[View Model Details](#)

[Multiple Primary Cancers](#)

[Restart](#)

[End Session](#)

If you have questions or comments, please contact [NIOSH](#)

SLIDE 5

Developed under contract with the
**National Institute for Occupational
 Safety and Health (NIOSH)**



SENE Oak Ridge Inc.
 Center for Risk Analysis

User's Guide / More Information / Contact NIOSH

Interactive RadioEpidemiological Program NIOSH-IREP v.5.5.1

Enter Dose Exposure Information

Dose entry can be either a single point value, or a probability distribution.
 Hit the "Submit Dose Data" button to submit entries back to the inputs page.

No.	Exposure Year	Exposure Rate	Selection of Radiation Type		Organ Dose (cSv)	Parameters u	
						1	2
1	1946	acute	photons E>250keV	Constant (value)	18	2	
2	1946	chronic	neutrons E=100keV-2MeV	Constant (value)	0.5	2	
3	1946	chronic	alpha	Constant (value)	4.5	2	
4	1946	chronic	photons E>250keV	Constant (value)	2	2	

SLIDE 6

NIOSH-Interactive RadioEpidemiological Program
Probability of Causation Results

Uploaded file: N/A
 Date of Run: 2/1/2007
 Time of Run: 2:31:16 PM
 NIOSH ID #: 123456
 Claimant Name: John Q. Doe

DOL District Office: CL
 NIOSH-IREP version: 5.5.1
 Analytica/ADE version: 3.0
 Claimant SSN: 123-45-6789

Claimant Cancer Diagnoses:

Primary Cancer #1: <u>N/A</u>	Date of Diagnosis: <u>N/A</u>
Primary Cancer #2: <u>N/A</u>	Date of Diagnosis: <u>N/A</u>
Primary Cancer #3: <u>N/A</u>	Date of Diagnosis: <u>N/A</u>
Secondary Cancer #1: <u>N/A</u>	Date of Diagnosis: <u>N/A</u>
Secondary Cancer #2: <u>N/A</u>	Date of Diagnosis: <u>N/A</u>
Secondary Cancer #3: <u>N/A</u>	Date of Diagnosis: <u>N/A</u>

Claimant Information Used In Probability of Causation Calculation:

Gender: <u>Male</u>	Race (skin cancer only): <u>N/A</u>
Birth Year: <u>1926</u>	Year of Diagnosis: <u>1966</u>
Cancer Model: <u>All Male Genitalia (185-187)</u>	Should alternate cancer model be run?: <u>No</u>
Smoking history (trachea, bronchus, or lung cancer only): <u>N/A</u>	

NIOSH-IREP Assumptions and Settings:

User Defined Uncertainty Distribution: Lognormal(1,1)
 Number of Iterations: 2000 Random Number Seed: 99

General Exposure Information:

Exposure #	Exposure Year	Organ Dose (cSv)	Exposure Rate	Radiation Type
1	1946	Constant =18	acute	photons E>250keV
2	1946	Constant =0.5	chronic	neutrons E=100keV- 2MeV

SLIDE 7

3	1946	Constant =4.5	chronic	alpha
4	1946	Constant =2	chronic	photons E>250keV

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	0.00 %
50th percentile	6.32 %
95th percentile	23.84 %
99th percentile	34.40 %