Washington University in St.Louis

Environmental Health & Safety **Radiation Safety Office**

7/31/07
72FR36526
(6)

August 1, 2007

Chief, Rulemakings, Directives, and Editing Branch
Division of Administrative Services
Office of Administration
U.S. Nuclear Regulatory Commission
Washington, DC 20555-0001

SUBJECT: Draft Guidance NUREG-1556, Volume 13, Rev. 1: "Consolidated Guidance About Materials Licenses Program-Specific Guidance About Commercial Radiopharmacy Licenses"

Dear Rulemakings, Directives, and Editing Branch Chief:

On behalf of Washington University in St. Louis (WU), Dr. Susan M. Langhorst, Ms. Sally Schwarz, Dr. Barry A. Siegel, and Dr. R. Gilbert Jost respectfully submit these comments on the Nuclear Regulatory Commission draft guidance, NUREG-1556, Volume 13, Rev. 1 (72 FR 36529, July 3, 2007). We appreciate NRC's efforts to enact the Energy Policy Act of 2005 expansion of definition for byproduct materials, especially as related to your attempt to minimize the impact these regulatory changes will have on the availability of radioactive drugs containing accelerator-produced radionuclides. We offer our comments in support of the continued availability of accelerator-produced radionuclides for research and development, as well as for medical use.

Problems with Interchangeable Use of Pharmacy Terms

In the first paragraph on page 1-1, the draft guidance states "...the phrases or terms, 'commercial radiopharmacy,' 'radiopharmacy,' 'nuclear pharmacy,' and 'pharmacy' are used interchangeably." We strongly **recommend** that NRC not include "pharmacy" as one of these interchangeable terms. We also **recommend** that a clarification statement be added noting that the interchangeable use of "commercial radiopharmacy," "radiopharmacy" and "nuclear

E-RIDS = ADM-03
Add = T. Taylor (TMT)

SUNSI Review Complete

Washington University in St. Louis, Campus Box 8053, 660 S. Euclid Avenue, St. Louis, MO 63110-1093
(314) 362-3476, *Fax*: (314) 362-4776, radsafety@wustl.edu, http://radsafety.wustl.edu

Template = ADM-013

pharmacy" does not necessarily mean the guidance applies for a non-commercial radiopharmacy or a non-commercial nuclear pharmacy.

Use of the Term "Pharmacy" – We **recommend** replacing all uses of the term "pharmacy" with "nuclear pharmacy," "radiopharmacy," or "pharmacy (radiopharmaceuticals)." The following examples show where the use of the term, "pharmacy", is giving either incorrect or unclear guidance.

Without use of a clarifying term such as "nuclear pharmacy," "radiopharmacy," or "pharmacy (radiopharmaceuticals)," the following statements imply a state pharmacy license is appropriate to become a commercial radiopharmacy:

Page 8-26 – "Licensure as a pharmacy by a State Board of Pharmacy; or..."

Page 8-27 – "Applicants must provide: Copies of their registration or license from a State Board of Pharmacy as a pharmacy..."

Page 8-30 – "PET radiopharmacies must demonstrate that they are ...licensed as a pharmacy by the State's Board of Pharmacy..."

Page C-9 – "Provide a copy of the registration or license from a State Board of Pharmacy as a pharmacy..."

Without the use of "nuclear pharmacy" or "radiopharmacy," the following statement may be confusing by suggesting an individual only needs pharmacy experience:

Pages 8-20, C-7 & D-5 – "The individual practiced at a pharmacy at a Government agency or Federally recognized Indian tribe before April 8, 2007 or at all other pharmacies before August 8, 2009, or an earlier date as noticed by NRC."

Issues Concerning Pharmacist Descriptions

In Section 8.7.2 Discussion, the draft guidance describes the sections of regulation defining the training and experience requirements to become an Authorized Nuclear Pharmacist (ANP) at a commercial radiopharmacy. We **recommend** that a statement be added to this section which discusses the "grandfathering" of a nuclear pharmacist who has used only accelerator-produced radioactive materials, discrete sources of Ra-226, or both for medical or nuclear pharmacy uses. We suggest the following paragraph be added at the end of this discussion section:

"Nuclear pharmacists who used accelerator-produced radionuclides or discrete sources of Ra-226 during the effective period of the waiver do not have to meet the requirements of 10 CFR 35.59, or the training and experience requirements in 10 CFR Part 35, Subpart B for those materials and uses. The criteria for such nuclear pharmacists are described in 10 CFR 32.72(b)(4) and acceptable documentation is discussed in Appendix G."

The statement under "State or Territory where Licensed" on page G-5 indicates that pharmacists are licensed to prescribe drugs. This statement is incorrect, and we **recommend** the statement be corrected to say that pharmacists are licensed to dispense drugs.

In Appendix G Part II. Preceptor Attestation (page G-6), the current regulatory definition of preceptor is quoted, and we note that nowhere is it indicated that the preceptor must have the same "authorization" as is sought by the individual whose training and experience is being verified by the preceptor.

Recommendation 1 – As NRC is preparing to "grandfather" individuals who have used accelerator-produced radionuclides to be an ANP (or an AU, AMP or RSO), there is an opportunity to bring the training and experience criteria for ANPs (AUs, AMPs and RSOs) more in line with the preceptor definition. We agree that a preceptor statement from a current ANP is appropriate for those individuals seeking to become an ANP by the alternative pathway. WU strongly **recommends** that the NRC Staff and, in particular, the Nuclear Regulatory Commissioners reconsider the need for an ANP preceptor statement for those individuals who are board-certified by an NRC-recognized specialty board. Each of the specialty boards recognized by the NRC have proven to the NRC that their board-eligible candidates meet the training and experience requirements for the type(s) of medical use for which they are recognized. In order to sit for a board exam, an individual requires the recommendation of a sponsor who verifies the individual has met all of the requirements to become board-certified. While this sponsor may not be an ANP, the sponsor is responsible to the board for recommending only individuals who meet the board's, and therefore the NRC's, requirements. Successful completion of the board exam by the individual gives further verification of the individual's training and experience. WU believes the current regulations imposing the additional requirement of an ANP preceptor statement is an unnecessary redundancy that has greatly complicated the process of approving an individual as an ANP, and has led to the trivialization of long-established radiopharmacy board-certification.

Recommendation 2 – We appreciate that NRC has taken care to ensure the continuing access of PET imaging techniques by allowing the "grandfathering" of individuals who have used accelerator-produced radionuclides to become ANPs (or AUs, AMPs or RSOs). We believe that NRC also "grandfathering" individuals who have received board-certification prior to NRC's recognition of a specialty board would be in line with the grandfathering for medical use of the new byproduct materials. In certain cases, such as those individuals who have been board certified by the American Board of Health Physics (ABHP) prior to January 1, 2005 and never named as RSO on a NRC or Agreement State license, an individual could not currently be named as an RSO based on their board-certification even though the ABHP made no changes in its certification process to receive NRC-recognition. WU also strongly **recommends** that NRC allow grandfathering of individuals who were board-certified prior to NRC-recognition for all specialty boards which receive NRC-recognition prior to the required implementation date, August 9, 2009, for the new byproduct definition.

Incorporation of a Commercial Radiopharmacy License into a Broad Scope Type A Medical License also Incorporating a License for Radioactive Material Produced Using an Accelerator

WU plans to incorporate a commercial radiopharmacy license into our overall broad scope license for the distribution of copper-64 (Cu-64), and possibly other accelerator-produced radionuclides, to other research entities for their production of radiopharmaceuticals for human research use. WU has been funded by the National Institutes of Health (NIH) for many years to supply other research entities with several different accelerator-produced radionuclides, with Cu-64 accounting for the majority of these transfers. WU's continued intent in supplying accelerator-produced radionuclides is to further the research and development of imaging techniques with eventual technology transfer to an entity that would commercially produce and distribute one or more of these radionuclides.

Since these research entities, which are located throughout the U.S., do not meet NRC's proposed definition for being in a "consortium" with WU, we will be obligated to become a "commercial" radiopharmacy, even though our distribution of accelerator-produced radionuclides for eventual human use will continue to be for noncommercial research and development. We plan to list separately a license item for Cu-64, and possibly other accelerator-produced radionuclides, and plan to identify purpose of use as 10 CFR 32.72.

Question – In Appendix D.5 (pages D-2 & D-3), the purpose of use is listed as 10 CFR 32.72 and 10 CFR 30.41. NRC has stated in the draft Federal Register Notice (SECY-07-0062, Enclosure 1, p.128):

> "In general, a PET radionuclide production facility may transfer excess PET radionuclides to other licensees that are authorized to receive such PET radionuclide transfer under 10 CFR 30.41."
>
> "An applicant's intent regarding noncommercial distribution, transfer, or commercial distribution will be evaluated as part of the licensing review process to ensure that the proper license or authorization is issued."

Does NRC agree a licensee that is required to obtain a commercial radiopharmacy license to cover a subset of its transfer of radionuclides, such as described here for WU's situation, is allowed to make non-commercial transfers under 10 CFR 30.41 for radionuclides not included in commercial radiopharmacy license purpose of use?

Question – What guidance does NRC give license applicants for 10 CFR 32.72 distribution of radionuclides that may contain other radionuclide contaminants? Should not guidance on how to describe these potential contaminants be included in this document? Examples of these types of radiopharmaceuticals that are widely used include:

Sm-153 Quadramet which can include Eu-154 and Eu-155

Tl-201 Thallous Chloride which can include Tl-200, Tl-202 and Pb-203

In-111 Indium Chloride which can include In-114m and Zn-65

Sealed Source Registry for New Byproduct Materials

On page 8-7, the draft guidance discusses what a radiopharmacy applicant should do if it possesses a sealed source containing the new byproduct material and there is no Sealed Source and Device (SSDR) certificate. NRC expects this applicant to provide information required under 10 CFR 30.32(g), which states:

> "An application for a specific license to use byproduct material in the form of a sealed source or in a device that contains the sealed source must either--
>
> (1) Identify the source or device by manufacturer and model number as registered with the Commission under § 32.210 of this chapter or with an Agreement State; or
>
> (2) Contain the information identified in § 32.210(c)."

10 CFR 30.32(g)(1) appears to be asking for the SSDR, which seems redundant since NRC requests this information because there is no SSDR. To meet 10 CFR 30.32(g)(2), 10 CFR 32.210(c) states:

> "The request for review of a sealed source or a device must include sufficient information about the design, manufacture, prototype testing, quality control program, labeling, proposed uses and leak testing and, for a device, the request must also include sufficient information about installation, service and maintenance, operating and safety instructions, and its potential hazards, to provide reasonable assurance that the radiation safety properties of the source or device are adequate to protect health and minimize danger to life and property."
>
> **Comment & Recommendation** – The information NRC requests may not be readily available to the applicant if the radiopharmacy purchased the source from someone else. If NRC asks for this information from every applicant possessing the sealed source, then it appears that NRC will be receiving multiple requests to do a safety evaluation for the same sealed source model. We **recommend** that NRC work directly with the sealed source manufacturers to begin conducting safety evaluations and issuing SSDR certificates. Guidance for applicants who only possess these sealed sources should be to provide NRC with the manufacturer name, source model number and general physical description, e.g., Ge-68 rod source 1/4" diameter & 8" long.

Security Issues

On page 8-12, the draft document provides guidance on verifying whether a transferee is allowed to receive the type, form and quantity of byproduct material to be transferred. Supplying copies of licenses has become problematic in the security conscious world of NRC Increased

Controls. In NRC's RIS 2005-31, "Control of Security-Related Sensitive Unclassified Non-Safeguards Information Handled by Individuals, Firms, and Entities Subject to NRC Regulation of the Use of Source, Byproduct, and Special Nuclear Material," Appendix 3, material licensees are told to withhold authorized quantities, manufacturers, model numbers and locations of sealed sources and devices exceeding threshold values. For some licensees, like WU, supplying a copy of the NRC license with multiple areas blacked out can look unprofessional and suspicious.

Comment & Recommendations – If NRC states the radiopharmacy should "verify that the address to which radioactive materials are delivered is an authorized location of use listed on the customer's license," and notes that the "most common form of verification" is possession of a "valid copy of the customer's NRC or Agreement State license", we are concerned that licensees will only accept copies of licenses as verification. We **recommend** either NRC delete mention of obtaining a copy of the license, or expand the explanation that another acceptable verification is a written certification by the licensee receiving the radioactive material that states the licensee is authorized by license or registration to receive the type, form, and quantity of byproduct material to be transferred, specifying the license or registration certificate number, issuing agency and expiration date. We also **recommend** that NRC include in this discussion that some licensees may choose to provide their own written verification and not to provide a copy of their license based on NRC guidance given in RIS 2005-31.

Comments, Suggestions and Questions on Specific Items in NUREG-1556, Vol. 13, Rev. 1 Draft

Page 3-1 – Definition of "Management" should be similar to that found in Vol. 11 (Broad Scope). We suggest it be modified to read:

> "'Management' refers to the processes for conduct and control of a Radiation Safety Program and to the individuals who are responsible for those processes and have *authority to provide necessary resources* to ensure safety and to achieve regulatory compliance."

Page 8-8 – To strengthen the idea that this draft document has been updated to include the new byproduct materials, we suggest that iodine-123 be included as an example for potentially volatile materials.

Page 8-20 – Should the statement, "*For an individual qualifying under 32.72(b)(5)*" be corrected to reference 32.72(b)(4)?

Pages 8-29 to 8-30 – The two bulleted items following Figure 8.3 should be deleted since they are repeated text.

Pages 8-45, 8-47 & C-11 – To strengthen the idea that this draft document has been updated to include the new byproduct materials, we suggest that performing Sr-82 and Sr-85 breakthrough measurements also be included for elution from a Rb-82 generator.

Page G-4 – The "[BOLD]" after IV. Recentness of Training should be deleted.

Page G-5 – The Note on this page states, "An individual that is board eligible will not be considered for this pathway until the individual is actually board-certified." Does NRC consider an individual to be board-certified when they have received written confirmation that they successfully completed their board exam?

Please contact the following individuals if you have any questions or concerns on the comments we have submitted on behalf of Washington University in St. Louis:

Susan M. Langhorst at (314) 362-2988 or langhors@msnotes.wustl.edu
Sally Schwarz at (314) 362-8426 or schwarzs@wustl.edu

Thank you for your consideration of our recommendations, comments, suggestions and questions.

Sincerely,

Susan M. Langhorst, Ph.D., CHP
Radiation Safety Officer

Barry A. Siegel, M.D.
Professor of Radiology and Medicine
Director, Division of Nuclear Medicine
Chair, Radiation Safety Committee
Chair, Radioactive Drug Research Committee

Sally Schwarz, R.Ph., M.S., BCNP
Associate Professor of Radiology
PET Production Radiopharmacist
Authorized Nuclear Pharmacist

R. Gilbert Jost, M.D.
Professor and Chair, Department of Radiology
Director, Mallinckrodt Institute of Radiology