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ADVISORY BOARD ON RADIATION AND WORKER HEALTH

NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

A LIMITED REVIEW OF ORAUT-OTIB-0082, REV. 00 PC-1 *DOSE RECONSTRUCTION METHOD FOR CHRONIC LYMPHOCYTIC LEUKEMIA*

Contract No. 211-2014-58081
SCA-TR-PR2014-0091, Revision 0

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October 2014

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S. Cohen & Associates: ***Technical Support for the Advisory Board on Radiation and Worker Health Review of NIOSH Dose Reconstruction Program***	Document No. SCA-TR-PR2014-0091 Effective Date: Draft – October 06, 2014 Revision No. Draft – 0
A Limited Review of ORAUT-OTIB-0082, Rev. 00 PC-1, ***Dose Reconstruction Method for Chronic Lymphocytic Leukemia***	Page 2 of 19
Task Manager: _____ Date: _____ U. Hans Behling, PhD, MPH	Supersedes: N/A
Project Manager: _____ Date: _____ John Stiver, MS, CHP	Reviewer(s): John Stiver

Record of Revisions

Revision Number	Effective Date	Description of Revision
0 (Draft)	10/06/2014	Initial issue.

TABLE OF CONTENTS

ABBREVIATIONS AND ACRONYMS

ABRWH or Advisory Board	Advisory Board on Radiation and Worker Health
ACS	American Cancer Society
AIC	Akaike Information Criterion
AP	anterior-posterior
CAD	Chronic Annual Dose (tool)
CFR	*Code of Federal Regulations*
CLL	chronic lymphocytic leukemia
DCAS	Division of Compensation Analysis and Support
DCF	dose conversion factor
DHHS	U.S. Department of Health and Human Services
dpm/d	disintegrations per minute/per day
EE	Energy Employee
EEOICPA	Energy Employees Occupational Illness Compensation Program Act of 2000
ET2	extrathoracic region 2
FR	Federal Register
GI	gastro-intestinal
GM	geometric mean
GSD	geometric standard deviation
HNM	highest nonmetabolic organ
Hp	penetrating dose
ICRP	International Commission on Radiological Protection
IMBA	Integrated Modules for Bioassay Analysis
IREP	Interactive RadioEpidemiological Program
keV	kiloelectron volt
LAT	lateral
LLI	lower large intestine
LN(ET)	extrathoracic lymph nodes
LN(TH)	thoracic lymph nodes
µ	micron
MDA	minimum detectable activity

MeV	mega-electron volt
NIOSH	National Institute for Occupational Safety and Health
ORAUT	Oak Ridge Associated Universities Team
OCAS	Office of Compensation Analysis and Support
ORNL	Oak Ridge National Laboratory
PA	posterior-anterior
POC	probability of causation
RBM	red bone marrow
SC&A	S. Cohen & Associates (SC&A, Inc.)
SI	small intestine
TBD	Technical Basis Document
TIB	technical information bulletin
ULI	upper large intestine

1.0 RELEVANT BACKGROUND INFORMATION

Among adults, chronic lymphocytic leukemia (CLL) is the most frequent form of leukemia in western countries, accounting for 30% of all leukemias. For the current year 2014, the American Cancer Society estimates 15,720 new cases of CLL among the 52,380 new cases of all leukemias (ACS 2014). Of the 15,720 new cases, 9,100 cases are expected to be males with a median age of 65 years at time of diagnosis. Given these incidence rates, it is reasonable to assume that a substantial number of Energy Employees (EEs) have been/will be diagnosed with CLL. NIOSH estimated that approximately 363 CLL cases may have been **diagnosed** that either filed claims that were rejected or were never filed due to knowledge that CLL was previously **not** considered a radiogenic cancer.

On March 21, 2011, the U.S. Department of Health and Human Services (DHHS) announced its intention in the Federal Register to treat CLL as a radiogenic cancer under the Energy Employees Occupational Illness Compensation Act of 2000 (EEOICPA) (FR 15268); and on February 6, 2012, the final rule was published that now regards CLL as being potentially caused by radiation.

As a result of this change and in compliance with Subpart D §81.10 of 42 CFR 81, a model was developed to derive estimates of radiation dose to a specific lymphocytic cell line that, after transformation and clonal expansion, gives rise to CLL. Details of this dosimetric CLL model were developed under contract by SENES Oak Ridge, Inc., and described in a 64-page report authored by A.J. Apostoaei and J.R. Trabalka. The report entitled, *Review, Synthesis, and Application of Information on the Human Lymphocytic System to Radiation Dosimetry for Chronic Lymphocytic Leukemia*, was issued in March 2012.

Based on technical information presented by Apostoaei and Trabalka (2012), NIOSH issued ORAUT-OTIB-0082, *Dose Reconstruction Method for Chronic Lymphocytic Leukemia* on December 20, 2012 (ORAUT 2012).

2.0 STATEMENT OF PURPOSE

Under the EEOICPA and Title 42, Part 82, *Methods for Radiation Dose Reconstruction Under the Energy Employees Occupational Illness Compensation Program Act of 2000*, of the *Code of Federal Regulations* (42 CFR Part 82), the Advisory Board on Radiation and Worker Health (Advisory Board or Board) is mandated to conduct an independent review of the methods and procedures used by the National Institute for Occupational Safety and Health (NIOSH) and its contractors for dose reconstruction.

As contractor to the Advisory Board, S. Cohen & Associates (SC&A) has been charged to support the Advisory Board in this effort by conducting critical reviews of ORAUT-OTIBs.

SC&A's review method is described in our report entitled, *A Protocol for the Review of Procedures and Methods Employed by NIOSH for Dose Reconstruction*, which was approved by the Advisory Board in November 2009 (SC&A 2009). In brief, SC&A identified the following objectives in its protocol to the Advisory Board, which have formed the basis for conducting past reviews:

Objective 1: Determine the degree to which procedures support a process that is expeditious and **timely** for dose reconstruction.

Objective 2: Determine whether procedures provide adequate guidance to be **efficient** in select instances where a more detailed approach to dose reconstruction would not affect the outcome.

Objective 3: Assess the extent to which procedures account for all potential exposures, and ensure that resultant doses are **complete** and based on adequate data.

Objective 4: Assess procedures for providing a **consistent** approach to dose reconstruction regardless of claimants' exposures by time and employment locations.

Objective 5: Evaluate procedures with regard to **fairness** and the extent to which the claimant is given the **benefit of doubt** when there are unknowns and uncertainties concerning radiation exposures.

Objective 6: Evaluate procedures for their approach to quantifying the **uncertainty** distribution of annual dose estimates that is consistent with and supports a U.S. Department of Labor probability of causation (POC) estimate at the upper 99% confidence level.

Objective 7: Assess the scientific and technical quality of methods and guidance contained in procedures to ensure that they reflect the **proper balance between current/ consensus scientific methods and dose reconstruction efficiency**.

For each of the above-cited seven general objectives, the review protocol was structured on a series of relevant questions contained in a checklist, which the SC&A reviewer used for rating a

given procedure. A rating system of 1 through 5 corresponded to the following answers: 1 = No (or Never), 2 = Infrequently, 3 = Sometimes, 4 = Frequently, 5 = Yes (or Always).

SC&A's assessment of ORAUT-OTIB-0082, however, will not adhere to the above-cited standard review protocol, which includes a critical evaluation of technical supporting documents and associated references, for the following reason:

In a written communique received on May 8, 2014, SC&A was given the following instruction regarding SC&A's review of ORAUT-OTIB-0082:

> . . . *please note this tasking does not include a review of the CLL risk model* [as presented by A. Julian Apostoaei and John R. Trabalka, 2012] *which was extensively peer-reviewed already.*

Correspondingly, SC&A's review of ORAUT-OTIB-0082 will not include the technical basis of the CLL risk model, but will be limited to the guidance/protocol for its implementation in dose reconstruction.

3.0 OVERVIEW OF OTIB-0082, REV. 00 PC-1

Of all cancers assessed under EEOICPA, estimating radiation dose(s) to cells suspected of giving rise to CLL is by far the most complex and challenging, as explained in the following statements cited in ORAUT-OTIB-0082:

> *CLL originates in the **B lymphocytes** rather than in a well-defined organ as with other cancers. These lymphocytes are distributed throughout the lymph system and, as noted in Review, Synthesis, and Application of Information on the Human Lymphatic System to Radiation Dosimetry for Chronic Lymphocytic Leukemia (Apostoaei and Trabalka 2012), they can travel throughout the body and their inventories in various compartments of the body can change significantly with age, gender, health status and other factors. **Estimation of dose to the cancer site for CLL cases requires the calculation of the radiation dose to this population of CLL precursor cells**. This is more complex than dose assessment to other cancer sites because CLL precursor cells can be present in different compartments of the lymphatic system throughout the body, and these compartments can receive substantially different doses. Because the B lymphocyte population in a given organ is not constant, probability distributions are used in the assessment.*
>
> *Current information indicates that CLL is produced by transformation of **mature, antigen-experienced B lymphocytes, possibly memory cells**, potentially anywhere in the body (i.e., including but not restricted to the bone marrow). This situation complicates an assessment of the risk of developing CLL of radiogenic origin because definition of an appropriate target organ or tissue is problematic because radiation doses from internally deposited radionuclides and from some types of external exposures can be very different at different locations within the body. B cells at different sites can thus receive markedly different doses.*
>
> *In the development of the CLL dosimetric model, information was analyzed to derive compartment-specific weights based on relative sizes of B-lymphocyte (more properly a B-cell precursor for CLL) pools to be used in estimating a weighted average radiation dose. Because of the variability and uncertainty in the distribution of these cells, probability distribution functions were assigned to the number of lymphocytes and to the fraction that represent B cells for each organ of interest. The final model consists of an average dose (and its uncertainty) obtained using weights based on the fractional distribution of B-lymphocyte precursors across **30 compartments for CLL**.* [Emphasis added.]
>
> *For **internal** dose calculation, the B lymphocytes compartments correspond to . . . a total of 28 organs must be assessed . . . Table 3-1 lists the corresponding organs to be assessed for each compartment of the CLL model* [in behalf of occupational internal, external, and medical dose].

> *However, this can be a **complicated process** and at a minimum is **very lengthy**, so specific issues associated with this calculation are addressed here. Although the CLL tool is mentioned, details of its use are not included here; these are addressed in the **tool user guide.*** [Emphasis added.]

As a convenience to the reader, Table 3-1 of ORAUT-OTIB-0082 is reproduced herein as Exhibit #1. In addition to the large number of organs that the model must consider, the complexity of the CLL model is further compounded by secondary variables that include the need to select (1) the type of medical x-ray examination administered and whether the beam was **poorly** or **properly** collimated, (2) the chemical form and solubility class for internalized radionuclides, (3) use of a special/blended dose conversion factor (DCF) (described in DCAS-RPT-004) representing the weighted fractions of DCF values for the 15 organs cited in Table 3-1 (Exhibit #1) for measured (or missed) external exposures to photons and neutrons, and (4) the potential assignment of geometry correction factors to glovebox work/uranium facilities and dose assignment to the **skin** (a compartment of the CLL model) from both penetrating and non-penetrating radiation. Guidance for the selection and use of these and other input parameters are provided in Section 4.0 of ORAUT-OTIB-0082.

EXHIBIT #1: Table 3-1. Correspondence of CLL model to ICRP-modeled organs.

Compartment of CLL dosimetry model	X-ray dose organ[a]	Internal dose organ	External dose organ
Lymph nodes			
Extrathoracic	Thyroid	LN(ET)	Thyroid
Thoracic	Lung	LN(TH)	Lung
Remainder	Ovaries	HNM[b]	Stomach[c]
Spleen	Spleen (lung or ovaries)	Spleen	Stomach[c]
Peyer's Patches	Colon (ovaries)	SI	Stomach[c]
Thymus	Thymus (lung)	Thymus	Thymus
Red bone marrow	Bone marrow	RBM	RBM
Tonsils	Esophagus (lung)	LN(ET)	Esophagus
Blood	Remainder	HNM[b]	Stomach[c]
Intestinal mucosa			
Small intestinal wall	Ovary	SI	Stomach[c]
Upper intestinal wall	Colon (ovaries)	ULI	Colon[c]
Lower large intestinal wall	Colon (ovaries)	LLI	Colon[c]
Respiratory mucosa			
Extrathoracic airways	Esophagus (lung)	ET2	Esophagus
Lung	Lung	Lung	Lung
Skin	Skin	Skin	Skin
Liver	Liver (lung or ovary)	Liver	Liver[c]
Vermiform appendix	Colon (Ovaries)	ULI	Colon[c]
Residual soft tissue			
Muscle	Remainder	Muscle	Remainder
Breast	Breast	Breast	Breast
Kidneys	Remainder	Kidney	Liver[c]
ST wall	Stomach (lung or ovaries)	Stomach	Stomach[c]
Pancreas	Pancreas (lung or ovaries)	Pancreas	Stomach[c]
Uterus	Uterus	Uterus	Uterus[c]
Urinary bladder wall	Urinary bladder (ovaries)	Bladder	Bladder[c]
Esophagus	Esophagus (lung)	Esophagus	Esophagus
Testes	Testes	Testes	Testes[c]
Thyroid	Thyroid	Thyroid	Thyroid
Prostate	Prostate (ovaries)	HNM[b]	Bladder[c]
Adrenals	Remainder	Adrenals	Remainder
Ovaries	Ovaries	Ovaries	Ovaries[c]

Source: ORAUT-OTIB-0082

3.1 REVIEW OF GUIDANCE FOR ESTIMATING INTERNAL CLL DOSE

Due to the fact that the CLL risk model identified 28 separate anatomical compartments with representation of CLL precursor cells, an assessment of the CLL internal dose in effect corresponds to a weighted dose assessment in behalf of 28 different organs/tissues cited in Column #3 of Exhibit #1.

Given the complexity of deriving weighted organ/tissue doses, NIOSH developed the **CLL Simulator Tool**, which allows the Integrated Modules for Bioassay Analysis (IMBA) and Chronic Annual Dose (CAD) Workbook files to be imported for calculating internal doses to all CLL organs simultaneously. In addition, the CAD Workbook was modified in order to create a separate file for each of the 28 organs/tissues, which can be used in the CLL Simulator Tool. OTIB-0082 also provides brief instructions for saving files in IMBA that can be imported into the CLL Tool.

Other tools that were modified or CLL-specific guidance added to address the complexity of the CLL risk model include (1) ORAUT-OTIB-0018 (*Internal Dose Overestimates for Facilities with Air Sampling Programs*), (2) ORAUT-OTIB-0054 (*Fission and Activation Product Assignment for Internal Dose-Related Gross Beta and Gross Gamma Analysis*), (3) ORAUT-OTIB-0049 (*Estimating Doses for Plutonium Strongly Retained in the Lung*), (4) ORAUT-OTIB-0011 (*Technical Information Bulletin: Tritium Calculated and Missed Dose Estimates*), (5) site-specific radionuclide chooser tools, and (6) site-specific internal environmental tools.

SC&A Comments Pertaining to Internal Dose Guidance for CLL Cases

SC&A was provided training on running the CLL Simulator Tool. Subsequently, we generated both IMBA and CAD files for a CLL claim, imported these files into the CLL Simulator Tool, and evaluated the internal doses generated by the tool.

In addition, SC&A assessed the modifications made to tools or changes to the dose reconstruction guidance for performing internal doses as specified in OTIB-0018 (ORAUT 2005), OTIB-0049 (ORAUT 2010), OTIB-0054 (ORAUT 2007), OTIB-0011 (ORAUT 2004), site-specific radionuclide chooser tools, and site-specific environmental tools. We were able to confirm that appropriate changes have been incorporated into these tools and the tools generated internal doses that included the weighted organs/tissues specified in OTIB-0082. In addition, we verified that guidance for using generic and site-specific tools had been appropriately updated to include changes required for performing best-estimates for CLL claims.

SC&A's evaluation of internal dose tools and technical guidance revealed no findings, but identified the following minor observation.

Observation #1. Section 4.2 of OTIB-0082 states the following: ". . . Although the CLL tool [for CLL internal dose] is mentioned, details of its use are not included here; these are addressed in the **tool user guide**." [Emphasis added.] Currently, however, a tool user guide does not exist; and unless a tool user guide is developed, this sentence should be removed from OTIB-0082.

3.2 REVIEW OF DCAS-RPT-004: CHRONIC LYMPHOCYTIC LEUKEMIA (CLL) DOSE CONVERSION FACTORS FOR DERIVING EXTERNAL DOSE

As shown in Exhibit #1, for external CLL dose calculation, there are 15 CLL compartments for which doses must be derived from dosimeter measurements and properly weighted to reflect fractional distribution of CLL precursor cells. The protocol for these blended CLL dose conversion factors (CLL-DCFs) is described in DCAS-RPT-004 (DCAS 2013) and is based on the following equation:

$$\text{CLL-DCF}_{\text{blended}} = \Sigma_{\text{organ}}\, \text{B-cell Fraction} \times \text{DCF}_{\text{organ}}$$

Important to note is that the $\text{DCF}_{\text{organ}}$ is defined by (1) radiation type (photons, neutrons, electrons), (2) energy, (3) exposure geometry, and (4) the recording of the external dose measurement [Roentgen, Hp(10), or $H^{*}(10)$]. Moreover, since both the $\text{DCF}_{\text{organ}}$ value and B-cell fraction represent probability distributions, their multiplicative product represents a sample value from each distribution. For **each** CLL-DCF, NIOSH employed a total of 50,000 interactions, which in turn were fitted to five standard probability distributions that included normal, lognormal-3 parameter,[1] lognormal-2 parameter, Weibull-3 parameter, and Weibull-2 parameter. To determine the **best fit** of the data among the five distributions, NIOSH employed the Akaike Information Criterion (AIC) and selected the fit(s) with the lowest AIC score (5), as provided in Appendix B of DCAS-RPT-004, and summarized in Table 4 of DCAS-RPT-004. As a convenience to the reader, Table 4 is reproduced herein as Table 1. Additionally, Table 2 provides the key for each parameter value of the five distribution types.

In order to properly apply the blended DCF values in dose reconstruction, NIOSH added a "CLL DCF" tab/spreadsheet with these CLL DCFs to all site-specific external dose calculation workbooks.

SC&A Comments Pertaining to DCAS-RPT-004 and External Dose Guidance for CLL Cases

SC&A critically reviewed the statistical approach described in DCAS-RPT-004, which correlates external dosimeter measurements to radiation doses received by B-lymphocytes (representing 15 anatomically separated compartments) by means of blended CLL DCFs. Blended DCFs were based on previously assessed DCF values cited in *External Dose Reconstruction Implementation Guide* (OCAS 2007) for select radiation types, energies, and exposure geometries using Monte Carlo techniques.

In addition, SC&A verified that the site-specific external dose calculation workbooks had been updated with the "CLL DCF" tab, and that the data entered into the spreadsheet associated with this tab were consistent with data provided in DCAS-RPT-004.

SC&A concurs with the methodology used to derive blended CLL DCF values, and there are no findings.

[1] Note: Due to software limitations, the lognormal-3 parameter distribution is not available for use.

Table 1: CLL Dose Conversion Factors (DCFs)

Photons – Standard	Program	AIC	Distribution Type	Parameter 1	Parameter 2	Parameter 3
AP, Hp(10), 20 keV	R Code	-260741	Weibull-3	22.47131	0.349317	-0.223322
	@Risk	-261126	Weibull-3	20.7300	0.3218	-0.1958
AP, Hp(10), <30 keV	R Code	-163211	Lognormal-2	-1.813092	0.289966	
	@Risk	-163749	Weibull-3	3.1523	0.1547	0.0316
AP, Hp(10), 30-250 keV	R Code	-115811	Weibull-3	7.199207	0.507184	0.179760
	@Risk	-115774	Weibull-3	7.4933	0.5264	0.1613
AP, Hp(10), >250 keV	R Code	-215872	Weibull-3	40.13267	0.924499	-0.045126
	@Risk	-216930	Weibull-3	40.0000	0.9134	-0.0337
AP, H*(10), 20 keV	R Code	-260926	Weibull-3	22.51689	0.349347	-0.223217
	@Risk	-260804	Weibull-3	18.9010	0.2951	-0.1692
AP, H*(10), <30 keV	R Code	-162595	Weibull-3	2.929355	0.147035	0.040620
	@Risk	-162782	Weibull-3	2.9167	0.1461	0.0417
AP, H*(10), 30-250 keV	R Code	-102949	Weibull-3	6.538252	0.527992	0.208968
	@Risk	-102681	Weibull-3	6.6675	0.5392	0.1980
AP, H*(10), >250 keV	R Code	-214109	Weibull-3	39.45216	0.937975	-0.043503
	@Risk	-214188	Weibull-3	40.0000	0.9492	-0.0548
AP, Exposure, 20 keV	R Code	-311040	Weibull-3	22.67735	0.213126	-0.137000
	@Risk	-311007	Weibull-3	22.6070	0.2126	-0.1365
AP, Exposure, <30 keV	R Code	-163352	Weibull-3	2.971961	0.147084	0.037963
	@Risk	-163447	Weibull-3	3.1430	0.1544	0.0309
AP, Exposure, 30-250 keV	R Code	-55009	Weibull-3	4.901520	0.660023	0.328846
	@Risk	-55182	Weibull-3	4.9724	0.6674	0.3215
AP, Exposure, >250 keV	R Code	-173835	Normal	0.902252	0.042539	
	@Risk	-173857	Normal	0.9024	0.0425	
ISO, H*(10), <30 keV	R Code	-293749	Lognormal-2	-3.006159	0.259159	
	@Risk	-293828	Lognormal-2	-3.0026	0.2580	
ISO, H*(10), 3-250 keV	R Code	-173300	Weibull-3	6.328391	0.252389	0.106626
	@Risk	-173544	Weibull-3	6.2922	0.2505	0.1083
ISO, H*(10), >250 keV	R Code	-205435	Weibull-3	4.770665	0.142480	0.523519
	@Risk	-206081	Weibull-3	4.9605	0.1465	0.5197
ISO, Exposure, <30 keV	R Code	-308204	Weibull-3	3.252577	0.037359	0.013826
	@Risk	-308245	Weibull-3	3.2695	0.0375	0.0137
ISO, Exposure, 3-250 keV	R Code	-139362	Weibull-3	6.379246	0.356836	0.106916
	@Risk	-139466	Weibull-3	6.4273	0.3590	0.1050
ISO, Exposure, >250 keV	R Code	-253408	Normal	0.656806	0.019196	
	@Risk	-253829	Normal	0.6567	0.0191	
Photons – Glovebox						
GL, AP, Hp(10), 20 keV	R Code	-153384	Weibull-3	4.573391	0.231926	0.035918
	@Risk	-153959	Weibull-3	4.5404	0.2294	0.0385
GL, AP, Hp(10), <30 keV	R Code	-73923	Weibull-3	2.618190	0.326542	0.065149
	@Risk	-74765	Weibull-3	2.5422	0.3158	0.0741
GL, AP, Hp(10), 30-250 keV	R Code	11108	Normal	1.353380	0.270388	
	@Risk	10711	Normal	1.3547	0.2693	
GL, AP, Hp(10), >250 keV	R Code	12631	Normal	1.730032	0.274537	
	@Risk	12653	Normal	1.7302	0.2746	

Table 1: CLL Dose Conversion Factors (DCFs) (continued)						
Photons – Glovebox	**Program**	**AIC**	**Distribution Type**	**Parameter 1**	**Parameter 2**	**Parameter 3**
GL, AP, Exposure, 20 keV	R Code	-203800	Weibull-3	4.600174	0.140813	0.021185
	@Risk	-203991	Weibull-3	4.4847	0.1374	0.0242
GL, AP, Exposure, <30 keV	R Code	-71732	Weibull-3	2.713886	0.343538	0.057365
	@Risk	-72049	Weibull-3	2.6518	0.3356	0.0654
GL, AP, Exposure, 30-250 keV	R Code	58114	Normal	1.945418	0.432643	
	@Risk	58593	Normal	1.9425	0.4347	
GL, AP, Exposure, >250 keV	R Code	19277	Normal	1.806214	0.293404	
	@Risk	19192	Normal	1.8060	0.2932	
Neutrons – Standard						
AP, Hp,slab(10), <10 keV	R Code	-14546	Weibull-3	4.354067	0.888335	0.699164
	@Risk	-14445	Weibull-3	4.7636	0.9649	0.6237
AP, Hp,slab(10), 10-100 keV	R Code	-38366	Lognormal-2	0.176877	0.138136	
	@Risk	-38538	Lognormal-2	0.1776	0.1378	
AP, Hp,slab(10), 0.1-2 MeV	R Code	-119373	Weibull-3	6.592743	0.450670	0.297627
	@Risk	-118907	Weibull-3	6.4519	0.4442	0.3042
AP, Hp,slab(10), 2-20 MeV	R Code	-123009	Weibull-3	6.284880	0.417064	0.611094
	@Risk	-121974	Weibull-3	6.4707	0.4329	0.5954
Neutrons – Glovebox						
GL, AP, Hp,slab(10), <10 keV	R Code	104679	Weibull-3	3.277786	2.325402	1.068565
	@Risk	105394	Weibull-3	3.3979	2.4149	0.9920
GL, AP, Hp,slab(10), 10-100 keV	R Code	81559	Lognormal-2	0.894352	0.223635	
	@Risk	81019	Lognormal-2	0.8960	0.2221	
GL, AP, Hp,slab(10), 0.1-2 MeV	R Code	17016	Normal	1.490459	0.286843	
	@Risk	16828	Normal	1.4921	0.2863	
GL, AP, Hp,slab(10), 2-20 MeV	R Code	38162	Normal	2.029914	0.354389	
	@Risk	38603	Normal	2.0320	0.3560	
Electrons						
Electrons – 1.5 MeV	R Code	-411625	Weibull-3	1.432950	7.2274e-3	4.6557e-5
	@Risk	-412382	Weibull-3	1.4000	0.0071	0.0002

Source: DCAS-RPT-004, Table 4

Table 2: Parameter Key for the Various Distribution Types

Distribution Type	Parameter 1	Parameter 2	Parameter 3
Lognormal-3	μ (GM = e^{μ})	σ (GSD = e^{σ})	Shift Factor (γ)
Lognormal-2	μ (GM = e^{μ})	σ (GSD = e^{σ})	
Weibull-3	k (Shape)	λ (Scale)	Shift Factor (θ)
Weibull-2	k (Shape)	λ (Scale)	
Normal	μ	σ	

Source: DCAS-RPT-004, Table 5

3.3 REVIEW OF GUIDANCE FOR ESTIMATING MEDICAL X-RAY DOSE TO COMPARTMENTS COMPRISING THE CLL MODEL

Section 4.1 of OTIB-0082 explains the basis for estimating doses to each of the compartments containing CLL precursor cells that may be exposed to occupational medical radiation associated with either a chest or lumbar spine x-ray examination. Dose estimates to each compartment are defined by the product of the incident air kerma and the compartment-specific DCFs assigned to organs shown in the second Column of Exhibit #1.

For the CLL compartment involving the skin, an entrance and exit skin dose is defined as well as the fraction of exposed skin, which varies from 0.19 for a properly collimated beam to 0.38 for a poorly collimated beam.

The effective organ to CLL precursor cells from occupational medical exposure is the sum of the weighted organ doses that takes into consideration uncertainties associated with each organ-specific DCF value and the weighted fraction of CLL cells.

For estimates of CLL medical x-ray doses, NIOSH developed CLL x-ray doses that were facility-specific, view-specific (e.g., PA or LAT), and facility-specific to given time periods. Variables among time periods included assigned organ doses and whether beams were properly or poorly collimated. A lookup table containing these values has been incorporated into each site-specific external dose calculation workbook as a single tab ("CLL X-ray Data").

SC&A Comments Pertaining to Occupational Medical Doses for CLL Cases

Our review of NIOSH's methodology and guidance pertaining to the assignment of medical x-ray dose to compartments indicate that they are consistent with existing models and, when properly adjusted to account for the distribution of CLL precursor cells among compartments, comply with the CLL risk model. In addition, SC&A reviewed all site-specific external dose calculation workbooks to ensure that the 'CLL X-ray Data" tab had been added and the data were consistent with TBD guidance.

There are no findings pertaining to estimates of medical x-ray doses applicable to the CLL risk model.

3.4 VALIDATION OF GUIDANCE PROVIDED IN ORAUT-OTIB-0082 IN DOSE RECONSTRUCTION

In an effort to assess the functionality of guidance provided in ORAUT-OTIB-0082, SC&A conducted a preliminary review of a CLL case assigned as part of our audit of the 19th set of dose reconstructions. A summary of the case specifics is provided below:

Case Overview

The Energy Employee (EE) worked at ORNL (X-10) as an [redacted] during the period [redacted]. Diagnosed with CLL in [redacted] ([redacted] years exposure, [redacted]

years latent period). NIOSH performed a partial dose reconstruction in May 2013, since this was sufficient to produce a POC of >50%.

External Dose

Recorded Photon/Neutron Doses – The EE was monitored for most of the 10-year employment period and external doses were calculated based on guidance in the X-10 TBD data and OTIB-0082. The most current version of the X-10 Calculation Workbook was used, which includes the CLL DCFs that were applied in this case.

Occupational Medical Doses – The EE was also assigned doses from occupational x-ray exams in accordance with OTIB-0082 and X-10 TBD guidance. The X-10 Calculation Workbook was used, and appropriate values from the CLL X-ray Data sheet were applied.

Internal Dose

Bioassay**s –** The EE was bioassayed for numerous radionuclides by urinalyses and whole body counts, with all results below the minimum detectable activity (MDA) levels. NIOSH used the urinalysis data to estimate internal dose in this case. Missed Pu-239 dose was based on ½ MDA = 0.5 × 0.06 dpm/d = 0.03 dpm/d.

IMBA **–** The missed intake value of 0.03 dpm/d (last bioassay on March 16, 1969) was used as the bioassay input into the IMBA program to provide a projected chronic intake of 3.57 dpm/d Type M, and 56.36 dpm/d Type S Pu-239 for the period 1960–1970. Type S was used in this case.

IMBA Report **-** An IMBA Report was created that included all the individual CLL organ/compartment annual doses for use in the CLL Simulator.

Type SS Pu **–** The organ doses in the IMBA Report for Type S Pu are then adjusted using the recommendations of OTIB-0049, Table 4-5, page 12, and page 14. For this case, this included the lungs, thoracic lymph nodes, extra-thoracic, gastro-intestinal (GI) tract, and systemic organs as per the Urinalysis column.

Multiple IMBA Reports **–** In general, an IMBA Report (that includes all the CLL organs) is generated for each radionuclide, and for each solubility type. For this case, a comparison is made between Pu-239 Type M, Type S, and Type SS, with Type SS resulting in the highest dose.

CLL Simulator **–** The IMBA Report for Pu-239 Type SS was then imported into the CLL Simulator 1.3.0, and the CLL calculation was performed. This created a CLL Report, which was compared to the IREP Input Table for use in the POC calculations.

ORAUT-OTIB-0082 Validation Summary Conclusions

From this preliminary evaluation and a spot check of calculations, doses, etc., it appears that, for this case, the dose reconstructor used the proper procedures and assigned the correct doses. The detailed calculations in the IMBA Report, CLL Simulator, POC calculations, etc., were not evaluated.

4.0 SUMMARY CONCLUSIONS

SC&A's assessment of ORAUT-OTIB-0082 was limited to the methodology and guidance needed to perform a dose reconstruction in behalf of a CLL claim. In recognition of the complexity of the CLL risk model, an extraordinary effort was required for the development of a new CLL internal dose tool, as well as the modification of numerous internal and external tools, in order to reduce the potentially time-consuming effort that would otherwise be required to perform a dose reconstruction. SC&A was able to verify that guidance and tools are adequate for deriving external and internal dose for CLL clams in accordance with ORAUT-OTIB-0082.

There were no findings associated with our review of ORAUT-OTIB-0082.

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