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NATIONAL INSTITUTE FOR OCCUPATIONAL SAFETY AND HEALTH

ADVISORY BOARD ON RADIATION AND WORKER HEALTH

TASK 3: REVIEW OF NIOSH/ORAUT PROCEDURES AND METHODS USED FOR DOSE RECONSTRUCTION

A PRELIMINARY REVIEW OF NIOSH'S PROGRAM EVALUATION REPORT OCAS-PER-009, "TARGET ORGANS FOR LYMPHOMAS"

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Task 3: Review of NIOSH/ORAUT Procedures And Methods Used For Dose Reconstruction **A PRELIMINARY REVIEW OF NIOSH'S PROGRAM EVALUATION REPORT OCAS-PER-009, "TARGET ORGANS FOR LYMPHOMAS"**	Page 2 of 44
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EXECUTIVE SUMMARY

During the Advisory Board on Radiation and Worker Health (Advisory Board or Board) conference call held on November 27, 2007, SC&A was directed to perform a review of Program Evaluation Report (PER)-009. The purpose of a PER is to establish a formal process for evaluating the effects of new information on previously adjudicated claims that have been denied. The PER process was developed by the National Institute for Occupational Safety and Health (NIOSH) in recognition that our scientific understanding of the factors that bear on a dose reconstruction is continually improving. In addition, new information could also come to light regarding the nature and types of exposures that a given worker might have experienced. When such new information becomes available, it is incumbent upon NIOSH to re-evaluate worker dose reconstructions that might be impacted by the new information.

As a result of ongoing reviews, it became apparent to NIOSH that the methods being used to reconstruct the doses to workers that contracted lymphoreticular neoplasms (cancer of the lymph nodes) required revision, revisions that could result in very large increases in the derived doses to the organs of concern and the possible reversal of previously denied claims.

The need for a revision to the dose reconstruction methodology became apparent when NIOSH recognized that its standard method for reconstructing the doses to workers with cancer of the lymph nodes, which made use of a surrogate organ, could substantially underestimate the doses to the affected lymph nodes. NIOSH's standard procedure for deriving doses to lymph nodes was based on the assumption that an upper bound on the doses to the organ of concern could be derived by using the colon (or the highest non-metabolic organ) as a surrogate organ. For reasons that are described in the main body of this report, this assumption could result in doses that are low by 2 to 3 orders of magnitude.

In order to address this issue, NIOSH implemented PER-009, which establishes a new protocol for reconstructing the doses to the organ of concern for workers with cancer of the lymph nodes. NIOSH used this new methodology to reconstruct the doses to all workers whose reconstructed doses could be impacted by this new procedure and whose claims were previously denied. The outcome of this process was the re-evaluation of 528 claims. Of these 528 claims, 152 previously denied claims were now granted compensation, 23 claims were returned to NIOSH for rework, and 348 claims remained denied.

Under Task Order 3, the Advisory Board requested that SC&A review the entire process under which the 528 lymphoma claims were reviewed. Our review process was divided into five subtasks, which are individually discussed in the main body of this report.

Our review concluded that OCAS-PER-009 reflects revisions to OCAS-TIB-012 and ORAUT-OTIB-0005, which correct previous deficiencies for the reconstruction of radiation doses to lymphatic tissues associated with the respiratory system. SC&A found that NIOSH was extremely thorough in ensuring that all cases that might be affected by the change in protocol were explicitly addressed.

Our review also identified two issues with potential significance to lymphoreticular neoplasms, but which may be outside of NIOSH's mandate under the Energy Employee Occupational Illness Compensation Program Act (EEOICPA) and its implementing regulations. Our primary concern pertains to the uncertainty associated with the assignment of a definitive International Classification of Diseases (ICD-9) code to a claimant's lymphoma, which in turn directs NIOSH to reconstruct radiation doses to a specific internal and external target organ. It is SC&A's understanding that this concern is outside the purview of NIOSH and may be more appropriately addressed by other agencies.

It is SC&A's opinion that, for various classes of lymphomas and/or stage of the neoplasm, there remains a substantial level of uncertainty regarding (1) the cell-line of origin for the neoplasm, and (2) the anatomical location where the neoplastic transformation and/or clonal expansion took place. While significant refinements in diagnostic methods have reduced the uncertainty in the classification of lymphomas in recent years, of greatest concern are claims in which the cancer diagnosis was made at a time when clinical data were inadequate for the assignment of an ICD-9 code. Uncertainties representing the assignment of ICD-9 codes are discussed in Section 4.3 of this report. As pointed out by NIOSH, the assignment of the ICD-9 code to a claimant's cancer is the sole responsibility of the Department of Labor (DOL). Hence, many of the findings provided in this report may pertain more to those aspects of the PER process under the purview of the DOL than under NIOSH.

A second concern raised by SC&A relates to smoking and its potential impacts on lymphomas associated with lymph nodes of the respiratory tract (LN_{TH} and LN_{ET}). The potential impact of smoking was not addressed in PER-009 and is briefly summarized in Section 5.2 of our report. Regarding the impact of smoking, NIOSH concluded that this is a highly technical issue that cannot be resolved by NIOSH at this time and may require a formal review by an ad hoc committee of scientific experts.

1.0 STATEMENT OF PURPOSE

To support dose reconstruction, the National Institute for Occupational Safety and Health (NIOSH) and the Oak Ridge Associated Universities Team (ORAUT) have assembled a large body of guidance documents, workbooks, computer codes, and tools. In recognition of the fact that all of these supporting elements in dose reconstruction may be subject to revisions, provisions exist for evaluating the effect of such programmatic revisions on the outcome of previously completed dose reconstructions. Such revisions may be prompted by document revisions due to new information, misinterpretation of guidance, changes in policy, and/or programmatic improvements.

The process for evaluating potential impacts of programmatic changes on previously completed dose reconstructions has been proceduralized in OCAS-PR-008, *Preparation of Program Evaluation Reports and Program Evaluation Plans,* (OCAS 2006a), Revision 2, dated December 6, 2006. This procedure describes the format and methodology to be employed in preparing a Program Evaluation Report (PER) and a Program Evaluation Plan (PEP).

A PER provides a critical evaluation of the effect(s) that a given issue/programmatic change may have on previously completed dose reconstructions. This includes a qualitative and quantitative assessment of potential impacts. Most important in this assessment is the potential impacts on the probability of causation (POC) of previously completed dose reconstructions with POCs of <50%.

As needed, a PEP may be issued that serves as a formal notification of an impending PER. The PEP provides a preliminary description of the issue(s) that will be addressed in the PER, and summarizes the likely scope of the effort required to complete the PER.

Under the existing Task Order 3 project, SC&A has been tasked by the Advisory Board to conduct a review of OCAS-PER-009, *Target Organs for Lymphoma* (OCAS 2007). In behalf of the PER review, SC&A performed five subtasks as authorized by the Board, each of which is discussed below.

2.0 SUBTASK 1: CONDUCT A CRITICAL REVIEW AND ANALYSIS OF THE "ISSUE" THAT SERVED AS THE BASIS FOR OCAS-PER-009 AND ASSESS THE CIRCUMSTANCE UNDER WHICH SC&A FIRST BECAME AWARE OF THE ISSUE

On April 2, 2008, the Procedures Review Work Group held a teleconference that specifically assessed Revision 0 of this draft report. Participants in this teleconference included persons representing NIOSH. It was during the teleconference that SC&A was first informed that NIOSH had initiated a formal technical review of issues leading up to PER-009 on or before November 2004. NIOSH explained that on or about July 2004, several members of the NIOSH team discussed the possible need to revise the protocol for reconstructing doses to lymph nodes. Coincidentally, in November 2004, SC&A completed and delivered a draft review of a dose reconstruction for a worker with cancer of the lymph nodes, and discussed the results with NIOSH and the Board. In that report, and during those discussions, SC&A was critical of the protocol and suggested strategies to improve the methods used to reconstruct doses to lymphatic tissue. In the original draft of this report, SC&A was under the impression that it was this review that was the genesis of the PER. However, SC&A was subsequently informed by NIOSH that SC&A's review apparently played no significant role in the genesis of the PER (see Attachment A-1, memorandum from NIOSH to the working group dated April 18, 2008, and Attachment A-2, NIOSH e-mail dated May 1, 2008). As further support for the need for this PER and as part of the PER process, NIOSH had several consultants prepare special reports on this subject, which are reproduced in Attachments B, C, and D. These attachments are discussed below.

3.0 SUBTASK 2: ASSESS NIOSH'S EVALUATION / CHARACTERIZATION OF THE ISSUE AND ITS POTENTIAL IMPACTS ON DOSE RECONSTRUCTION

3.1 REGULATORY BASIS FOR OCAS-PER-009

Section § 82.18(b) of Title 42 Part 82 of the *Code of Federal Regulations* (42 CFR 82) states that, ". . . NIOSH will calculate the dose to the organ or tissue of concern using the appropriate current metabolic models published by ICRP."

Specifically, Section I.G. of the Preamble to the Final Rule for 42 CFR 82 states that, ". . . at this time NIOSH will use the new ICRP respiratory tract model for assessing doses due to the **inhalation** of radioactive particles[1]" [emphasis added]. [Note: Footnote 1 in this citation identifies *ICRP Publication 66: Human Respiratory Tract Model for Radiological Protection* (ICRP 1993).]

3.2 RELEVANT BACKGROUND INFORMATION

For energy employees, inhalation is likely the dominant route for radionuclides to enter the body. Once inhaled, the fate and radiological consequence for a given radionuclide is determined by numerous physical, chemical, and biological factors. Important factors include particle size of the airborne contaminant, its solubility in aqueous media, and its biochemical/metabolic role in human physiology. Collectively, these variables will determine the initial distribution of the airborne contaminant within the respiratory tract, and subsequently the rate(s) of clearance from the respiratory tract, absorption into blood, and/or translocation to and retention by other organs/tissues. All of these factors, as well as the unique radiological properties of the inhaled radionuclides, will determine the radiation dose to individual tissues.

A comprehensive discussion of the complex variables that may affect the radiological consequences of an inhalation exposure is beyond the scope of this review. Instead, the discussion that follows will focus only on those aspects of the inhalation exposure pathway that may impact the radiation dose to lymphatic/hematopoietic tissues and affect their risk to cancer induction.

3.3 OVERVIEW OF THE ICRP RESPIRATORY MODEL

A model for the deposition behavior of airborne particulates in the respiratory tract is characterized in ICRP Publication 66 (ICRP 1993). Figure 1 identifies those compartments in which inhaled particulates may be initially deposited. Inspection of Figure 1 identifies the following compartments:

- Extrathoracic Airways – The extrathoracic airways consist of two distinct regions designated as ET_1 and ET_2. For this discussion, tissues associated with ET_1 are not considered relevant. ET_2 represents the posterior nasal passages, nasopharynx, oropharynx, and larynx.

- Thoracic Airways – Particulates that enter the thoracic airways may be deposited in the bronchi (BB), bronchioles (bb), and the alveolar interstitium (AI).

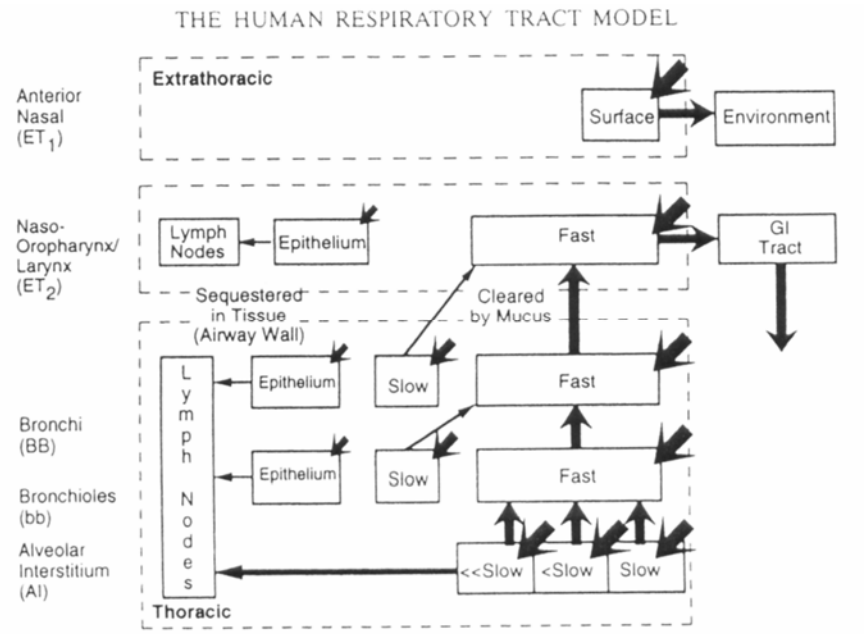

Figure 1. Respiratory Tract Compartment for which Inhaled Particles May Be Deposited
(Source: ICRP 1993)

3.3.1 Deposition Fractions within Respiratory Tract

Particle deposition within the respiratory tract is heavily affected by the particle size distribution, with larger particles differentially depositing in the upper airways. Additional factors affecting the fractional deposition include the age and, therefore, the anatomical dimensions of the individual's airways, and the individual's breathing rate, breathing style (nasal or oro-nasal), and other factors that influence inertial impaction and Brownian diffusion.

Table 1 identifies initial deposition fractions in each of the major regions of the respiratory tract for 5-micrometer (μm) AMAD aerosol inhaled by an adult male nose breather.

Table 1. Compartmental Deposition Fractions
(Source: ICRP 1993, Table F-1)

Region	Deposition Fraction
ET_1	0.34
ET_2	0.40
BB	0.018
Bb	0.011
AI	0.053
Total	0.82

Figures 2 and 3 graphically illustrate reference deposition values for each major compartment as a function of particle size. Reference values are for the adult male nose or mouth breather with a respiration rate of 1.2 cubic meters (m^3) per hour. Important to note are the variable and oscillating deposition fractions for ET_1 and ET_2. For very small particles (i.e., 0.001 µm), the deposition fractions for ET_1 and ET_2 are about 0.4 each (or 0.8 for both). With increased particle size, the deposition fractions decrease and reach a low point for particle sizes of about 0.1 µm before rising again to a plateau of about 0.4 fraction for particle sizes of a few microns.

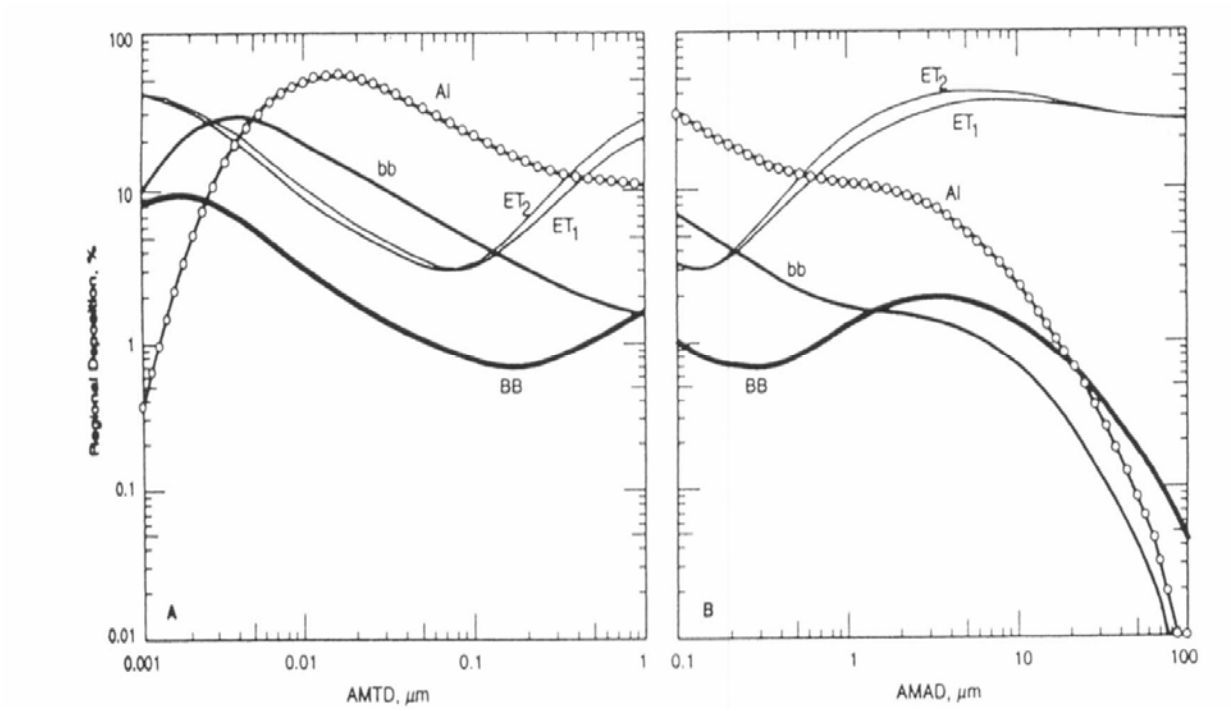

Figure 2. Fractional Deposition in Each Region of Respiratory Tract for Reference Worker (Normal Nose Breather)
(Source: ICRP 1993)

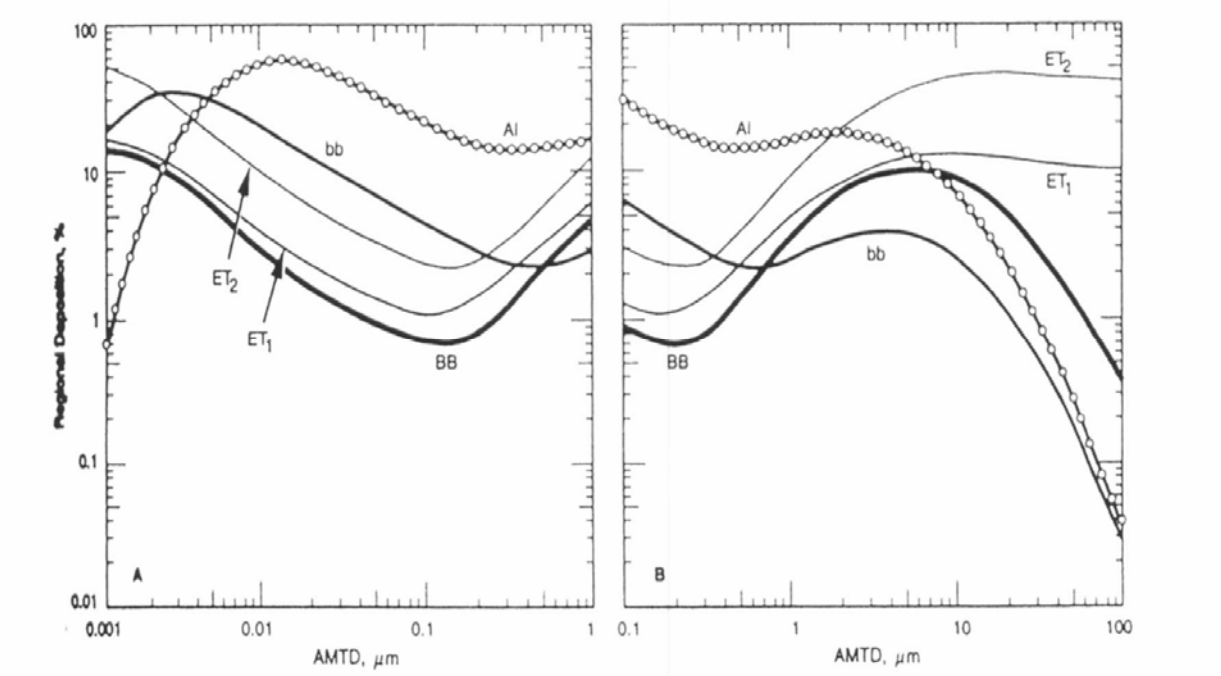

Figure 3. Fractional Deposition in Each Region of Respiratory Tract for Reference Worker (Mouth Breather)
(Source: ICRP 1993)

3.3.2 The ICRP Respiratory Tract Clearance Model

When inhaled particles deposit onto the epithelial lining of the respiratory tract, their rate of removal by absorption and/or mechanical means is highly variable. The ICRP model assumes that particles deposited within the anterior nasal passages (i.e., ET_1 region) are removed by extrinsic means (nose blowing, wiping, etc.) and will, therefore, not be considered within the context of this report.

Material deposited in the nasopharynx, oropharynx, and larynx (or ET_2 region) is subject to rapid clearance in the layer of fluid/mucus that covers this portion of the respiratory tract.

Particles deposited in the thoracic airways representing the BB and bb regions are subject to modest ciliary clearance rates, while materials deposited in the AI region (which is further subdivided among compartments AI_1, AI_2, and AI_3) are successively cleared more slowly. Figure 4 depicts the various compartments of the respiratory tract and provides reference/ clearance rates expressed in terms of the fraction of the material cleared from a given compartment per day (d^{-1}) for completely **insoluble** material. Heavy solid lines define the directional transport over airway surfaces towards the ET_2 compartments, where such particles are swallowed and enter the GI tract. Besides ciliary clearance, a secondary clearance mechanism of **insoluble** particles involves **alveolar macrophages** (AM) that have phagocytized particulate matter and subsequently migrate to regional lymph nodes, where these phagocytic cells may stay for long periods of time. For the ET_2 region, removal by phagocytic alveolar macrophages relocate particulates to extrathoracic lymph nodes (LN_{ET}), while macrophages in

thoracic compartments transfer particles to thoracic lymph nodes (LN_{TH}). Table 2 provides summary data for the clearance rates between individual compartments and their corresponding half-times. Inspection of Table 2 indicates that particles directly deposited in the ET_2 compartment have a rapid clearance rate of 100 d^{-1}, which corresponds to a half-time of 10 minutes. Thus, following an acute exposure, nearly all insoluble materials initially deposited in ET_2 are transferred to the GI tract within the first hour of exposure.

Of interest here, however, are clearance rates from AI_3 to LN_{TH}, bb_{seq} to LN_{TH}, BB_{seq} to LN_{TH}, and ET_{seq} to LN_{ET}. Once macrophages bearing radioactive microparticulates enter a lymph node, the particulates are likely to be released and sequestered within the node for long periods of time. The mean residence time of microparticulates in LN_{TH}/LN_{ET} is estimated at 10,000 days. Histologically, lymph nodes are dense, encapsulated bundles of cells, which, in addition to macrophages, include bone marrow-derived or B-lymphocytes, and thymus-derived or T-lymphocytes. It is estimated that there are more than 600 lymph nodes in the human body, and their size varies from a few millimeters to more than a centimeter. Collectively, the weight of lymph nodes in the adult is estimated between 400 g and 800 g.

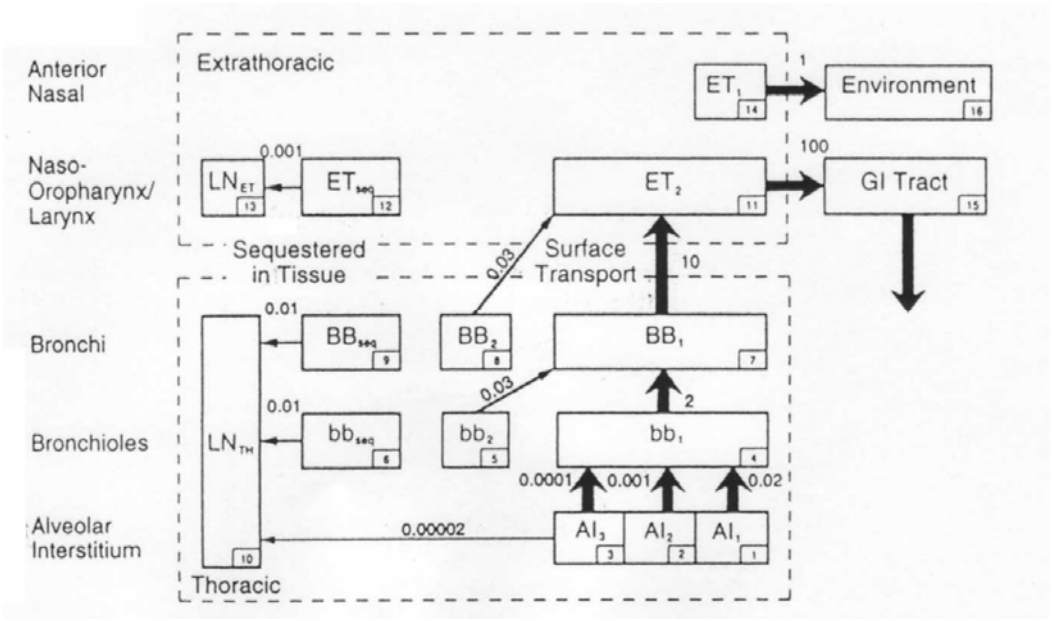

Figure 4. Compartment Model to Represent Time-Dependent Particle Transport from Each Region
(Source: ICRP 1993)

Table 2. ICRP Respiratory Tract Reference Clearance Rates for Insoluble Particulates

Clearance Rates			
From	**To**	**Rate (d^{-1})**	**Half-Time**
AI_1	bb_1	0.002	35 d
AI_2	bb_1	0.001	700 d
AI_3	bb_1	0.0001	7000 d
AI_3	LN_{TH}	0.00002	—
bb_1	BB_1	2	8 h
bb_2	BB_1	0.03	23d
bb_{seq}	LN_{TH}	0.01	70 d
BB_1	ET_2	10	100 min
BB_2	ET_2	0.03	23 d
BB_{seq}	LN_{TH}	0.01	70 d
ET_2	GI tract	100	10 min
ET_{seq}	LN_{ET}	0.001	700 d

3.3.3 Radiological Impacts to Lymph Nodes

Radiation exposure to lymph nodes associated with the respiratory tract are maximized when the inhaled radio-contaminant (1) emits an alpha particle, (2) is highly insoluble, and (3) has a long physical half-life. Thus, lung clearance of microparticulates to regional lymph nodes with small tissue mass results in large time-integrated doses that are well above those of lung tissues. For illustration, ICRP 66 derived 50-year committed effective dose equivalent (CEDE) values for a 1-Bq intake of a long-lived Type S radionuclide emitting a 5.15 MeV alpha particle (Table 3). Inspection of Table 3 shows that in time, LN_{TH} and LN_{ET} will experience doses that are well above those of the lung.

Table 3. Regional Committed Dose Equivalents for Intake of 1 Bq of a Long-Lived, Type S Alpha-Emitter
(Source: ICRP 1993)

Respiratory Tract Region	CEDE (rem)
Extra Thoracic:	
- ET_2	7.94E-03
- LN_{ET}	1.45E-02
Thoracic:	
- BB_{bsal}	5.90E-04
- $BB_{secretory}$	6.44E-03
- bb	3.24E-03
- AI	3.96E-03
- LN_{TH}	5.36E-02

3.4 NIOSH'S RESPONSE TO THE ISSUE

On October 24, 2005, NIOSH issued a white paper entitled, *NIOSH Re-examination of Lymphoma Target Organ Selection* (Ulsh 2005). The White Paper acknowledged that, in the past, dose reconstruction for cancers of the lymphatic and hematopoietic tissues may have been improperly based on the "highest nonmetabolic organ [HNMO]." NIOSH concluded that the use of the HNMO as surrogate tissue for thoracic and extra-thoracic lymph nodes for dose reconstruction may have resulted in dose estimates that were far below those involving select lymphatic tissues.

During technical discussions with NIOSH on April 29, 2008, NIOSH explained that they used the HNMO approach because that approach served them well for other non-metabolic cancers. In addition, NIOSH recognized that the risk coefficients for cancer of the lymph nodes were derived primarily based on epidemiological investigations of Hiroshima and Nagasake exposures, where the populations experienced uniform whole-body exposure to penetrating radiation. Hence, the risk coefficients for cancer of lymphatic tissues were originally derived based on data where all of the lymphatic tissue was acutely exposed. For the purpose of dose reconstruction of workers who might have inhaled highly insoluble alpha emitters, only a small fraction of the lymphatic tissue would have been exposed. Hence, at the time of the development of the original protocol, NIOSH judged that there were off-setting factors (i.e., though the dose to selected lymph nodes might be substantially higher than those derived using the HNMO approach, the risk coefficient cancer of lymphatic tissue, as derived from data associated with uniform whole-body exposures, would tend to overestimate the risk.) However, upon further reflection (see Attachments A, B, and C), NIOSH determined that there was a need to revise the protocol for reconstructing these to lymphatic tissue.

Enclosed herein as Appendices A, B, and C are the full text of the NIOSH White Paper and the supporting documents by Drs. M. Crowther[1] and K. Eckerman,[2] respectively. Revision 0 of OCAS-TIB-012 (OCAS 2005), issued August 15, 2005, reflects recommendations by Dr. Crowther. Subsequently, as a result of comments and suggestions provided by Dr. Eckerman, additional revisions were incorporated in Revision 1 of OCAS-TIB-012 (OCAS 2006b), issued on February 10, 2006. Concurrently, on February 10, 2006, *Internal Dosimetry Organ, External Dosimetry Organ, and IREP Model Selection by ICD-9 Code,* ORAUT-OTIB-0005, Revision 02 PC-1 (ORAUT 2006) was issued, which incorporated organ selections identified in OCAS-TIB-012.

Our review of these documents confirms that NIOSH fully understood the need and technical basis for developing OCAS-TIB-012 and revising ORAUT-OTIB-0005.

[1] Mark Crowther, M.D., MSc., FRCPC, McMaster University, Canada, was hired as a NIOSH consultant.
[2] Keith Eckerman, Ph.D., Oak Ridge National Laboratory, Oak Ridge, Tennessee, was hired as a NIOSH consultant.

4.0 SUBTASK 3: ASSESS NIOSH'S SPECIFIC SOURCES OF INFORMATION TO ENSURE THE CREDIBILITY OF THE CORRECTIVE ACTION AND ITS CONSISTENCY WITH CURRENT/CONSENSUS SCIENCE

It is SC&A's opinion that the core technical issue of OCAS-PER-009 is complex and multi-disciplinary. Corrective action, therefore, not only requires a thorough understanding of radiological models used to quantify the transfer of radio-particulates from the respiratory tract to regional lymph nodes, but also requires a keen understanding of the immunological, cytological, and oncological features that characterize cells and tissues of the lymphatic system. Lastly, it is equally important to recognize clinical limitations that surround the detection, diagnosis, and classification of lymphomas. This is especially true for claims in which the diagnosis was made decades ago.

To provide a level of scientific/clinical expertise, NIOSH enlisted the advice of two outside experts. The first, Mark Crowther, MD, is board certified in internal medicine and hematology. As a result of personal communications with Dr. Crowther that include his consultant report (see Appendix B), NIOSH drafted and issued OCAS-TIB-012, Revision 0 on August 15, 2005.

As acknowledged in NIOSH's White Paper, OCAS-TIB-012 **Revision 0** was subsequently forwarded to Dr. Keith Eckerman, an internationally recognized health physicist, who authored extensive publications related to internal dosimetry and biokinetic modeling. Dr. Eckerman recommended substantial changes, which were incorporated in Revision 1 of OCAS-TIB-012 (OCAS 2006b). As explained by NIOSH in its commentary dated April 18, 2008, the majority of Dr. Eckerman's recommendations were concerned primarily with internal dosimetry issues related to the classification of lymph nodes as LN(TH) and LN(ET), and the magnitude of the resulting doses to those organs.

A review of Dr. Crowther's report (see Appendix B) suggests that even **today,** a substantial level of ambiguity exists in defining the specific cell-line of origin, as well as the primary anatomical location that gave rise to a cancer associated with lymphatic and hematopoietic tissues. Under the Energy Employee Occupational Illness Compensation Program Act of 2000 (EEOICPA), the need to assign a highly definitive International Classification of Diseases (ICD-9) code for cancers diagnosed many years ago is even further hampered by diagnostic/clinical methods that by today's standards are crude at best.

Presented below are excerpts from a standard medical reference text published nearly 30 years ago that further illustrates the difficulties/ambiguities that surround the diagnosis and classification of lymphoreticular neoplasms over time (Beeson et al. 1979).

4.1 EXCERPTS FROM SECTION SEVEN, § 500 – LYMPHORETICULAR NEOPLASMS (BEESON ET AL., 1979)

> *Lymphoreticular neoplasms arise in lymphocytic cells, reticulum cells, or primitive precursor cells… The lymphoreticular cells are located primarily in lymph nodes, thymus, spleen, and liver, but components of the lymphoreticular*

system are also found in the submucosal areas of the respiratory and gastrointestinal tracts as well as the marrow. . .

Lymphoreticular tumors may become clinically apparent as single or multiple tumors in the ***lymph nodes, spleen****, or* ***gastrointestinal tract and may or may not involve the bone marrow****. Since lymphocytes and macrophages also normally occur in the peripheral blood,* ***lymphoreticular tumor cells may circulate*** *. . . The term malignant lymphoma commonly refers to patients who present predominately with solid tumors and must be further classified as to cell type, i.e., histiocytic, lymphocytic, or Hodgekin's… When the marrow and peripheral blood manifestations are prominent as contrasted to tumor or nodal enlargement, the term leukemia or leukemic phase is applied. Thus, in patients with lumphoreticular neoplasms, one sees a complete spectrum from localized tumors only to multiple tumors, leukemias, and mixtures.* ***The presentation at time of diagnosis reflects only a point in time, and the natural progression – untreated or after ineffective therapy – is toward dissemination…***

The ***current approach*** *to classification of lymphoreticular neoplasms, as well as the previously applied terms, is shown in the accompanying table* [reproduced as Table 4 below]. *The use of this classification and the appreciation of* ***chronologic changes*** *in cell type should clear up many of the* ***previous difficulties*** *with confusing names that encompassed* ***grossly different prognostic categories****.*

The diagnosis of lymphoreticular neoplasms ***must always*** *be based on adequate tissue biopsy. Occasionally, multiple biopsies may be needed before the decision as to* ***pathologic classification*** *can be definitively made…* ***cytochemical*** *studies will help clarify the specific cell type and degree of differentiation.*

More recently*, specific markers of the cell surface such as immunoglobulin receptors, complement receptors, immunoglobulin fluorescence, or rosette cell formation have classified cell variants that* ***heretofore were difficult or impossible to categorize****.* [Emphasis added.]

Table 4. Classification of Lymphoreticular Neoplasms*

Proposed Name	Old Name
Lymphoma, Lymphocytic type, well differentiated	Lymphosarcoma
Lymphoma, Lymphocytic type, poorly differentiated	Lymphosarcoma
Lymphoma, histiocytic type	Reticulum cell sarcoma
Lymphoma, mixed lymphocytic-histocytic type	Mixed lymphoma
Lymphoma, undifferentiated pleomorphic type	Stem cell lymphoma
Lymphoma, undifferentiated Burkitt type	Stem cell lymphoma

* From Beeson et al., 1979

4.2 EXCERPTS FROM § 501 – NON-HODGKIN'S LYMPHOMAS (BEESON et al., 1979)

The diagnosis and classification of a lymphoma must be based on careful evaluation of biopsy material. However, in certain instances it may be ***difficult*** *to distinguish benign from malignant disorders.* ***Misinterpretation*** *with respect to histopathologic subclassification are also* ***common****. Frequently the distinction between* ***leukemia*** *and* ***lymphoma*** *cannot be made on the basis of biopsy alone…*

The non-Hodgekin's lymphomas have traditionally been classified according to their morphology under the light microscope. Most of the terminologies used to describe and classify these disorders were proposed long ***before*** *the* ***remarkable developments in immunology of recent years.*** *… As newer techniques in immunology have been applied to the study of the non-Hodgekin's lymphomas, several* ***new classification*** *systems have been suggested.* [Emphasis added.]

4.3 SUMMARY CONCLUSIONS REGARDING THE RELIABILITY OF ICD-9 CODES FOR DOSE RECONSTRUCTION OF LYMPHOMAS

From these statements, it is only fair to conclude that past and even present-day methods for the classification of neoplasms of the reticuloendothelial tissues were/are inconsistent and subject to a high degree of uncertainty. Contributing factors include (1) changes in cancer nomenclature, (2) improved diagnostic equipment and methods for the detection and staging of the cancer, and (3) changes in clinical protocols used to identify the origin of the neoplastic cell lines. Of special concern for some claimants is the time of cancer diagnosis and classification of their cancer that may pre-date the ICD-9 codes, which were first introduced in 1977.

Even when the assignment of an ICD-9 code is regarded with absolute accuracy, the site of exposure/cell-transformation is **not** absolute, as acknowledged by NIOSH in OCAS-TIB-012. For Tables 1, 3, 4, 8, 11, 13, and 14 of OCAS-TIB-012, a significant number of cancers are identified for which the internal target organ is either HNMO or bone marrow, along with either of the following cautionary statements:

- *The site of occurrence is the* ***most likely*** *site of the original injury.* [Emphasis added.]
- *Therefore, the* ***most plausible*** *site of original radiation injury is the bone marrow.* [Emphasis added.]

While SC&A does not question NIOSH's conclusion of a "most likely" or "most plausible" site of the original radiation injury, the need to give the claimant the benefit of doubt must be considered, as specified under 42 CFR 82. Uncertainty regarding the site of the original injury may even include acute lymphocytic leukemia (ICD-9 code 204), which, according to OCAS-TIB-012, consistently identifies the bone marrow as the only potential internal target organ. For example, § 497 in Beeson et al. 1979 states the following:

> ***Acute lymphocytic leukemia*** *arises in lymphoid tissue and is* ***ordinarily*** *first manifest by its presence in marrow. In some instances thymic infiltration precedes overt marrow disease, but it is not known whether the initial leukemogenic event in man is usually* ***extramedullary*** *[i.e., outside the bone marrow]. **Many** instances of **lymphosarcoma** of various cell types culminate in an acute leukemic phase which bears some resemblance to acute **lymphocytic leukemia.*** [Emphasis added]

Thus, a derived internal dose for an alpha-emitting Type S radionuclide (that is falsely based on the red bone marrow as its internal organ when, in fact, the site of injury may have involved LN_{ET} or LN_{TH}) would underestimate the real dose by about 2 orders of magnitude.

As acknowledged in the Executive Summary of this report, assignment of an ICD-9 code is the exclusive responsibility of the DOL and is, therefore, outside of NIOSH's purview. Regardless of which federal agency bears responsibility, SC&A believes that we have an obligation to communicate these concerns to the Board.

5.0 SUBTASK 4: EVALUATE THE PER'S STATED APPROACH FOR IDENTIFYING THE UNIVERSE OF POTENTIALLY AFFECTED DOSE RECONSTRUCTIONS; OR ASSESS THE CRITERIA BY WHICH A SUBSET OF POTENTIALLY AFFECTED DOSE RECONSTRUCTIONS WAS SELECTED FOR RE-EVALUTION

As previously noted, **internal** doses to lymph nodes versus HNMO may differ by as much as 2 or even 3 orders of magnitude. In addition, the issuance of OCAS-TIB-012 Revision 1 changed the **external** target organ from bone marrow to various other organs for many forms of lymphoma. This, too, increased the dose and the resulting POC.

As part of the plan for resolution and corrective action, NIOSH issued OCAS-PEP-009 (OCAS 2006c) on December 8, 2006. In behalf of OCAS-PEP-009, a query of the NIOSH OCAS Claims Tracking System (NOCTS) database identified that prior to February 10, 2006, a total of 528 lymphoma claims had been processed with POCs less than 50% and were, therefore, subject to re-evaluation under OCAS-PER-009.

NIOSH re-evaluated the dose reconstructions for all 528 affected lymphoma claims using the revised guidance documents. The following conclusions for the re-evaluation were reported by NIOSH in OCAS-PER-009 on March 8, 2007:

> *This report is issued indicating a resolution to each of the 528 claims re-evaluated. Of the 528 claims, 23 had been returned to NIOSH for rework for various reasons. These claims were updated using the current dose reconstruction methods so no evaluation under this PER was necessary. Five claims have no current method of dose reconstruction. NIOSH will ask that these claims be returned for rework based on the revision to the lymphoma target organ. Of the remaining 500 claims, 152 claims were found to now result in a probability of causation of greater than 50%, while the remaining 348 claims resulted in the probability of causation remaining below 50%.*

5.1 PRELIMINARY CONCLUSIONS AND RECOMMENDATIONS

Under Subtask 5, SC&A is required to conduct audits of dose reconstructions selected by the Advisory Board that were affected by OCAS-PER-009. At this time, the Board's Work Group on Procedures Review has **not** selected dose reconstructions for SC&A's review. Thus, the final subtask will not commence until the Work Group presents SC&A with its selection of dose reconstructions.

We believe that the audits of these cases should have two objectives. The first pertains to confirming that, given the ICD-9 code assigned by NIOSH, SC&A would confirm that the dose reconstructions were performed in accordance with the current procedures. The second objective would be to assess the degree to which the benefit of the doubt was given to the claimant when assigning ICD-9 codes, taking into consideration the uncertainties and challenges associated with the diagnosis of these types of cancers. SC&A recognizes that this second objective is concerned

with matters that might be outside the purview of NIOSH. Hence, we look to the Board for guidance on whether it is appropriate for the audit to look into this particular issue.

If the Board elects to limit the audit to the first objective, we believe a random sample of three dose reconstructions from the re-evaluated claims will fulfill the objectives of this assignment.

If the Board judges that the audit should try to achieve both objectives, it is SC&A's opinion that a meaningful selection process will require additional information that characterizes a subset of perhaps 10 dose reconstructions from among the 348 dose reconstructions from which 3 dose reconstructions will be selected for audit. This could be accomplished as follows:

- Classify re-evaluated claims based on their original approach used for dose reconstruction, i.e., maximized or best estimate
- Classify re-evaluated claims based on (1) change to the internal target organ, (2) change to the external target organ, and (3) change to both internal and external organs
- Identify the POC of the individual re-evaluated claim
- Identify those re-evaluated claims for which **internal** exposures included (or should have included) in-vivo/in-vitro bioassay data for U, Pu, Am, and/or Th

This information can be readily summarized for each of the 10 dose reconstructions in a spreadsheet, as illustrated in Table 5.

Table 5. Sample Information

DR ID #	ICD-9 Code	Target Organ		DR Method		POC (%)		Year of Cancer Diagnosis	Exposure to α-Emitters
		Internal	External	Original	New	Original	New		
Claim 001	200.84	LN_{TH}	Lung	Maximized	Best Estimate	18%	46%	1976	U, Pu
↓									
Claim 348									

5.2 SMOKING AS MODIFYING AGENT THAT MAY REQUIRE FURTHER CONSIDERATION

Smoking causes histological and cytological alterations within the respiratory tract. Most relevant to this discussion is the impairment of the tracheobronchial mucociliary transport/clearance mechanism. The impaired ciliary clearance mechanism of a smoker implies a longer residency time of particulates in the lung and a likely shift towards lung clearance by alveolar macrophages that involve LN_{TH} and LN_{ET}. ICRP (1993) notes the following:

> *. . . A major cytologic feature in smokers is a considerable increased alveolar macrophages population . . . Whereas a nonsmoker usually has about **5 billion** macrophages, a smoker might have as many as **70 billion** or more.*
> [Emphasis added.]

It is safe to assume that the more than 14-fold increase in alveolar macrophages among smokers will profoundly increase the transfer of activity to LN_{TH} and LN_{ET}. The ICRP, however, offers no further discussion on the radiological impacts of smoking. In the absence of information, a reasonable approach might assume that the increased number of alveolar macrophages would proportionately increase the fractional amount of radioactivity transferred to and concentrated in the regional lymph modes.

On the basis of first principles, it is only reasonable to conclude that the elevated number of alveolar macrophages would significantly enhance the relocation of respired radioparticulates to LN_{TH} and LN_{ET} and proportionately raise their radiation exposure. In brief, for a common inhalation intake, smokers are likely to be at greater risk for lymphoma than non-smokers.

During the procedures review work group teleconference on April 2, 2008, NIOSH stated that there are many uncertainties associated with modeling the biokinetics of the clearance of particles deposited in the deep lung and transferred to thoracic lymph nodes for smokers. In addition, due to changes in the morphology of the lymph nodes of smokers and the radiation doses that lymph nodes of smokers experience due to natural radioactivity in tobacco, along with other confounding factors, it is not possible at this time to explicitly address this issue, given the state of the scientific understanding of this subject. SC&A agrees with this perspective and suggests that this subject might best be addressed by NIOSH as a global scientific issue.

6.0 SUBTASK 5: CONDUCT AUDITS OF DOSE RECONSTRUCTIONS SELECTED BY THE ADVISORY BOARD, WHICH WERE AFFECTED BY OCAS-PER-009

Before reviewing specific dose reconstructions for compliance with OCAS-TIB-012, SC&A also assessed the Integrated Modules for Bioassay Analysis (IMBA) software (ACJ 2002) in order to verify its consistency with the ICRP Publication 66 (ICRP 1993) for deriving dose estimates for select tissues. Specifically, SC&A assessed dose ratios among tissues as given in Table 24 of ICRP Publication 66 and compared these to dose ratios calculated by IMBA. For this comparison, SC&A ran IMBA using the following arbitrary input parameters:

(1) A 24-hour urine sample yielded an excretion of 1 dpm/day for Pu-239, Type S

(2) The inhalation intake was confined to a single acute exposure that occurred 30 days prior to the date of urine collection

(3) CEDE values were calculated for 5 μm and 1 μm particles

Table 6 provides the corresponding CEDE values for various regions of the respiratory tract, lymph nodes (LN_{TH} and LN_{ET}), and other organs/tissues. Important to note is that the two highest doses correspond to LN_{TH} and LN_{ET}. For example, the dose to LN_{TH} is more than 10 times the dose to the lung and more than 100 times that of the red bone marrow. A comparison of IMBA dose ratios with ratios defined in Table 24 of ICRP Publication 66 shows nearly identical values (small differences can be attributed to the fact that ICRP values are based on a hypothetical alpha emitter of 5.15 MeV particles with no beta/gamma emission).

6.1 AUDIT OF DOSE RECONSTRUCTIONS INVOLVING LYMPHOMAS

This section will be completed following receipt of dose reconstructions selected by the Work Group.

Table 6. Dose Distribution for a Single Acute Intake of Pu-239

IMBA Generated CEDE Values			
5 µm Particles		**1 µm Particles**	
Target Organs	**Equivalent Dose (rem)**	**Target Organs**	**Equivalent Dose (rem)**
Adrenals	1.52E+00	Adrenals	1.73E+00
Urinary Bladder	1.52E+00	Urinary Bladder	1.73E+00
Brain	1.52E+00	Brain	1.73E+00
Breast	1.52E+00	Breast	1.73E+00
Gall Bladder	1.52E+00	Gall Bladder	1.73E+00
Heart Wall	1.52E+00	Heart Wall	1.73E+00
Kidneys	3.81E+00	Kidneys	4.34E+00
Liver	1.87E+02	Liver	2.13E+02
Muscle	1.52E+00	Muscle	1.73E+00
Ovaries	1.16E+01	Ovaries	1.33E+01
Pancreas	1.52E+00	Pancreas	1.73E+00
Testes	1.19E+01	Testes	1.35E+01
Thyroid	1.52E+00	Thyroid	1.73E+00
R.B.M.	4.37E+01	R.B.M.	4.98E+01
Bone Surface	8.81E+02	Bone Surface	1.00E+03
Stomach	1.53E+00	Stomach	1.74E+00
S.I.	1.53E+00	S.I.	1.74E+00
U.L.I.	1.60E+00	U.L.I.	1.77E+00
L.L.I.	1.76E+00	L.L.I.	1.84E+00
Skin	1.52E+00	Skin	1.73E+00
Spleen	1.52E+00	Spleen	1.73E+00
Thymus	1.52E+00	Thymus	1.73E+00
Uterus	1.52E+00	Uterus	1.73E+00
ET	7.75E+02	ET	2.49E+02
Lung	4.55E+02	Lung	4.70E+02
Colon	1.67E+00	Colon	1.80E+00
ET1	1.56E+01	ET1	5.88E+00
ET2	7.75E+02	ET2	2.49E+02
LN(ET)	1.40E+03	LN(ET)	4.48E+02
BBsec	6.32E+02	BBsec	3.82E+02
BBbas	5.78E+01	BBbas	2.61E+01
bb	3.23E+02	bb	3.64E+02
AI	6.85E+02	AI	8.28E+02
LN(TH)	4.82E+03	LN(TH)	4.89E+03
Esophagus	1.52E+00	Esophagus	1.73E+00
Gonads	1.19E+01	Gonads	1.35E+01
Spare	0.00E+00	Spare	0.00E+00
Remainder	1.92E+00	Remainder	1.88E+00

7.0 REFERENCES

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APPENDIX A-1: NIOSH MEMORANDUM DATED APRIL 18, 2008

April 18, 2008

NIOSH Comments on SC&A's Draft of SCA-TR-Task3-0008, Rev. 1
A Preliminary Review of NIOSH's Program Evaluation Report OCAS-PER_009
Target Organs for Lymphomas

SCA-TR-TASK3-0008, Rev. 1, Page 5:

As a result of ongoing internal reviews, including the review of dose reconstructions performed by SC&A, it became apparent to NIOSH that the methods being used to reconstruct the doses to workers that contracted lymphoreticular neoplasms (cancer of the lymph nodes) required revision; revisions that could result in very large increases in the derived doses to the organs of concern and the possible reversal of previously denied claims.

NIOSH comment:

As discussed during the April 2, 2008 conference call, the SC&A review of dose reconstructions was not a contributor to NIOSH's decision to review target organ selection for cancers of the lymphatic/hematopoietic system. The review comment made by SC&A (see exhibit #1 on page 10) referred to a case of Hodgkin's lymphoma. The revision to our approach in selecting organs for Hodgkin's lymphoma remains unchanged from the time that this case was completed. That is, the site of diagnosis is considered to be the site of origin for Hodgkin's lymphoma. Thus, our response to the review comment is still valid.

NIOSH's decision to review our approach to dealing with lymphomas was initiated by informal oral comments made to NIOSH by members of the public, which preceded SC&A's dose reconstruction review.

SCA-TR-TASK3-0008, Rev. 1, Page 5:

The need for a revision to the dose reconstruction methodology became apparent when NIOSH recognized that its standard method for reconstructing the doses to workers with cancer of the lymph nodes was fundamentally flawed. NIOSH's standard procedure for deriving doses to lymph nodes was based on the erroneous assumption that an upper bound on the doses to the organ of concern could be derived by using the colon (or the highest non-metabolic organ) as a surrogate organ.

NIOSH comment:

NIOSH has never stated or concluded that our previous dose reconstruction methodology was "fundamentally flawed". The previous methodology accurately reflected our scientific understanding of the issue at the time. Subsequently, new information became available and NIOSH revised our dose-reconstruction methodology accordingly. This is an example of NIOSH seriously considering comments received from members of the public, and our commitment that dose reconstruction methodology be based on the best available scientific information.

SCA-TR-TASK3-0008, Rev. 1, Page 5:

Our review concluded that OCAS-PER-009 reflects revisions to OCAS-TIB-012 and ORAUT-OTIB-0005, which correct previous deficiencies for the reconstruction of radiation doses to lymphatic tissues associated with the respiratory system.

NIOSH comment:

In other instances in SC&A's report, this issue is characterized as a "problem" with NIOSH's previous dose-reconstruction methodology. NIOSH does not concur with the implication that this issue represents a "problem" or "deficiency" in the previous dose reconstruction methodology. The previous methodology accurately reflected our scientific understanding of the issue at the time. The methodology was revised to reflect the latest scientific information.

SCA-TR-TASK3-0008, Rev. 1, Page 6:

It is SC&A's opinion that for various classes of lymphomas and/or stage of the neoplasm, there remains a substantial level of uncertainty regarding (1) the cell-line of origin for the neoplasm, and (2) the anatomical location where the neoplastic transformation and/or clonal expansion took place. While significant refinements in diagnostic methods have reduced the uncertainty in the classification of lymphomas in recent years, of greatest concern are claims in which the cancer diagnosis was made at a time when clinical data were inadequate for the assignment of an ICD-9 code.

NIOSH comment:

NIOSH agrees that there are certain classes of lymphomas for which there exist current and historic uncertainties regarding the cells of origin, and where in the body radiation might interact with these cells to subsequently form a neoplasm. This uncertainty is the reason NIOSH has chosen to make the very claimant-favorable assumption that these interactions may have occurred, for example, in the thoracic lymph nodes for non-Hodgkin's lymphomas.

NIOSH, however, disagrees with SC&A's opinion that these uncertainties apply to Hodgkin's lymphoma and a few other classes of lymphoma which involve immobile cells forming the lymphatic system. The ability to accurately distinguish between Hodgkin's and non-Hodgkin's lymphoma has existed for close to a hundred years. While understanding of the origins of these diseases has certainly evolved over the years, the contemporary assignment of the ICD-9 code reflects this accumulated knowledge. That is, the ICD 9 codes are assigned by DOL to each cancer at the time the application is received from the claimant. For situations where the medical files are unclear or contain ambiguity, DOL has the ability to provide NIOSH with codes that reflect this uncertainty. NIOSH strongly disagrees with SC&A's argument that the described historical uncertainties of the origins and etiology of certain lymphomas impacts the reliability of ICD-9 code assignment, which occurs when the claim is filed.

SCA-TR-TASK3-0008, Rev. 1, Page 6:

Regarding the impact of smoking, NIOSH concluded that this is a highly technical issue that cannot be resolved by NIOSH and may require a formal review by an ad hoc committee of scientific experts.

NIOSH comment:

NIOSH does not recall stating this conclusion. Rather, it is NIOSH's opinion that SC&A's arguments regarding the potential impact of smoking are speculative in nature, and the current scientific evidence is not sufficient to justify the adoption of SC&A's position. NIOSH believes that a general increase in macrophage activity due to smoking must be considered in the context of a number of factors, including: 1) the concomitant intake of natural radioactivity in cigarette smoke; 2) the increase in the mass of the lymph nodes due to accumulation of deposited smoke particles; and 3) the sequestering of dozens of known chemical carcinogens in the lymph nodes by the macrophages.

SCA-TR-TASK3-0008, Rev. 1, Page 8:

On April 2, 2008, the Procedures Review Work Group held a teleconference that specifically assessed Revision 0 of this draft report. Participants in this teleconference included persons representing NIOSH. It was during the teleconference that SC&A was first informed that NIOSH had initiated a formal technical review of issues leading up to PER-009 on or before November 2004. Specific dates and details surrounding the circumstances, which may have served as the initial trigger for OCAS-PER-009 were neither discussed during the teleconference nor provided in a white paper enclosed herein as Appendix A. Therefore, what follows below is only a partial and incomplete assessment of the circumstances that may have served as the basis for OCAS-PER-009.

NIOSH comment:

NIOSH responded to specific inquiries from SC&A regarding the date the NIOSH white paper was issued. SC&A never consulted NIOSH regarding our motivation for initiating our investigation of the target organ selection issue for lymphatic/hematopoietic cancers. NIOSH was unaware that this was an issue upon which SC&A was reporting until we received SC&A's draft report. Revision 0 of this report stated that SC&A's review of a dose-reconstruction contributed to NIOSH's decision to review this issue. NIOSH addressed SC&A's statement during the April 2, 2008 Working Group meeting, yet Revision 1 of SC&A's report (page 5) still makes this claim.

It is NIOSH's opinion that our motivation for investigating this issue is not germane to the technical adequacy of our resulting revisions to target organ selection. If this is an issue that SC&A feels the need to discuss in their report, then the reported timeline and motivations for our investigation should be accurate.

SCA-TR-TASK3-0008, Rev. 1, Page 17:

Enclosed herein as Appendices A, B, and C are the full text of the NIOSH White Paper and the supporting documents by Drs. M. Crowther[1] and K. Eckerman,[2] respectively. Revision 0 of OCAS-TIB-012 (OCAS 2005), issued August 15, 2005, reflects recommendations by Dr. Crowther. Subsequently, as a result of comments and suggestions provided by Dr. Eckerman, substantial revisions were incorporated in Revision 1 of OCAS-TIB-012 (OCAS 2006b), issued on February 10, 2006.

NIOSH comment:

SC&A's statement can be interpreted as implying that the recommendations of Dr. Eckerman conflicted with those of Dr. Crowther, and that this necessitated revision of OCAS-TIB-012. While it is understandable how SC&A could have come to this conclusion, it is not entirely accurate. Revision 0 of OCAS-TIB-012 reflected NIOSH's discussions with Dr. Crowther regarding the possible origins of various classes of lymphoma. Dr. Crowther does not have expertise in internal modeling of radionuclide transport and deposition. The classification of lymph nodes as LN(TH) and LN(ET), and the magnitude of the resulting doses to those organs, is a health physics designation, specific to internal modeling. To cover this aspect of the issue, we solicited Dr. Eckerman's review. As SC&A notes, and as discussed in NIOSH's white paper, Dr. Eckerman recommended that we select LN(TH) rather than LN(ET) if our criteria was claimant favorability. We accepted Dr. Eckerman's recommendation and revised OCAS-TIB-012 accordingly.

SCA-TR-TASK3-0008, Rev. 1, Page 18:

Dr. Eckerman recommended substantial changes, which were incorporated in Revision 1 of OCAS-TIB-012 (OCAS 2006).

NIOSH comment:

As discussed in NIOSH's white paper, the most substantial change recommended by Dr. Eckerman was the selection of LN(TH) rather than LN(ET), because the former is claimant-favorable.

SCA-TR-TASK3-0008, Rev. 1, Page 18:

*A review of Dr. Crowther's report (see Appendix B) suggests that even **today,** there exists a substantial level of ambiguity for defining the specific cell-line of origin, as well as the primary anatomical location that gave rise to a cancer associated with lymphatic and hematopoietic tissues. Under Energy Employee Occupational Illness Compensation Program Act of 2000 (EEOICPA), the need to assign a highly definitive International Classification of Diseases (ICD-9) code for cancers diagnosed many years ago is even further hampered by diagnostic/clinical methods that by today's standard are crude at best.*

NIOSH comment:

NIOSH questions SC&A's interpretation of Dr. Crowther's report. Dr. Crowther, who is a highly qualified hematologist, reviewed our revised target organ selections and concurred with our revisions.

NIOSH agrees that there are certain classes of lymphomas for which there exist current and historic uncertainties regarding the cells of origin, and where in the body radiation might interact with these cells to subsequently form a neoplasm. This uncertainty is the reason NIOSH has chosen to make the very claimant-favorable assumption that these interactions may have occurred, for example, in the thoracic lymph nodes for non-Hodgkin's lymphomas. However, NIOSH disagrees with SC&A's application of these uncertainties to Hodgkin's lymphoma and a few other classes of lymphoma which involve immobile cells forming the lymphatic system. The ability to accurately distinguish between Hodgkin's and non-Hodgkin's lymphoma has existed for close to a hundred years. While understanding of the

origins of these diseases has certainly evolved over the years, the contemporary assignment of the ICD-9 code reflects this accumulated knowledge. NIOSH strongly disagrees with SC&A's argument that the described historical uncertainties of the origins and etiology of certain lymphomas in any way impacts the reliability of ICD-9 code assignment, which occurs when the claim is filed.

The EEOICPA prescribes that the benefit of the doubt be given to the claimant when science alone is insufficient to choose between multiple plausible alternatives. However, the alternatives must be *plausible*. The very radiogenicity of Hodgkin's disease (and similar lymphomas) is questionable, as no consistent relationship between ionizing radiation exposure and Hodgkin's disease has been observed in the many radioepidemiological studies conducted to date. If SC&A's recommendations were accepted, it would result in Hodgkin's disease being one of the most compensated cancers in the EEOICPA program. This is inconsistent with the epidemiological evidence. Combined with the opinion of a well-qualified hematologist, this suggests that SC&A's recommendations are not scientifically plausible.

SCA-TR-TASK3-0008, Rev. 1, Pages 18-19:

EXCERPTS FROM SECTION SEVEN, § 500 LYMPHORETICULAR NEOPLASMS (BEESON ET AL., 1979)

Lymphoreticular neoplasms arise in lymphocytic cells, reticulum cells, or primitive precursor cells . . . The lymphoreticular cells are located primarily in lymph nodes, thymus, spleen, and liver, but components of the lymphoreticular system are also found in the submucosal areas of the respiratory and gastrointestinal tracts as well as the marrow. . .

Lymphoreticular tumors may become clinically apparent as single or multiple tumors in the ***lymph nodes, spleen****, or* ***gastrointestinal tract and may or may not involve the bone marrow****. Since lymphocytes and macrophages also normally occur in the peripheral blood,* ***lymphoreticular tumor cells may circulate*** *. . . The term malignant lymphoma commonly refers to patients who present predominately with solid tumors and must be further classified as to cell type, i.e., histiocytic, lymphocytic, or Hodgekin's . . . When the marrow and peripheral blood manifestations are prominent as contrasted to tumor or nodal enlargement, the term leukemia or leukemic phase is applied. Thus, in patients with lumphoreticular neoplasms, one sees a complete spectrum from localized tumors only to multiple tumors, leukemias, and mixtures.* ***The presentation at time of diagnosis reflects only a point in time, and the natural progression – untreated or after ineffective therapy is toward dissemination****. . .*

The ***current approach*** *to classification of lymphoreticular neoplasms, as well as the previously applied terms, is shown in the accompanying table* [reproduced as Table 4 below]. *The use of this classification and the appreciation of* ***chronologic changes*** *in cell type should clear up many of the* ***previous difficulties*** *with confusing names that encompassed* ***grossly different prognostic categories****.*

*The diagnosis of lymphoreticular neoplasms **must always** be based on adequate tissue biopsy. Occasionally, multiple biopsies may be needed before the decision as to **pathologic classification** can be definitively made . . . . **cytochemical** studies will help clarify the specific cell type and degree of differentiation.*

***More recently**, specific markers of the cell surface such as immunoglobulin receptors, complement receptors, immunoglobulin fluorescence, or rosette cell formation have classified cell variants that **heretofore were difficult or impossible to categorize**.* [Emphasis added.]

NIOSH comment:

NIOSH has not reviewed the textbook cited by SC&A, however, we note that the quoted section speaks generally about lymphoreticular neoplasms, which would include all lymphomas. There is nothing in the quoted text which suggests that there is ambiguity differentiating between Hodgkin's and non-Hodgkin's lymphoma, which is the relevant question for target organ selection.

SCA-TR-TASK3-0008, Rev. 1, Page 19-20:

EXCERPTS FROM § 501 – NON-HODGKIN'S LYMPHOMAS (BEESON ET AL., 1979)

*The diagnosis and classification of a lymphoma must be based on careful evaluation of biopsy material. However, in certain instances it may be **difficult** to distinguish benign from malignant disorders. **Misinterpretation** with respect to histopathologic subclassification is also **common**. Frequently the distinction between **leukemia** and **lymphoma** cannot be made on the basis of biopsy alone….*

*The non-Hodgekin's lymphomas have traditionally been classified according to their morphology under the light microscope. Most of the terminologies used to describe and classify these disorders were proposed long **before** the **remarkable developments in immunology of recent years.** . . . As newer techniques in immunology have been applied to the study of the non-Hodgekin's lymphomas, several **new classification** systems have been suggested.* [Emphasis added.]

NIOSH comment:

It is unclear why SC&A quoted the 29-year old Beeson text regarding uncertainties relevant to non-Hodgkin's lymphoma. NIOSH has already addressed this uncertainty. NIOSH agrees that there are current and historic uncertainties regarding the cells of origin, and where in the body radiation might interact with these cells to subsequently form a neoplasm in the case of non-Hodgkin's lymphoma. This uncertainty is the reason NIOSH has chosen to make the very claimant-favorable assumption that these interactions may have occurred, for example, in the thoracic lymph nodes. However, NIOSH disagrees with SC&A's opinion that these uncertainties apply to Hodgkin's lymphoma and a few other classes of lymphoma which involve immobile cells forming the lymphatic system. The ability to accurately distinguish between Hodgkin's and non-Hodgkin's lymphoma has existed for close to a hundred years. While understanding of the origins of these diseases has certainly evolved over the years, the

contemporary assignment of the ICD-9 code reflects this accumulated knowledge. NIOSH strongly disagrees with SC&A's argument that the described historical uncertainties of the origins and etiology of certain lymphomas in any way impacts the reliability of ICD-9 code assignment, which occurs when the claim is filed.

SCA-TR-TASK3-0008, Rev. 1, Page 20:

From these statements, it is only fair to conclude that past and even present-day methods for the classification of neoplasms of the reticuloendothelial tissues were/are inconsistent and subject to a high degree of uncertainty.

NIOSH comment:

NIOSH agrees that there are current and historic uncertainties regarding the cells of origin, and where in the body radiation might interact with these cells to subsequently form a neoplasm in the case of non-Hodgkin's lymphoma. This uncertainty is the reason NIOSH has chosen to make the very claimant-favorable assumption that these interactions may have occurred, for example, in the thoracic lymph nodes. However, NIOSH disagrees with SC&A's opinion that these uncertainties apply to Hodgkin's lymphoma and a few other classes of lymphoma which involve immobile cells forming the lymphatic system. The ability to accurately distinguish between Hodgkin's and non-Hodgkin's lymphoma has existed for close to a hundred years. While understanding of the origins of these diseases has certainly evolved over the years, the contemporary assignment of the ICD-9 code reflects this accumulated knowledge. NIOSH strongly disagrees with SC&A's argument that the described historical uncertainties of the origins and etiology of certain lymphomas in any way impacts the reliability of ICD-9 code assignment, which occurs when the claim is filed.

SCA-TR-TASK3-0008, Rev. 1, Page :

*Even when the assignment of an ICD-9 code is regarded with absolute accuracy, the site of exposure/cell-transformation is **not** absolute, as acknowledged by NIOSH in OCAS-TIB-012. For Tables 1, 3, 4, 8, 11, 13, and 14 of OCAS-TIB-012, a significant number of cancers are identified for which the internal target organ is either HNMO or bone marrow, along with either of the following cautionary statements:*

- *The site of occurrence is the **most likely** site of the original injury. [Emphasis added.]*
- *Therefore, the **most plausible** site of original radiation injury is the bone marrow. [Emphasis added.]*

While SC&A does not question NIOSH's conclusion of a "most likely" or "most plausible" site of the original radiation injury, the need to give the claimant the benefit of doubt must be considered, as specified under 42 CFR 82.

NIOSH comment:

The need to give the benefit of the doubt to the claimant is exactly what motivated NIOSH to revise the target organ assignment for non-Hodgkin's lymphoma. However, EEOICPA does not prescribe that NIOSH ignore scientific plausibility. SC&A's recommendations regarding Hodgkin's lymphoma are not scientifically plausible.

The text from OCAS-TIB-012 quoted by SC&A reflects prudent scientific caution. The weight of the current scientific evidence suggests that it is plausible that non-Hodgkin's lymphoma could have originated anywhere in the body, and benefit of the doubt dictates that NIOSH make claimant-favorable assumptions for target organ selection for this disease. The weight of the current scientific evidence also indicates that for Hodgkin's disease (and similar lymphomas), the site of occurrence is the most likely site of original radiation injury, and this is also reflected in OCAS-TIB-012.

Of course NIOSH cannot guarantee with absolute certainty that future scientific evidence won't indicate changes from the procedures in OCAS-TIB-012, and it is unreasonable for SC&A to predicate its recommendations upon such a demand. If future scientific evidence reverses current understanding on this issue, NIOSH will revise our procedures accordingly.

SCA-TR-TASK3-0008, Rev. 1, Page 20:

Uncertainty regarding the site of the original injury may even include acute lymphocytic leukemia (ICD-9 code 204), which, according to OCAS-TIB-012, consistently identifies the bone marrow as the only potential internal target organ. For example, § 497 in Beeson et al. 1979 states the following:

> ***Acute lymphocytic leukemia*** *arises in lymphoid tissue and is* ***ordinarily*** *first manifest by its presence in marrow. In some instances thymic infiltration precedes overt marrow disease, but it is not known whether the initial leukemogenic event in man is usually* ***extramedullary*** *[i.e. outside the bone marrow]. **Many** instances of **lymphosarcoma** of various cell types culminate in an acute leukemic phase which bears some resemblance to acute **lymphocytic leukemia**.* [Emphasis added]

NIOSH comment:

The report by Dr. Crowther clearly states, "In general, anything currently classified as a Leukemia (including those discussed below that I feel should be reclassified as leukemia) should be classified as red bone marrow under IMBA applicable organ". Dr. Crowther does not make an exception for ALL. Dr. Crowther's report describes that semantic arguments could probably be made about whether every single case fits this description, however the weight of the current scientific evidence suggests bone marrow as the appropriate target organ for ALL. It is NIOSH's opinion that ignoring the advice of a highly qualified hematologist on the basis of a 29-year old textbook is not prudent.

SCA-TR-TASK3-0008, Rev. 1, Page 23:

It is safe to assume that the more than 14-fold increase in alveolar macrophages among smokers will profoundly increase the transfer of activity to LN_{TH} and LN_{ET}. The ICRP, however, offers no further discussion on the radiological impacts of smoking. In the absence of information, a reasonable approach might assume that the increased number of alveolar macrophages would proportionately increase the fractional amount of radioactivity transferred to and concentrated in the regional lymph modes.

NIOSH comment:

SC&A has presented no evidence that there is any correlation whatsoever between the number of alveolar macrophages and additional incorporation of radioactivity in the thoracic or extrathoracic lymph nodes. Even if such a correlation could be made, the overall increase in risk associated with this activity would have to be modeled, as previously described, in the context of all relevant information. To our knowledge, this information does not exist. The ICRP apparently did not feel that the scientific evidence justified making any recommendations on this issue. If SC&A has any evidence in this regard, NIOSH would be very interested in reviewing it.

SCA-TR-TASK3-0008, Rev. 1, Page 23:

On the basis of first principles, it is only reasonable to conclude that the elevated number of alveolar macrophages would significantly enhance the relocation of respired radioparticulates to LN_{TH} and LN_{ET} and proportionately raise their radiation exposure.

NIOSH comment:

History is replete with reasonable-sounding speculations that are nonetheless wrong. NIOSH cannot base dose-reconstructions on unproven speculation. If SC&A has any evidence to back up these arguments, NIOSH would be very interested in reviewing it.

SCA-TR-TASK3-0008, Rev. 1, Page 23:

During the Procedures Review Work Group teleconference on April 2, 2008, NIOSH stated that ". . . Due to the technical nature of this issue, a credible/quantitative assessment may be outside the scope of NIOSH's responsibility."

NIOSH comment:

NIOSH does not recall making this statement as it is written. We did state that this is a highly technical issue; however, we do not recall asserting that an issue being highly technical puts it outside NIOSH's responsibility. We also stated our position that SC&A was inappropriately selecting factors which might increase the dose, but neglecting factors which might decrease the dose (such as increased mass of the thoracic lymph nodes). We concluded the current scientific evidence does not support making the adjustments for smoking that SC&A is recommending.

APPENDIX A-2: NIOSH E-MAIL DATED MAY 1, 2008

K. Behling

From: Ulsh, Brant A. (CDC/NIOSH/OD) [bau6@cdc.gov]
Sent: Thursday, May 01, 2008 3:01 PM
To: jmauro@scainc.com; H. Behling
Cc: Neton, Jim (CDC/NIOSH/OD); Elliott, Larry J. (CDC/NIOSH/OD); Sundin, David S. (CDC/NIOSH/OD)
Subject: Lymphoma information

John and Hans:
Recall that during our lymphoma conference call on April 29, I talked about a discussion I had with David Richardson and Richard Miller in the Washington DC subway. It was during this discussion that they raised the issue of lymphoma target organs to me. This discussion occurred on my way back to the airport following a meeting on chronic lymphocytic leukemia sponsored by another group in NIOSH. The date of this discussion was July 21, 2004. I want to emphasize again that this discussion was unrelated to the topic of the meeting - I just remember that it occurred after that particular meeting. Upon my return to the office, I raised the issue with Jim Neton, and he told me that he had been thinking about this issue for some time. It was at this point (on or about July 22, 2004) that Jim directed me to look into this issue further, and the end result of this process was OCAS-TIB-0012, which I authored.

Since I am not routinely involved in SC&A's dose-reconstruction reviews and NIOSH activities related to them, I had not even seen SC&A's dose-reconstruction audit results, which your report states were submitted to NIOSH on November 1, 2004. That's why I was very surprised by SC&A's statement that, "As a result of ongoing internal reviews, **including the review of dose reconstructions performed by SC&A, it became apparent to NIOSH that the methods being used to reconstruct the doses to workers that contracted lymphoreticular neoplasms (cancer of the lymph nodes) required revision**;..." (emphasis added).

I hope this clarifies things and gives you the background information you need.

Regards,
Brant

APPENDIX B: NIOSH WHITE PAPER

White Paper:
NIOSH Re-examination of Lymphoma Target Organ Selection

Questions have arisen regarding target organ selection for cancers of the lymphatic and hematopoietic systems. Current NIOSH guidance is for a medical review to be conducted for cases of lymphoma. In the past, these reviews have relied on the listed biopsy location for determination of appropriate target organs and this determination has frequently been "highest nonmetabolic organ" for internal target organ, and a nearby organ has been used as a surrogate for external target organ. NIOSH has re-examined the appropriateness of this strategy of target organ selection in light of the current scientific literature on the diagnosis and etiology of the various forms of lymphoma.

To assist in its review, NIOSH sought the expert advice of Dr. Mark Crowther, Associate Professor of Medicine at McMaster University in Hamilton, Ontario. Dr. Crowther has board-certifications in internal medicine and hematology.

This re-examination has revealed that for many non-Hodgkin's lymphomas, there are two problems in selecting target organs for organ-specific radiation dose reconstruction. First, the site of occurrence of the tumor is not necessarily the site of original radiation injury. Non-Hodgkin's lymphoma is a disease involving malignant lymphocytes. Unlike the case for most primary solid tumors, where the tumor results from the interaction of radiation with immobile cells, radiation could have interacted with these lymphocytes anywhere in the lymphatic system, and then formed a tumor elsewhere.

The second problem is that the site listed in the diagnosis may not actually be the site of primary involvement. Rather, it is common to list the site of the biopsy, which is selected based primarily on convenience, that is, as indicated by clinical symptoms and ease of surgical access.

In such cases, selection of target organs will be based on claimant-favorable assumptions (*i.e.,* assumptions that result in higher organ doses) and professional judgment about plausible sites of original radiation injury. In many cases, the thoracic lymph nodes associated with the lungs will be selected for two reasons: (1) due to the insoluble nature of many of the radionuclides energy employees could inhale, the dose to these organs is typically higher than the dose to other organs. (2) a significant fraction of the total lymphoid organ mass occurs in the thoracic cavity, in close proximity to the lungs, making this selection plausible. For the subset of lymphomas where tumor location is informative about the probable site of original radiation injury (*e.g.,* Hodgkin's disease, lymphosarcoma, etc.), this information will be considered in target organ selection.

Note that this guidance pertains only to the selection of appropriate target organ as the site of radiation injury (i.e., for calculation of effective radiation dose during the dose reconstruction process.) It has no bearing on the selection of the appropriate IREP cancer risk model, nor does it impact the risk models themselves.

Following extensive telephone and email consultations with Dr. Crowther, NIOSH prepared OCAS-TIB-012: Selection of internal and external dosimetry target organs for lymphatic/hematopoietic cancers. This technical information bulletin reviewed current NIOSH procedure regarding the target organ selection for lymphatic/hematopoietic cancers, as specified in ORAUT-OTIB-0005: IMBA organ, external dosimetry organ, and IREP model selection by ICD-9 code.

OCAS-TIB-012 was then subjected to further review by Dr. Keith Eckerman of Oak Ridge National Laboratory (ORNL). Dr. Eckerman, a recognized expert in internal dosimetry and a member of the International Commission on Radiological Protection (ICRP), provided several suggestions, the most significant of which was to select the thoracic lymph nodes [LN(TH)], rather than the extrathoracic lymph nodes [LN(ET)], for internal target organs in situations where the site of original radiation injury is unknown. Dr. Eckerman's proposal, as noted in his attached review, was based on the fact that it is a plausible choice and that it is also claimant-favorable, as doses to LN(TH) are typically higher than doses to LN(ET). This suggestion was incorporated into Revision 1 of OCAS-TIB-012.

Concurrent with preparation of OCAS-TIB-012, NIOSH began a program evaluation report to identify completed lymphoma dose-reconstructions with a probability of causation <50% at the upper 99th percentile credibility limit which may be affected by the revised organ selection guidance. Approximately 500 cases requiring re-examination have been identified. Further action on this re-examination, as well as implementation of OCAS-TIB-012 for currently uncompleted cases, is pending review by the Advisory Board on Radiation Worker Health, as requested by the Board at its meeting on October 19, 2005.

APPENDIX C: DR. CROWTHER REPORT

Consultant's Report
Dose Reconstruction Project
Dr Mark Crowther, MD, MSc, FRCPC

General comments:

In general, anything currently classified as a Leukemia (including those discussed below that I feel should be reclassified as leukemia) should be classified as red bone marrow under IMBA applicable organ, rather than "medical review." Thus, in my opinion, all of the "leukemias" should be classified similarly to the classification currently used for acute myeloid leukemia (ICD9 205) and others. One could have a complicated semantic argument about whether all leukemias originate in the marrow; clearly, some do not but we presume that the majority do. Presumably the exposure causing the leukemia occurred in the marrow although again one could probably find examples where this is not true. Similarly, non-marrow exposures are probably responsible for the "lymphomas" and other non-leukemic hematologic malignancies. However, again, one would have a hard time finding good quality scientific evidence to back this up and there is no doubt that there are examples of non-leukemic hematologic malignancies where the exposure occurred in the marrow (early in leukocyte development) or in other non-marrow and non-lymphatic sites.

For the purposes of this proposal I would include organs such as the thymus within the "lymphatic system" since it would be difficult to pin down any particular diseases which occurred within or outside the thymus. The lymphatic system can be assumed to spread widely throughout the body and although concentrated in the chest and abdomen it has components throughout the body. It is my understanding that the lymphatic system is classified within the "remainder" category.

All forms of hematological malignancy (with the possible exception of limited stage Hodgkin's disease) are assumed to be widely disseminated at presentation; thus they are treated with systemic therapy. Hodgkin's disease is assumed to start at a single location and spread to contiguous lymph node groups. Thus, classifying a specific site of exposure for non-Hodgkin's hematological malignancies is illogical; even if the bulk of disease is confined to a single location (for example massive lymphadenopathy in the left cervical region) it cannot be assumed that this was the site of original exposure. Similarly, if a patient had a limited exposure (for example, radiation exposure confined to a limb) and later presented with a lymphoma at a remote site, it cannot be assumed that they are unrelated, since the exposed organ (in this case the lymphoreticular system) is not confined to a discrete body section or organ.

I presume that the classification "leukemia, less CLL" is a carryover from the concept that CLL is not a radiation related disease. As noted, many disorders (for example Sezary syndrome and hairy cell leukemia as well as some forms of indolent lymphomas such as small lymphocytic lymphoma) behave very similarly to CLL and would best be classified as a CLL like disorder. However, it appears to me this would require the generation of a new IREP model since it is not included in this document.

I realize that you are confined to ICD codes however many of the diseases presented are illogical; for example, I'm not sure what "subacute leukemia" is and many of the disorders (such as leukemias limited to body cavities) are also illogical.

Specific review comments:

202.2 SEZARY DISEASE AND ALL SUBTYPES (202.20 TO 202.28)

This would generally be regarded as a form of leukemia and thus probably is better classified as a "red bone marrow" disorder, rather than "Remainder." Under IREP model I would suggest that they should be classified as a leukemia, although it would difficult to classify them as "leukemia, less CLL" since they all behave like CLL.

202.4 LEUKEMIA RETICULENDOTHELIAL AND HAIRY CELL LEUKEMIA (202.4 TO 202.48)

These would generally be regarded as a form of leukemia and thus probably is better classified as a "red bone marrow" disorder, rather than "Remainder." Under IREP model I would suggest that they should be classified as a leukemia, although it would be difficult to classify them as "leukemia, less CLL" since they all behave like CLL.

204.1 TO 204.11 CHRONIC LYMPHOID LEUKEMIA

These are regarded as a form of leukemia and thus should be classified as a "red bone marrow" disorder, rather than "NA". Under IREP model I would suggest that they should be classified as a leukemia, (cannot, logically, be classified as "leukemia, less CLL" ; see comments above).

205.0 TO 205.11 ACUTE MYELOID LEUKEMIA

Not clear to me why they are classified as "Leukemia, less CLL AND Acute Myeloid Leukemia" – this classification is illogical since they are acute myeloid leukemia.

APPENDIX D: DR. ECKERMAN REPORT

Target Organs for Lymphatic and Hematopoietic Cancers
Comments/Suggestions by K. F. Eckerman

Introduction

The lymphatic system consists of bone marrow, spleen, tonsils, nodes, and thymus. The only nodes explicitly addressed in dosimetric models are those associated with the respiratory system in the head (ET) and thorax (TH). The number of nodes in the body has been indicated to be between 600 – 700; 8-37 in the arm pits, at least 50-60 in the lung, and 200-500 in the mesentery (ICRP 1975). The same mass has been estimated for the extrathoracic lymph nodes [LN(ET)] and thoracic lymph nodes (LN(TH)} in adults; the value being 12 and 15 g in the female and male, respectively (ICRP 1994). If the 60 nodes in the lung have a mass of 15 g, then the mass of the 600 nodes of the body would be 150 g. ICRP publications do not indicate a mass for the body's lymph nodes.

General Comment

The following statement appears frequently in the proposed technical information bulletin.

> *Due to the insoluble nature of many of the radionuclides …the dose to the extrathoracic lymph nodes [LN(ET)] is typically higher than the dose to HNMO.*

While the statement is true, the thoracic lymph nodes [LN(TH)] are generally more highly irradiated that the extrathoracic nodes, at least in ICRP's calculations. This is typically the case for in most radionuclides of U, Th, Pu, Am, and Cm. Apparently IMBA differs for the standard calculations on this matter? Furthermore the LN(TH) are present in the thoracic not LN(ET) as apparently assumed here.

Specific Comments:

Table 1: ICD 200 – 200.18

Below are my suggested changes by ICD for the internal – all externals accepted.

a. 200.00 LN(TH)
b. 200.01 LN(ET)
c. 200.02 LN(TH)
d. 200.04 LN(TH)
e. 200.05 Colon
f. 200.06 Colon
g. 200.08 LN(TH)
h. 200.10 LN(TH)
i. 200.11 LN(ET)
j. 200.12 LN(TH)
k. 200.14 LN(TH)
l. 200.15 Colon

m. 200.16 Colon
n. 200.18 LN(TH)

Table 2: ICD 200.2-200.28
Change all the internals target organs to LN(TH). Note the last sentence of the discussion following the table suggest that a large fraction of the lymph mass is in the thorax and yet the extrathoracic lymph was cited in the table. From the introduction the thoracic lymph is probably only about 1/10 of the total lymph node mass.

Table 3: ICRP 200.8 – 200.08
Below are my suggested changes by ICD for the internal – all externals accepted.
a. 200.8 LN(TH)
b. 200.80 LN(TH)
c. 200.81 LN(ET)
d. 200.82 LN(TH)
e. 200.84 LN(TH)
f. 200.85 Colon
g. 200.86 Colon
h. 200.88 LN(TH)
Here again the discussion following the table associated LN(ET) with the thorax! Also the statement that the HNMO is the "claimant-favorable choice" is not clear since it rules out a metabolic organ. For insoluble materials the target of 200.85 and 200.86 is suggested above to be the colon rather than HNMO. Maybe these should be HNMO or Colon to be claimant favorable.

Table 4: ICD 201-201.98
Below are my suggested changes by ICD for the internal – all externals accepted.
a. 201 LN(TH)
b. 201.0 LN(TH)
c. 201.00 LN(TH)
d. 201.01 LN(ET)
e. 201.02 LN(TH)
f. 201.04 LN(TH)
g. 201.05 Colon
h. 201.06 Colon
i. 201.08 LN(TH)
j. 201.1 LN(TH)
k. 201.10 LN(TH)
l. 201.11 LN(ET)
m. 201.12 LN(TH)
n. 201.14 LN(TH)
o. 201.15 Colon
p. 201.16 Colon
q. 201.18 LN(TH)
r. 201.2 LN(TH)
s. 201.20 LN(TH)

t. 201.21 LN(ET)
u. 201.22 LN(TH)
v. 201.24 LN(TH)
w. 201.25 (Colon)
x. 201.26 (Colon)
y. 201.28 LN(Th)
z. 201.4 LN(TH)
aa. 201.40 LN(TH)
bb. 201.41 LN(ET)
cc. 201.42 LN(TH)
dd. 201.44 LN(TH)
ee. 201.45 Colon
ff. 201.46 Colon
gg. 201.48 LN(TH)
hh. 201.5 LN(TH)
ii. 201.50 LN(TH)
jj. 201.51 LN(ET)
kk. 201.52 LN(TH)
ll. 201.54 LN(TH)
mm. 201.55 Colon
nn. 201.56 Colon
oo. 201.58 LN(TH)
pp. 201.6 LN(TH)
qq. 201.60 LN(TH)
rr. 201.61 LN(ET)
ss. 201.62 LN(TH)
tt. 201.64 LN(TH)
uu. 201.65 Colon
vv. 201.66 Colon
ww. 210.68 LN(TH)
xx. 201.70 LN(TH)
yy. 201.71 LN(ET)
zz. 201.72 LN(TH)
aaa. 201.74 LN(TH)
bbb. 201.75 Colon
ccc. 201.76 Colon
ddd. 201.78 LN(TH)
eee. 201.9 LN(TH)
fff. 201.90 LN(TH)
ggg. 201.91 LN(ET)
hhh. 201.92 LN(TH)
iii. 201.94 LN(TH)
jjj. 201.95 Colon
kkk. 201.96 Colon
lll. 201.98 LN(TH)

Table 5: ICD 202-202.08
Change all internal target organs to LN(TH). Externals look OK.

Table 6: ICD 202.1 – 202.18
Use skin for the internal targets since it is explicit in the calculations.

Table 7: ICD 202.2 – 202.28
Same treatment as in Table 6 is suggested.

Table 8: ICD 202.3- 202.38
Since these cancers are found in connective tissue, which is a component of all solid organs, why not use the highest dose to a solid organ as the estimate for internal exposure. I would exclude bone surface from this list.

Table 9: ICD 202.4 – 202.48
OK

Table 10: ICD 202.5-202.58
Same comment at for Table 6 and 7.

Table 11: ICD 202.6-202.68
a. 202.6 LN(TH)
b. 202.60 LN(TH)
c. 202.61 LN(ET)
d. 202.62 LN(TH)
e. 202.64 LN(TH)
f. 202.65 Colon
g. 202.66 Colon
h. 202.68 LN(TH)

Table 11: ICD 202.8 – 202.98
Change all internal targets to LN(TH).

Table 13: ICD 203-203.01
OK

Table 14: ICD 203.1 -208.91
OK

References

ICRP 1975. Report of the Task Group on Reference Man. ICRP Publication 23, Pergamon Press, Oxford, United Kingdom.

ICRP 1994. Human Respiratory Tract Model for Radiological Protection. ICRP Publication 66, Ann. ICRP 24(1-3).