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July 3, 2007

Chief,
Rulemakings, Directives and Editing Branch
Division of Administrative Services
Office of Administration
U.S. Nuclear Regulatory Commission
Washington, DC 20555-00001

RE: NUREG-1556, Volume 21, "Consolidated Guidance About Materials Licenses Program – Specific Guidance About Possession Licenses for Production of Radioactive material Using an Accelerator"; Draft Guidance Document for Comment. Federal Register Vol. 72, No. 102, May 29, 2007.

These comments concerning the draft NUREG-1556, Volume 21, are submitted on behalf of the Council on Radionuclides and Radiopharmaceuticals (CORAR). CORAR members include manufacturers and shippers of diagnostic and therapeutic radiopharmaceuticals, life science research radiochemicals and sealed sources used in therapy, diagnostic imaging and calibration of instrumentation used in medical applications. CORAR membership also includes manufacturers and operators of cyclotrons used to manufacture PET radionuclides and operators of cyclotrons in the commercial production of other radiopharmaceuticals. CORAR has an interest in ensuring that these products can be made available as needed for the delivery of quality patient treatment and care and the regulation of both byproduct and accelerator-produced radioactive material to ensure the safety of workers, patients and other members of the public.

General Comments

CORAR appreciates the work that went into development of this guidance under such time constraints and welcomes its publication. One general comment concerns the potential for conflicting guidance between this volume, Volume 13 on Commercial Radiopharmacy Licenses, and Volume 12 on Manufacturing and Distribution. Many of the commercial PET radiopharmacies currently operate as a hybrid of a radiopharmaceutical manufacturing and as a radiopharmacy due to the unique rules governing PET radiopharmaceuticals. We urge consideration of this in the development of guidance that will apply to licensing of these facilities. In addition, one should consider the fundamental conflict between engineering controls used to insure compliance with Good Manufacturing Practices for drug manufacturing, and those commonly employed for control of contamination from radioactive materials. Resolving this conflict may require a novel approach and recognition that perhaps a radionuclide with a

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(TMT)

low volatility hazard can be safely handled in a positive pressure space in order to guarantee sterility of the final product.

A second general comment concerns the issue of "grandfathering" as provided for extensively in the proposed rules published July 28, 2006. An excerpt from page 42964, third column, first full page, is given below:

> *Further, to ensure the availability of NARM (which includes PET) radioactive drugs and biologics, individuals who may include nuclear pharmacists among others, responsible for the production of PET radionuclides at the cyclotron facilities under the NRC waiver issued on August 31, 2005, will be "grandfathered" and will not be required to meet new training and experience requirements as long as their duties and responsibilities under the new license do not significantly change. When adding these individuals to a license, the applicant will be required to document that these individuals were responsible for the production of PET radionuclides using a cyclotron or accelerator during the period the waiver was in effect.*

There is no discussion of grandfathering in the draft of Volume 21, and this could be critical to ensuring the continued supply of accelerator produced radiopharmaceuticals during and after implementation of the final rules. We request that discussion be included in section 8-7 and in the suggested response for Item 7 of NRC Form 313 on page C-3. Further, there was discussion earlier in the rulemaking process regarding classification of service personnel for accelerators. These individuals are critical to ensuring the reliability of accelerators used to produce radiopharmaceuticals on a timely basis, but may not possess the academic background suggested in section 8.7.2 of the draft. In the interest of ALARA as much time as possible is usually allowed from the last production cycle of the accelerator until the beginning of maintenance on the unit. Under a Nuclear Pharmacy type of license, it could be required that an ANP is present whenever this work is taking place, when it is often on a shift opposite of the normal Pharmacist's production schedule. We suggest that a combination of training, outside of academia, and experience be more broadly defined. For example, many accelerator service personnel come from a military background and may not have had formal coursework in the physical sciences or engineering fields, but nevertheless have been provided extensive radiation safety training from either the employer/licensee or from the accelerator manufacturer.

Specific Comments

1. **Page iii** – first paragraph of Abstract
   This guidance document should be used for activities that take place once radioactive materials are produced by the accelerator, which include material in the target and associated activation products, to the transfer or distribution of material to another license for preparation of the final product (e.g., radioactive drugs).

   Suggested rewording of this sentence is as follows:
   This guidance document should be used for activities that take place once radioactive materials are produced by the accelerator, which includes material in the target and the associated activation products **in the accelerator along with its associated shielding (if applicable)**, to the **point of** transfer or distribution of material to another license or **licensee** for preparation of the final product (e.g., radioactive drugs).

   We are requesting emphasis on the scope of the newly defined by-product to include activation products in the cyclotron itself as well as in the surrounding shielding, whether self-shielded or in a bunker. Production of the final product often takes place at the same facility. Volume 13 covers radiopharmacy licensees but not necessarily radiopharmaceutical manufacturing.

2. **Page 5-2 - Section 5.3** - Paper Format and Electronic Format

There is discussion in this section about NRC's intent to move to a "faster and more efficient" processing of electronic applications "in the future."

It seems pointless to include "Electronic Format" in the title of this section when there really isn't an electronic application option. In addition, we strongly urge NRC to move to provide the option of electronic submission of applications as soon as possible.

3. **Page 8-1** - paragraphs three and four

   Include mention of material selection and its impact on creation of activation products in the discussion on ALARA in paragraphs three and four in order to highlight this issue for licensees.

4. **Page 8-2** – Discussion section under "Timely Notification of Transfer of Control"

   It is often difficult or impossible for licensees to meet this requirement as often the RSO is not at a level to be made aware of such a change in the business prior to its execution. The best that can be expected is for immediate notification when the RSO is made aware of the change.

5. **Page 8-4** – Sentence under Figure 8.1

   This sentence is essentially a repeat of the last sentence on Page 8-3.

6. **Page 8-5** – Second paragraph in the Criteria discussion of Section 8.5.1

   Some reasonable and practical guidance is needed here on how to determine the radionuclides and quantity of activity that is expected in various locations (e.g. cyclotron components, targets and target systems, vault shielding, etc) in addition to the discussion provided on sealed sources. The added guidance should be based on established licensing practices used by the Agreement States.

7. **Page 8-7** – First bullet under "For unsealed materials:"

   This is impractical guidance. It is unreasonable to assume that licensees would be able to identify and list on the license each and every distinct location where radioactive materials may exist as a result of activation from accelerator operation. Licensees should be allowed to follow the practice endorsed by the Agreement States where an estimate of activity is determined (with a maximum for any radionuclide stated) for atomic numbers 1 - 83, in any chemical/physical form, with a general authorized use provided (e.g. target loading and irradiation, transfer of target materials, storage of induced radioactivity in cyclotron components and related equipment and facilities).

8. **Page 8-8** - Section 8.5.2. Financial Assurance and Recordkeeping for Decommissioning

   There is no guidance in this section related to financial assurance for decommissioning of accelerator facilities with the exception of the statement, "most accelerator facilities will be required to comply... because of activation materials... produced by operation."

   Considering this document is intended for accelerator operators, it would be very useful for some detailed guidance to be provided here to enable licensees to determine how and to what extent they may be subject to the financial surety requirements. This guidance should include a provision for some PET cyclotron operators to establish a threshold of operational parameters

below which it has been demonstrated that activation of ancillary facilities would not result in accumulated activities subject to decommissioning plans, cost estimates and financial assurance.

9. **Page 8-14** – Discussion under section 8.7.1

   The first sentence differs from other guidance where the RSO is responsible for oversight on implementation, and not directly for the program's implementation.

10. **Page 8-15** – last paragraph and top of the following page

    The requirement for a "specialist in the field of radiation protection" directly implies that a Health Physicist would be the minimum qualification for RSO at accelerator facilities with curie quantities of radioactivity and differs substantially from RSO requirements at Nuclear Pharmacy licensees. Curie quantities of radioactive materials, with much longer half-lives or that present internal dose concerns, are also handled safely at Nuclear Pharmacy licensees by ANPs. This appears to come from guidance developed for Manufacturing and Distribution licensees and should not be applied to all accelerator facilities. In many cases, the facility will also be operating as a Nuclear Pharmacy licensee and this would appear to require that a single licensee would need a Health Physicist as RSO on one license and an Authorized Nuclear Pharmacist (ANP) on the Nuclear Pharmacy license. CORAR recognizes the NRC's concern with respect to the higher potential for radiation exposure from PET radionuclides but urges the NRC to consider the extensive operating experience at the many such PET radiopharmacies currently licensed by Agreement States where ANPs have served well as RSO on the license. The inclusion of an accelerator into the facility should not by itself require such a high threshold for the position of RSO.

    In addition, CORAR requests that guidance be included here and elsewhere as appropriate to address the issue of "grandfathering" as discussed extensively in the proposed rulemaking documentation.

11. **Page 8-17** – last paragraph discussing service provider licenses

    In the last paragraph it states, "accelerator manufacturers or companies that provide repair and/or maintenance service to licensed accelerator facilities may need to possess an NRC service provider license or equivalent Agreement State license."

    While a service provider may be subject to registration requirements for servicing an accelerator as a radiation-producing machine, this should be retained within the jurisdiction of the relevant state agencies. Regarding the "handling of radioactive materials" produced by accelerator operation in the course of providing repair or maintenance services; this should be allowed without an NRC or Agreement State service provider license if the accelerator operator licensee has a provision that allows for this work to be done by a contracted service provider. Since this is a licensing guide for accelerator operators, this provision should be included in the discussion on authorized users. Some States do not list individual names on the service license.

12. **Page 8-20** – first bullet under "Response from Applicant"

    This needs further explanation because much information in a license application is considered binding i.e. is treated by inspectors or licensing as a license condition.

13. **Page 8-23** – Auditor Techniques

Observation of Emergency Procedure implementation is not normally observed during an audit.

14. **Page 8-31** – Last sentence

This assertion does not necessarily follow from the preceding sentence. Some accelerator facilities will fall into the greater than 10% rule and require monitoring. Most radiation exposure to staff at an accelerator facility comes from activated material or the target material and not from prompt radiation fields around the accelerator during operation.

15. **Page 8-34** – First bullet under "Criteria"

Clarify that this is for radioactive material outside of the DOT cycle. Properly marked and labeled packages awaiting transport are in the DOT cycle and not subject to the public dose limits in 10 CFR 20.

16. **Page 8-37** - Figure 8.10

The picture is intended to show the use of appropriate shielding (apparently in a nuclear pharmacy operation), out of context, but suggests a situation that does not employ best practices with regard to ALARA and dosimeters are not apparent as they are in other illustrations. For example, there are multiple unshielded containers in proximity to the extremities and no evidence of any remote or extended handling devices within reach. The handling is also done on a bench top which would generally be unacceptable for dispensing of radiopharmaceuticals. This picture should be left out of the guidance or replaced with a more acceptable example.

17. **Page 8-38** – Discussion regarding security procedures

It is not clear why the presence of "hot cells" qualifies as an unusual need for greater security. The other two examples are fairly well understood. Please clarify or remove the reference to hot cells.

18. **Page 8-39** - Figure 8.11

This figure shows several poor practices. No safety glasses or extremity dosimeter, and kneeling on a potentially contaminated floor in order to clean up a spill.

19. **Page 8-41** – Figure 8.13

Detector needs to be closer to surveyed object. Generally a distance of one to two inches is specified for personal contamination surveys.

20. **Page D-1** - SAMPLE PRODUCTION MATERIALS LICENSE

This is an impractical approach. It is unreasonable to assume that licensees would be able to identify and list on the license each and every distinct location where radioactive materials may exist as a result of activation from accelerator operation. This approach fails to take into consideration the fact that there are likely more radionuclides (due to target material impurities) present in the target foils than just the radionuclides provided (Co-60 and Zn-65) on the sample license. This is one example of why licensees should be allowed to follow the practice endorsed by the Agreement States where an estimate of activity is determined (with a maximum for any

radionuclide stated) for atomic numbers 1 - 83, in any chemical/physical form, with a general authorized use provided (e.g. target loading and irradiation, transfer of target materials, storage of induced radioactivity in cyclotron components and related equipment and facilities).

This document should also provide some guidance on how the activity is to be determined for the various radionuclides that are expected to be produced in activated components and associated equipment and facilities.

21. **Page G-1** – General comment on this section

The guidance in this section is lacking discussion on critical topics including, but not limited to, target handling systems, shielding of activated machine components and control of access to areas such as vaults where there are very high levels of radiation due to prompt interaction of primary beam with targets and surrounding materials.

22. **Page G-1** – second to last bullet

Glove boxes and hot cells are very rarely sealed- too expensive and not necessary for gamma-beta emitters.

23. **Page G-2** – last bullet

This statement is overly simplistic and does not take into account the variety of accelerator facilities with different design and operational requirements. This statement is not accurate for a number of situations and should be removed or replaced with more appropriate guidance to consider in the engineering of ventilation systems on a case-by-case basis. For instance, one wouldn't want a high air flow in a vault where there is loose surface contamination since this could create an unnecessary airborne hazard.

24. **Page G-3** – Fourth bullet

One must recognize the potential for radiation damage to electronics and possible need for replacement in areas with potentially high radiation fields or contamination levels.

25. **Page H-5** – last paragraph discussion on error limits

Some types of spirometers also use gas displacement i.e. bubble spirometers.

26. **Page I-1** – Table on "Doses to Members of the Public", left column

This section should include another mention of radiation from licensed and "unlicensed" sources being considered in total by the NRC for purposes of demonstrating compliance with the limits.

27. **Page I-2** – Third paragraph under "Measurements" – "Due to the uncertainty of this type of discharge, it **is** important to perform..."

Suggest replacing "**is...**" with "**may be...**" in order to be more general.

28. **Page I-2** – First paragraph under "Calculation Method"

Should make reference to the guidance included in NRC Regulatory Guide 4.20, "Constraints on Release of Airborne Radioactive Materials to the Environment for Licensees Other Than Power Reactors."

29. **Page I-4** – Table I.1 Standard Occupancy Factors

CORAR requests reference to the guidance from the NCRP in Report 147 (page 31) on the use of occupancy factors in planning and assessing public doses. We suggest that these newer occupancy factors be incorporated into Table I.1 on page I-4.

30. **Page J-2** – In the box titled "Example 2:" - first bullet

It is not clear why high density materials would need to be layered properly in order to be effective shielding for F-18. It is no longer considered standard practice to have low density materials first to shield beta or positron radiation followed by higher density materials to deal with *bremsstrahlung* and gammas. Any *bremsstrahlung* generated by positrons will be adequately shielded by consideration of the two 511 keV photons also associated with each decay.

31. **Page J-2** – In the box titled "Example 2:" - second bullet

What would be considered "each use"? Generally accepted practice is for surveys to be completed as soon as practical at the end of work involving radioactive materials. Personnel contamination surveys are more frequent depending on use.

32. **Page J-5** – Note in the middle of the page.

The criteria provided for minor and major radioactive spills need to include the distance from the source at which the 50 mR/h criteria apply.

33. **Page L-1** – First paragraph

This section needs to discuss the distinction between radiation produced by the accelerator (not regulated by NRC) and radiation emitted from radioactive material produced by the accelerator (regulated by NRC), and then provide guidance on how this distinction is taken into account when radiation level surveys are performed.

34. **Page L-3** – Table L.2

A strange arrow character is located immediately in front of "Ci". It appears this should be the Greek symbol for "micro" and was perhaps a result of translation between different programs.

35. **Page L-4** - Table L.4 - Isotope Groups

Several commonly produced radionuclides are not included. We recommend adding I-123 to Group 2, In-111, Ga-67, and Pb-201 to Group 3, and C-11 and N-13 to Group 4.

36. **Page L-5** – Table L.5 - Acceptable Surface Contamination Levels

I-129 and I-133 are a lesser hazards due to the very low-specific activity of one and the short half-life of the other. All radioiodines should be listed with the gamma-beta emitters as those levels of contamination would not pose an internal contamination hazard.

37. **Page L-8** – First paragraph

    A revised report, ANSI/HPS N13.1-1999 was issued in 1999 to supersede the 1969 report. We suggest you reference the new version. This should also be updated in the References to Appendix L, page L-10. The US EPA has updated their regulatory references to the newer standard.

38. **Page P-9** – paragraph under "Return Waste"

    Additional discussion in this section would be helpful to clarify that residual material contained in returned syringes and vials has a very short half-life and that this material can readily decay to background, enabling used syringes and vials to be returned to the PET producer without being categorized as "radioactive waste."

Minor Grammatical Comments

In at least two locations the article, "a", is used in front of the abbreviation NRC. This seems occur when "A" is the first letter of a sentence (see for example last paragraph of page 8-3 and first paragraph on page 8-4). The proper article for a word that begins with a vowel sound is "an". "An" is used throughout the text in other places.

Throughout the document the term "radioisotope(s)" is used to refer to generic radionuclides. It is more proper when referring to many radioisotopes of many elements to refer to them as radionuclides. The term radioisotopes is more properly used when referring to a single element, not several or all elements.

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Thank you for the opportunity to submit comments on this draft NUREG document. If, in consideration of these recommendations, you or your staff need additional information from CORAR or have any questions, please contact me at 865-218-2595

Sincerely,

Roger Moroney, CHP
Council on Radionuclides and Radiopharmaceuticals