

**NON-CONCURRENCE PROCESS**

**SECTION A - TO BE COMPLETED BY NON-CONCURRING INDIVIDUAL**

TITLE OF DOCUMENT <b>RIS 2008-XX Licensing Requirements for Sentinel Lymph Node Biopsy</b>		ADAMS ACCESSION NO. <b>ML081620152</b>
DOCUMENT SPONSOR <b>Cindy Flannery</b>		SPONSOR PHONE NO. <b>(301) 415-0223</b>
NAME OF NON-CONCURRING INDIVIDUAL <b>Donna-Beth Howe, Ph.D.</b>		PHONE NO. <b>(301) 415-7848</b>

DOCUMENT AUTHOR    
  DOCUMENT CONTRIBUTOR    
  DOCUMENT REVIEWER    
  ON CONCURRENCE

TITLE	ORGANIZATION
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**REASONS FOR NON-CONCURRENCE**

I am non-concurring on the RIS because the RIS does not provide an adequate technical basis for concluding that the surgical removal of sentinel lymph nodes when using a radiation probe to identify the localization of the radioactive material is not a licensed localization activity under 10 CFR 35.200. Exempting this procedure from specific licensing would require rulemaking and adding it to 10 CFR Part 30, "Exemptions." The technical basis conclusions in the RIS are not based upon critical data or address the effect expected increases in use of this or similar procedures will have. Although the Commission does not have a "below regulatory concern" policy, the foundation for the technical basis appears to be founded on "below regulatory concern" principles. The RIS signifies a significant shift in NRC's established policy and sets precedence for not regulating unsealed byproduct material and the use of byproduct material in humans without a thorough vetting and examination of the unintended consequences.

**Background:**

Sentinel lymph node biopsy is an interesting medical procedure. Unlike most other nuclear medicine procedures, the patient is already diagnosed with a suspicious tumor and scheduled for surgery. The timing of the nuclear medicine procedure is based upon the availability of the surgeon to perform the excision. It cannot be performed so far in advance that the pathology changes in such a way that there are additional sentinel lymph nodes or too soon before surgery to prevent the technetium labeled sulfur colloid from being taken up by each sentinel lymph node. The surgeon's role is to insure the correct tissue is excised and sent to the pathologist. It is the pathologist that makes the final diagnosis and determining where additional lymph nodes need to be removed. The nuclear medicine procedure is performed to identify the tissue that the surgeon will excise and the pathologist will examine. In most other nuclear medicine procedures, radioactive materials are either used early in the process of determining a diagnosis or later to monitor the treatment.

Sentinel lymph node biopsy is an established procedure that is increasing in use with the increase in early stage identification of breast cancer. Further, its use will be expanding for other cancers and diseases as other early detection practices improve. As described, there are three groups of individuals that will handle radioactive material during this process. The nuclear medicine group that will receive the material contained in a syringe, inject the material directly into the patient. Because the radioactivity is labeled to colloidal particles, it essentially remains at the injection site, is taken up slowly by the local lymphatic system, and is not rapidly dispersed in the body for breakdown and removal. There is little if any contamination associated with this part of the procedure. The second group is the surgical staff. This group will handle the largest amount of unsealed and uncontained radioactive material once the incision is made. This group has the largest potential for contaminating equipment and areas. The final group is the pathology laboratory which will

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SIGNATURE <i>Donna-Beth Howe</i>	DATE <i>7 July 2008</i>
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receive only the tissue extracted. It too will handle unsealed and uncontained radioactive material but less than the surgical staff. The amount of radioactive material involved is dependent not only on the radioactivity in the patient but also the number of patients sent to the surgical practice. Technical Basis for

Non-Concurrence:

The overriding issue in determining the licensing status of the surgeon's role in sentinel lymph node biopsy is determining whether the surgeon meets the criteria in 10 CFR 30.3, "Activities requiring license." The pertinent part of this requirement is 10 CFR 30.3(a) because sections (b) and (c) address implementation of the NARM rule. 10 CFR 30.3(a) states: "except as provided in paragraphs (b)(2), (b)(3), (c)(2), and (c)(3) of this section and for persons exempt as provided in this part and part 150 of this chapter, no person shall manufacture, produce, transfer, receive, acquire, own, possess, or use byproduct material except as authorized in a specific or general license issued in accordance with the regulations in this chapter." If you cannot get over this hurdle, all other arguments concerning decoupling, low radiation risk, etc., in the RIS are moot.

If the surgeon is not using or transferring byproduct material, then the surgeon's activities in surgically excising the sentinel lymph node or the tumor itself is not licensed. The transferring issue includes two aspects: (1) whether the surgeon is transferring radioactive material to the pathology laboratory or (2) if it can be demonstrated that the radioactive material being sent is below the requirements in 10 CFR 30.18, "Exempt quantities," the pathology laboratory does not have to receive the material from a licensed entity. The RIS describes two ways of approaching sentinel lymph node biopsy procedures.

The first approach is simply as an imaging procedure. The NRC or Agreement State licensed medical authorizer user performs the administration under the provisions of 10 CFR 35.200, keeps the patient for a short period of time or has the patient return at some specified time to be imaged. (As with other Tc-99m procedures, 10 CFR 35.75 is not an issue because the activities administered are too low to require hospitalization for radiation reasons.) The AU uses the information on the image to mark the skin where the sentinel lymph node(s) is (are) located to identify the tissue to be excised and sent to pathology. While the nuclear medicine authorized user is providing the information resulting from the image, the authorized user can also provide information on when the activity in the injection site and in the sentinel lymph node is expected to be below 100 microcuries. (Since surgery may be from 1 to 18 hours after injection, there may be reduction in radioactivity at the injection site due to radioactive decay.) This information can be used to ensure the pathology laboratory receives tissue samples with less than 100 microcuries. (This is important because the surgeon may send additional tissue from the injection site to pathology.) The nuclear medicine authorized user only needs to administer the minimum activity of Tc-99m to provide a readable image. The image can be used to estimate the percent uptake of the sentinel lymph node(s) and the activity at surgery can be estimated by decay correction.

In the first approach, the surgeon is not using byproduct material and the pathology laboratory receives exempt quantities and does not need to demonstrate that the material was received from a licensee.

In the second approach, regardless of the production of an image, the surgeon uses a radiation detection probe to determine the localization of the radioactivity in the sentinel lymph node. The surgeon is using **byproduct material. This is a medical use regulated under 10 CFR 35.200, "Use of unsealed byproduct material for imaging and localization studies for which a written directive is not required."** Because

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**the surgery is already scheduled and the nuclear medicine group is working with the surgical group, the nuclear medicine authorized user knows that the surgeon is using a probe. An important part of the authorized user's determination of the activity to be administered to the patient is determining if there will be enough activity at the time of surgery for the surgeon to detect the sentinel lymph node. Additional radiation is given to the patient to account for the decay of the material at the time of surgery and the activity that must be present in the tissue for the surgeon to perform the localization procedure.**

10 CFR 30.18, "Exempt quantities," does not exempt persons from meeting the requirements in 10 CFR Part 35. Even if the total activity of the TC-99m at the surgical site (i.e., the combination of the activities at the injection site and in the sentinel lymph nodes) were below 100 microcuries when the surgeon used the radiation probe to perform the localization procedure, the surgeon could not perform the procedure under 10 CFR 30.18. Specifically 10 CFR 30.18(a) states "Except as provided in paragraphs (c) through (e) of this section, any person is exempt from the requirements for a license set forth in section 81 of the Act and from the regulations in parts 30 through 34, 36, and 39 of this chapter to the extent that such person receives, possesses, uses, transfers, owns, or acquires byproduct material in individual quantities, each of which does not exceed the applicable quantity set forth in § 30.71, Schedule B. Paragraphs (c) and (d) refer to commercial distribution.

Therefore, in the second approach, the surgeon is not exempt from licensing. The surgeon can either be independently licensed (decoupled from the 10 CFR 35.200 licensee) for the localization procedure or perform the procedure under the supervision of an authorized user (and the 35.200 licensee) as discussed in the TAR response. The "technical basis" described in the RIS can be used as a starting point for regulating the "decoupled" localization and surgical excising of the radioactive tissue under 10 CFR 35.1000, "Other medical uses of byproduct material or radiation from byproduct material." This would provide an interim solution if the staff wants to use the "technical basis" as a starting point for not requiring the surgeon performing the "decoupled" localization and surgical excising of the radioactive tissue to have a specific medical use license.

#### Solution / Path Forward:

In the draft TAR response, the licensing of a stand alone surgeon was addressed but removed in the final response because the applicant had not requested it. At that time the training and experience requirements in 10 CFR 35.190 were thought to be a suitable model because of the activities involved. Because of the limited isotopes involved (only Tc-99m at this time) and uniform surgical procedures, the total hours could be reduced to include the hours of clinical experience in the 8 hours of classroom and laboratory training and specific work experience would be tailored to the task required for the safe use of the material during and after the surgery. Corresponding changes to the RSO requirements could be made for this simple program. No changes to the RSO requirements would be needed for an existing licensed facility.

The cost of licensing a free standing surgical office that routinely performs radioactive sentinel lymph node surgery would come under fee category 7C. The fees for such a license fee category 7C are \$2,300 for an application and \$6,000 annually. If the surgical operation meets the definition of a small business (gross annual receipts between \$350,000 and \$ 5 million) the annual fee is reduced to \$2,300. These fees should not keep a surgeon from providing the services.

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I would recommend, in light of the unsealed and uncontained nature of the radioactive material and the increasing use of sentinel lymph node procedures, as well as the potential increase in similar uses of byproduct material by surgeons (or other physicians), that NRC consider introducing a general license for the medical use of similar procedures tied to a registration procedure similar to that existing for *in vitro* laboratories. The general license issued to the physician could specify the maximum activity and short half-life radionuclides the general licensee could have in a year for each radionuclide, if such a limit exists, and provide general radiation safety procedures for the general licensee on the back of the registration form. These procedures could focus on reduction of contamination, decay-in-storage time frames for disposal, restriction to short half-life isotopes of low safety significance, and minimum operational training with the probes being used. This general license like the *in vitro* laboratory general license would not include a licensing fee, registration fee, annual fee or other cost to the licensee, if cost to the surgeon is a concern.

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**SECTION B - TO BE COMPLETED BY NON-CONCURRING INDIVIDUAL'S SUPERVISOR**

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ORGANIZATION FSME/DMSSSA	

COMMENTS FOR THE DOCUMENT SPONSOR TO CONSIDER

- I HAVE NO COMMENTS
- I HAVE THE FOLLOWING COMMENTS

I have reviewed the package, including the ACMUI transcripts, and agree with the position taken in the RIS.

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SIGNATURE 	DATE 11/11/2008
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COMMENTS FOR THE DOCUMENT SPONSOR TO CONSIDER



I HAVE NO COMMENTS



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*R E Zelac, Ph.D. 10/22/08*

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06/02/2008

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**SECTION C - TO BE COMPLETED BY DOCUMENT SPONSOR**

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ORGANIZATION  
FSME/MSSA/MSEA

ACTIONS TAKEN TO ADDRESS NON-CONCURRENCE

NRC staff requested an OGC opinion regarding whether the regulations allow the surgical excision of the lymph nodes to be "decoupled" from the procedure that involves administration of Tc-99m. OGC concluded that the surgical excision can be decoupled from the provisions of 10 CFR 35.200 (i.e., administration of the radionuclide), and that exempting surgical facilities from the requirements for a license is legally supportable.

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