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Dose Reconstruction
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Oak Ridge Associated Universities | NV5|Dade Moeller | MJW Technical Services

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Lymphocytic Leukemia**

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Subject Expert(s): Elizabeth M. Brackett, Jo Ann Jenkins, Matthew H. Smith

Document Owner
Approval:

Signature on File
Elizabeth M. Brackett, Document Owner

Approval Date: 04/12/2021

Concurrence:

Signature on File
John M. Byrne, Objective 1 Manager

Concurrence Date: 04/12/2021

Concurrence:

Signature on File
Scott R. Siebert, Objective 3 Manager

Concurrence Date: 04/12/2021

Concurrence:

Vickie S. Short Signature on File for
Kate Kimpan, Project Director

Concurrence Date: 04/12/2021

Approval:

Signature on File
Timothy D. Taulbee, Associate Director for Science

Approval Date: 04/29/2021

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ACRONYMS AND ABBREVIATIONS

AWE	atomic weapons employer
CLL	chronic lymphocytic leukemia
DCF	dose conversion factor
DHHS	U.S. Department of Health and Human Services
DOE	U.S. Department of Energy
EEOICPA ET2	Energy Employees Occupational Illness Compensation Program Act of 2000 extrathoracic region 2 (posterior nasal passage, larynx, pharynx, and mouth)
FR	<i>Federal Register</i>
HNM	highest nonmetabolic organ
ICRP	International Commission on Radiological Protection
IDOT	Internal Dosimetry Tool
IMBA	Integrated Modules for Bioassay Analysis
in.	inch
IREP	Interactive RadioEpidemiological Program
LLI	lower large intestine
LN(ET)	extrathoracic lymph nodes
LN(TH)	thoracic lymph nodes (trachea, bronchi, bronchioles, alveolar ducts, and sacs)
mrem	millirem
NIOSH	National Institute for Occupational Safety and Health
ORAU ORAUT	Oak Ridge Associated Universities ORAU Team
RBM	red bone marrow
SI	small intestine
SRDB Ref ID	Site Research Database Reference Identification (number)
TIB	technical information bulletin
U.S.C.	<i>United States Code</i>
ULI	upper large intestine

1.0 INTRODUCTION

Technical information bulletins (TIBs) are not official determinations made by the National Institute for Occupational Safety and Health (NIOSH) but are rather general working documents that provide historical background information and guidance to assist in the preparation of dose reconstructions at particular sites or categories of sites. They will be revised in the event additional relevant information is obtained about the affected site(s), such as changing scientific understanding of operations, processes, or procedures involving radioactive materials. TIBs may be used to assist NIOSH staff in the completion of individual dose reconstructions.

In this document the word “facility” is used to refer to an area, building, or group of buildings that served a specific purpose at a U.S. Department of Energy (DOE) or Atomic Weapons Employer (AWE) facility. It does not mean, nor should it be equated to, an “AWE facility” or a “DOE facility.” The terms AWE and DOE facility are defined in 42 *United States Code* (U.S.C.) 7384l(5) and (12) of the Energy Employees Occupational Illness Compensation Program Act of 2000, respectively.

In a final rule published in the *Federal Register* (FR) on March 21, 2011 [77 FR, p. 5711; U.S. Department of Health and Human Services (DHHS) 2012], the department included chronic lymphocytic leukemia (CLL) as a radiogenic cancer under the Energy Employees Occupational Illness Compensation Program Act of 2000 (EEOICPA).

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* [Apostoaiei 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 (1) CLL precursor cells can be present in different compartments of the lymphatic system throughout the body and (2) 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.

2.0 PURPOSE

A model was developed to determine a meaningful radiation dose for the assessment of radiological risk of CLL; complete details of this dosimetry model can be found in Apostoaiei and Trabalka [2012]. This TIB provides guidance on the application of this model.

Attributions and annotations, indicated by bracketed callouts and used to identify the source, justification, or clarification of the associated information, are presented in Section 5.0.

3.0 GENERAL MODEL

3.1 BACKGROUND

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 defining an appropriate target organ or tissue is problematic. Radiation doses from internally deposited radionuclides and some types of external exposures can be very different at different locations within the body. B cells at different sites can therefore 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.

3.2 CORRESPONDENCE OF MODELED ORGANS

There is not a complete one-to-one correspondence between the regions that are included in the estimates of inventories of CLL precursors and the organs and tissues for which radiation doses are estimated from International Commission on Radiological Protection (ICRP) models. Table 4-1 lists the corresponding organs to be assessed for each compartment of the CLL model. Where a direct correspondence was not available, a description of the CLL compartment and the assignments in ORAUT-OTIB-0005, *Internal Dosimetry Organ, External Dosimetry Organ, and IREP Model Selection by ICD-10 Code* [Oak Ridge Associated Universities (ORAU) Team (ORAUT) 2019a], were used to determine the appropriate organ.

4.0 GUIDANCE

4.1 MEDICAL X-RAY DOSE

Dose from medical X-ray exposure to each of the compartments that make up the CLL model in Table 4-1 is determined in the usual way as the product of the incident air kerma and the dose conversion factors (DCFs). As described in ORAUT-OTIB-0006, *Dose Reconstruction from Occupational Medical X-Ray Procedures* [ORAUT 2019b], substitute DCFs are used for organs in the model without unique DCFs as shown in parentheses in Table 4-1. If two organs are listed in parentheses, the substitute DCF depends on the X-ray examination (typically chest or lumbar spine). Each organ dose is then weighted by the fraction of CLL precursor cells in each organ according to the CLL model.

The organ dose assignment for CLL is the sum of the weighted organ doses after appropriately combining the uncertainty distributions using Monte Carlo methods and accounting for the statistical correlation of the incident air kerma with the various organs.

The skin dose from X-ray exposure for the purpose of CLL is a fraction of the entrance and exit dose based on an estimate of the fraction of total exposed skin for poorly and properly collimated beams. The area of exposed skin is 3,074 cm² (14 by 17 in. on each of the entrance and exit sides) for properly collimated beams and twice that (6,148 cm²) for poorly collimated beams [ORAUT 2019b]. The total skin area for females (16,000 cm²) from ORAUT-OTIB-0017, *Interpretation of Dosimetry Data for Assignment of Shallow Dose* [ORAUT 2005a], should be used to calculate the skin dose fraction because it yields a slightly higher fractional result. It is assumed that all of the area of the beam (both poorly and properly collimated) is the same as the area of exposed skin. Table 4-2 provides the exposed skin fractions for estimating the skin dose.

Table 4-1. Correspondence of CLL model to ICRP-modeled organs.^a

Compartment of CLL dosimetry model	X-ray dose organ ^b	Internal dose organ	External dose organ
Lymph nodes–extrathoracic	Thyroid	LN(ET)	Thyroid
Lymph nodes–thoracic	Lung	LN(TH)	Lung
Lymph nodes–remainder	Ovaries	HNM ^c	Stomach ^d
Spleen	Spleen (lung or ovaries)	Spleen	Stomach ^d
Peyer's patches	Colon (ovaries)	SI	Stomach ^d
Thymus	Thymus (lung)	Thymus	Thymus
Red bone marrow	Bone marrow	RBM	RBM
Tonsils	Esophagus (lung)	LN(ET)	Esophagus
Blood	Remainder	HNM ^c	Stomach ^d
Intestinal mucosa–small intestinal wall	Ovary	SI	Stomach ^d
Intestinal mucosa–upper intestinal mucosa–intestinal wall	Colon (ovaries)	ULI	Colon ^d
Lower large intestinal wall	Colon (ovaries)	LLI	Colon ^d
Respiratory mucosa–extrathoracic airways	Esophagus (lung)	ET2	Esophagus
Respiratory mucosa–lung	Lung	Lung	Lung
Skin	Skin	Skin	Skin
Liver	Liver (lung or ovary)	Liver	Liver ^d
Vermiform appendix	Colon (ovaries)	ULI	Colon ^d
Residual soft tissue–muscle	Remainder	Muscle	Remainder
Residual soft tissue–breast	Breast	Breast	Breast
Residual soft tissue–kidneys	Remainder	Kidney	Liver ^d
Residual soft tissue–stomach wall	Stomach (lung or ovaries)	Stomach	Stomach ^d
Residual soft tissue–pancreas	Pancreas (lung or ovaries)	Pancreas	Stomach ^d
Residual soft tissue–uterus	Uterus	Uterus	Uterus ^d
Residual soft tissue–urinary bladder wall	Urinary bladder (ovaries)	Bladder	Bladder ^d
Residual soft tissue–esophagus	Esophagus (lung)	Esophagus	Esophagus
Residual soft tissue–testes	Testes	Testes	Testes ^d
Residual soft tissue–thyroid	Thyroid	Thyroid	Thyroid
Residual soft tissue–prostate	Prostate (ovaries)	HNM ^c	Bladder ^d
Residual soft tissue–adrenals	Remainder	Adrenals	Remainder
Residual soft tissue–ovaries	Ovaries	Ovaries	Ovaries ^d

- ET2 = extrathoracic region 2 (posterior nasal passage, larynx, pharynx, and mouth); LLI = lower large intestine; LN(ET) = extrathoracic lymph nodes; LN(TH) = thoracic lymph nodes (trachea, bronchi, bronchioles, alveolar ducts, and sacs); RBM = red bone marrow; SI = small intestine; ULI = upper large intestine.
- An organ in parentheses after the listed organ indicates the substitute organ DCF to be used to assess the dose to the listed organ. If there are two organs in parentheses, the substitute DCF depends on the X-ray examination (typically chest or lumbar spine).
- See ORAUT-OTIB-0060, *Internal Dose Reconstruction* [ORAUT 2018], for guidance on selection.
- Organs that could require application of a glovebox geometry correction factor from DCAS-TIB-0010, *Best Estimate External Dose Reconstruction for Glovebox Workers* [NIOSH 2011], or of the geometry correction factor from DCAS-TIB-0013, *Selected Geometric Exposure Scenario Considerations for External Dose Reconstruction at Uranium Facilities* [NIOSH 2010].

Table 4-2. Exposed skin fractions used to estimate skin dose.^{a,b}

Exposure type	Estimated skin dose
Properly collimated beam	(entrance + exit skin dose) (0.19)
Poorly collimated beam	(entrance + exit skin dose) (0.38)

- Exposure area is 3,074 cm² (14 by 17 in. on each of the entrance and exit sides) for properly collimated beams and twice that (6,148 cm²) for poorly collimated beams [ORAUT 2019b].
- The total skin area for females (16,000 cm²) used to calculate the skin dose fraction [ORAUT 2005a].

4.2 INTERNAL DOSE

For internal dose calculation, the B lymphocyte compartments correspond to 25 organs, so doses to all of them must be calculated to determine the CLL dose to be entered into the Interactive RadioEpidemiological Program (IREP). However, one of the 25 corresponds to the highest nonmetabolic organ (HNM), which can be one of several organs depending on the particular circumstances of the exposure. Bone surface, brain, gall bladder, and heart wall are possible HNM organs but are not included in the internal organ correspondence list. Therefore, a total of 28 organs must be assessed for the internal dose determination.

As a general rule, assessment of the CLL internal dose is equivalent to assessing a claim with cancers of 28 different organs. This is a complicated process and at a minimum is very lengthy, so specific issues associated with this calculation are addressed here.

4.2.1 Best Estimates

When a best estimate is needed, parameters must be consistent across all organs. For example, the material type for a given intake of a radionuclide must be the same for all organs. Note that this does not preclude the assignment of multiple material types for a given nuclide. This can happen when one type is maximizing for a fitted dose while a different type is more favorable to the claimant for the missed dose. However, a consistent material type must be used across all organs for the fitted doses and, similarly, a consistent material type must be used for the missed dose calculation for all organs.

When comparing missed versus fitted dose, annual doses should be compared after running the CLL tool rather than comparing the missed and fitted annual doses to the individual organs before the values are input to the CLL tool.

4.2.2 Integrated Modules for Bioassay Analysis

The Integrated Modules for Bioassay Analysis (IMBA) calculates all organ doses simultaneously. To generate a report that includes doses for all organs, click the **Select all** option on the **Equivalent Doses** page. The CLL tool will import all organs necessary for performing the dose calculation.

4.2.3 Web CAD

The chronic annual dose tool Web CAD has been modified to create files for all relevant organs. A single file is created with separate worksheets for each organ.

4.2.4 Type Super S Material

Intakes of highly insoluble forms of plutonium are calculated using the Internal Dosimetry Tool (IDOT). Refer to ORAUT-OTIB-0049, *Estimating Doses for Plutonium Strongly Related in the Lung* [ORAUT 2020b] for type super S applicability and the *IDOT User Guide* for information on the use of the tool [ORAUT 2020a]. Doses can be calculated with Web CAD or IDOT. The output reports include all organs needed for the CLL calculation, which can be imported into the CLL tool.

4.2.5 Tritium

Dose from tritiated water is most often calculated using the tritium tool (Tritium Doses from Urine Data Workbook) as documented in ORAUT-OTIB-0011, *Technical Information Bulletin: Tritium Calculated and Missed Dose Estimates* [ORAUT 2004], because IMBA will not directly calculate the dose from measured tritiated water in urine samples. The tritium tool generates only a single list of doses, which are applicable to all organs. These doses must be entered into the CLL tool for all relevant organs.

IMBA is used to assess doses from stable metal tritides (see ORAUT-OTIB-0066, *Calculation of Dose from Intakes of Special Tritium Compounds* [ORAUT 2020c]), so the Section 4.2.1 guidance can be followed.

4.2.6 Overestimates for Facilities with Air Sampling Programs

This overestimating method is applicable to CLL cases in accordance with ORAUT-OTIB-0018, *Internal Dose Overestimates for Facilities with Air Sampling Programs* [ORAUT 2005b]. Each organ in the CLL model must be assessed.

4.2.7 Radionuclide Chooser

The Radionuclide Chooser tool is used to determine the radionuclide and material type combination that is most favorable to the claimant from a whole-body count in which many nuclides are reported. In the case of CLL, this information is necessary for the 28 organs of interest; Radionuclide Chooser can be used to determine the maximizing radionuclide and type combination for each of these organs. Once this list is generated, IMBA is run for each of these nuclides for input to the CLL tool.

4.2.8 Environmental Doses

Environmental doses are typically relatively small, so maximizing material types can be used for each organ for a best estimate.

4.2.9 Reactor Mixes

ORAUT-OTIB-0054, *Fission and Activation Product Assignment for Internal Dose-Related Gross Beta and Gross Gamma Analyses* [ORAUT 2015], is used to assign radionuclide-specific intakes of mixed fission and activation products when air sampling or urinalysis data associated with reactors or reactor fuels are available only as gross or total beta activity or gross or total gamma activity. Based on an analysis of the CLL organ distribution and the material types yielding the largest dose for each, it was determined that the material type for each nuclide in the ORAUT-OTIB-0054 mixture can be fixed for CLL analysis. These types are given in Table 4-3. The ORAUT-OTIB-0054 tool assigns the appropriate material type.

Table 4-3. Material types to be assigned for ORAUT-OTIB-0054 CLL analyses.

Radionuclide	Type	Radionuclide	Type
Ce-141	S	Pr-143	S
Ce-144	S	Ru-103	S
Co-60	S	Ru-106	S
Cs-134	F	Sr-89	F
Cs-137	F	Sr-90	F
Eu-154	M	Y-90	S
I-131	F	Y-91	M
Nb-95	S	Zr-95	M
Pm-147	M		

4.3 EXTERNAL DOSE

For external dose calculation, the B lymphocyte compartments correspond to 15 organs as listed in Table 4-1. These organs were selected based on the availability of data for DCFs from OCAS-IG-001, *External Dose Reconstruction Implementation Guideline* [NIOSH 2007] and surrogate organ guidance in ORAUT-OTIB-0005 [ORAUT 2019a].

To properly account for the correlation of external dose between dosimeter measurements and the individual organs in Table 4-1, a special DCF has been derived and is used to determine the dose to the appropriate CLL compartments. As described in DCAS-RPT-004, *Chronic Lymphocytic Leukemia (CLL) Dose Conversion Factors* [NIOSH 2012], this blended CLL DCF consists of the weighted fractions of the DCF values in association with the 15 organs in Table 4-1. Dose should be calculated using Monte Carlo techniques to combine distributions for measured (or missed) dose, the blended CLL DCF distribution, and distributions for factors such as neutron-to-photon ratios. Descriptions of the applications of Monte Carlo methods for external dose are outlined in OCAS-IG-001 [NIOSH 2007].

Table 4-1 lists the organs that could require application of a geometry correction factor due either to glovebox work as described in DCAS-TIB-0010, *Best Estimate External Dose Reconstruction for Glovebox Workers* [NIOSH 2011], or to work at uranium facilities as described in DCAS-TIB-0013, *Selected Geometric Exposure Scenario Considerations for External Dose Reconstruction at Uranium Facilities* [NIOSH 2010]. In situations where a geometry correction factor is needed, a blended CLL DCF incorporating the factor (either as a distribution or as a constant) should be used [NIOSH 2012].

Dose assignment to the skin – both penetrating and nonpenetrating – is done in accordance with the guidance in ORAUT-OTIB-0017 [ORAUT 2005a]. Shallow dose (typically open window - shielded) should be assigned to the skin organ without any transmission correction factors due to the small fraction (0.064%) of dose that is assigned to the skin compartment in the CLL model. As described earlier in this section, dose assigned as electrons should use a blended CLL DCF consisting of the skin, testes, breast, and bone marrow organs. Missed shallow dose is assigned in the same manner as all other deep organs (i.e., open window and shielded values are not assessed to determine limit of detection and radiation type). In addition, due to the small area of skin that is associated with extremity dose (<5% of skin area with the hands), the overall dose to the skin from extremity dose is likely to be ≤ 1 mrem (i.e., over 31 rem of extremity dose would be needed to equal 1 mrem of dose to the skin of the extremities). Therefore, extremity dose is not included in the model implementation. Similarly, dose from skin contamination incidents – unless it is a case of whole-body or large-area contamination – should not be added to the skin dose. Situations that involve large-area contamination can be addressed using the guidance in ORAUT-OTIB-0017 [ORAUT 2005a].

5.0 ATTRIBUTIONS AND ANNOTATIONS

All information requiring identification was addressed via references integrated into the reference section of this document.

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