

Summary of NIOSH's Re-examination of Lymphoma Target Organ Selection

Current NIOSH practice for the selection of target organs involving lymphomas is to obtain a medical review by a physician to determine the site of origin. In the past, these reviews have relied on the listed biopsy location to identify the appropriate target organ. The result of this determination has frequently been to use the highest non-metabolic organ¹ as the internal dose target organ, and to use a nearby organ as a surrogate for the 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 issues with NIOSH's method of selecting target tissues for organ-specific radiation dose reconstruction. First, the site of occurrence of the tumor is not necessarily the site of the 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 or circulatory system, and then formed a tumor elsewhere. The second issue 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 diagnostic access.

Because the site of origin of non-Hodgkin's lymphomas can not be determined with any confidence, NIOSH proposes to modify the selection of target organs so that the dose to the highest plausible organ is used in the dose reconstruction. For internal dose, the thoracic lymph nodes associated with the lungs will be selected because the dose to this tissue from exposure via inhalation of insoluble radioactive material is always higher than the dose to other organs. For external dose, the lungs will be selected for B-cell lymphomas as the target organ because a significant fraction of the total lymphoid organ mass occurs in the thoracic cavity. For T-cell lymphomas, the thymus will be selected.

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.), the information related to the site of diagnosis will be considered in target organ selection.

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 a number of telephone and email consultations with Dr. Crowther, NIOSH prepared revision 0 of OCAS-TIB-012: *Selection of internal and external dosimetry target organs for lymphatic/hematopoietic cancers*. This technical information bulletin reviewed the current NIOSH procedure regarding the target organ selection for lymphatic/hematopoietic cancers, as specified

¹ In this context, the highest non-metabolic organ refers to the organ with the highest internal dose that is not explicitly described as concentrating the radionuclide under investigation. In current ICRP model terminology, it is equivalent to the highest dose assigned to "other soft tissues."

in ORAUT-OTIB-005: *IMBA organ, external dosimetry organ, and IREP model selection by ICD-9 code.*

Prior to the release of this procedure, however, 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 initiated a review 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 the several hundred currently uncompleted cases, has been suspended pending review by the Advisory Board on Radiation Worker Health, as requested by the Board at its meeting on October 19, 2005. To facilitate the Board's review, the three documents relevant to this issue: 1) Draft OCAS-TIB-012 rev. 1; 2) report on target organ selection from Dr. Mark Crowther; and, 3) review of OCAS-TIB-012 rev. 1 by Dr. Keith Eckerman, are attached.