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Subject Expert(s): Elizabeth M. Brackett, Matthew H. Smith, Elyse M. Thomas

Approval:	Signature on File Elizabeth M Brackett, Document Owner	Approval Date:	12/03/2012
Concurrence:	Signature on File John M. Byrne, Objective 1 Manager	Concurrence Date:	11/29/2012
Concurrence:	Signature on File Edward F. Maher, Objective 3 Manager	Concurrence Date:	11/28/2012
Concurrence:	Vickie S. Short Signature on File for Kate Kimpan, Project Director	Concurrence Date:	11/29/2012
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PUBLICATION RECORD

EFFECTIVE DATE	REVISION NUMBER	DESCRIPTION
12/04/2012	00	New document initiated to describe the use of the chronic lymphocytic leukemia model and to provide guidance to dose reconstructors on its application. Incorporates formal internal and NIOSH review comments. Training required: As determined by the Objective Manager. Initiated by Elizabeth M. Brackett.

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ACRONYMS AND ABBREVIATIONS

CAD	Chronic Annual Dose (tool)
CLL	chronic lymphocytic leukemia
DCF	dose conversion factor
DHHS	Department of Health and Human Services
DOE	U.S. Department of Energy
EEOICPA	Energy Employees Occupational Illness Compensation Program Act of 2000
ET2	extrathoracic region 2
FR	Federal Register
HNM	highest nonmetabolic organ
HTO	tritiated water
ICRP	International Commission on Radiological Protection
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
mrem	millirem
NIOSH	National Institute for Occupational Safety and Health
ORAU	Oak Ridge Associated Universities
RBM	red bone marrow
SI	small intestine
SRDB Ref ID	Site Research Database Reference Identification (number)
TIB	technical information bulletin
U.S.C.	United States Code
ULI	upper large intestine
§	section or sections

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). TIBs may be used to assist NIOSH staff in the completion of individual dose reconstructions.

In this document, the word "facility" is used as a general term for an area, building, or group of buildings that served a specific purpose at a site. It does not necessarily connote an "atomic weapons employer facility" or a "Department of Energy (DOE) facility" as defined in the Energy Employees Occupational Illness Compensation Program Act of 2000 [42 U.S.C. § 7384l(5) and (12)].

In a notice of proposed rulemaking published in the Federal Register (FR) on March 21, 2011, the U.S. Department of Health and Human Services (DHHS) proposed to treat chronic lymphocytic leukemia (CLL) as a radiogenic cancer under the Energy Employees Occupational Illness Compensation Program Act of 2000 (EEOICPA) (76 FR 15268). On February 6, 2012, the final rule was published. Under the final rule, CLL will now be treated as being potentially caused by radiation and as potentially compensable under EEOICPA. This reverses an earlier decision by DHHS to exclude this cancer from consideration.

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.

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 Apostoaei 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 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.

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 3-1 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-9 Code,* were used to determine the appropriate organ (ORAUT 2011a).

4.0 GUIDANCE

4.1 MEDICAL X-RAY DOSE

Dose from medical X-ray exposure to each of the compartments comprising the CLL model in Table 3-1 is determined in the usual way, as the product of the incident air kerma and the dose conversion factors (DCFs). Substitute DCFs are used for organs in the model without unique DCFs – as described in ORAUT-OTIB-0006, *Dose Reconstruction from Occupational Medical X-Ray Procedures* (ORAUT 2011b) – and are shown in parentheses in Table 3-1. 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 skin exposed for poorly and properly collimated beams. The area of exposed skin is 3,074 cm^2 (14- by 17-in. on each of the entrance and exit sides) for properly collimated beams, and an area twice this size (6,148 cm^2) for poorly collimated beams (ORAUT-OTIB-0006, ORAUT 2011b). The total skin area for females (16,000 cm^2) from ORAUT-OTIB-0017, *Interpretation of Dosimetry Data for Assignment of Shallow Dose* (ORAUT 2005a) will 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 4-1 provides the exposed skin fractions for estimating the skin dose.

4.2 INTERNAL DOSE

For internal dose calculation, the B lymphocytes compartments correspond to 25 organs, so doses to all 25 of these organs must be calculated to determine the CLL dose to be entered into the Interactive RadioEpidemiological Program (IREP). However, one of these 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. 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.

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]

a. 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).
b. See ORAUT-OTIB-0060, *Internal Dose Reconstruction*, (ORAUT 2007a) for guidance on selection.
c. 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 the geometry correction factor from DCAS-TIB-0013, *Selected Geometric ExposureScenario Considerations for External Dose Reconstruction at Uranium Facilities* (NIOSH 2010).

Table 4-1. 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)

a. Exposure area is 3,074 cm^2 (14- by 17-in. on each of the entrance and exit sides) for properly collimated beams, and twice this area (6,148 cm^2) for poorly collimated beams (ORAUT (2011b)).
b. The total skin area for females (16,000 cm^2) used to calculate the skin dose fraction ORAUT (2005a).

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 vs. 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 Chronic Annual Dose Tool

The Chronic Annual Dose (CAD) Tool has been modified to create files for all relevant organs. A separate file is created for each organ.

4.2.4 Type Super S Material

Adjustment factors from ORAUT-OTIB-0049, *Estimating Doses for Plutonium Strongly Retained in the Lung* (ORAUT 2010) for Type super S material are organ dependent, so the doses to each organ must be adjusted before entry in the CLL tool. The dose to all organs from Type S plutonium must first be assessed, using a consistent set of assumptions for all organs.

4.2.5 Tritium

Dose from tritiated water (HTO) 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 HTO 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 2007b), so 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, as allowed by 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 Chooser tool is used to determine the radionuclide and material type combination that is most favorable to the claimant from a whole-body count where 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

The environmental tool can be used for each organ of interest; one file for each organ in the CLL model must be generated for input to the CLL tool. Although this tool selects the maximizing material type for each organ and these types are not necessarily the same across all organs, environmental doses are typically relatively small so this can be used for a best estimate.

4.2.9 Reactor Mixes

The tool implementing ORAUT-OTIB-0054, *Fission and Activation Product Assignment for Internal Dose-Related Gross Beta and Gross Gamma Analyses* (ORAUT 2007c), selects the maximizing material type for each radionuclide in the mixture based on the organ of interest. If a best estimate is not needed, the files that are generated for each organ of the CLL model can be used as is. As noted in Section 4.2.1, the material type for a given radionuclide must be the same for all organs when a best estimate is needed.

4.3 EXTERNAL DOSE

For external dose calculation, the B lymphocytes compartments correspond to 15 organs as listed in Table 3-1. 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 2011a).

In order to properly account for the correlation of external dose between dosimeter measurements and the individual organs listed in Table 3-1, a special dose conversion factor has been derived and is used to determine the dose to the appropriate CLL compartments. This blended CLL DCF – as described in DCAS-RPT-004, *Chronic Lymphocytic Leukemia Dose Conversion Factors* - is comprised of the weighted fractions of the DCF values associated with the 15 organs listed in Table 3-1 (NIOSH 2012). 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) and ORAUT-OTIB-0012, *Technical Information Bulletin: Monte Carlo Methods for Dose Uncertainty Calculations* (ORAUT 2005c).

Organs that could require application of a geometry correction factor due to glovebox work as described in DCAS-TIB-0010, *Best Estimate External Dose Reconstruction for Glovebox Workers* (NIOSH 2011) - or due 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) - are identified in Table 3-1. In situations where a geometry correction factor is

needed, a blended CLL DCF incorporating the factor (either as a distribution or as a constant) will 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-shallow) 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. In addition, due to the small area of skin that is associated with extremity dose (<5% of skin area is associated 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 skin-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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