U.S. Nuclear Regulatory Commission
Advisory Committee on the Medical Use of Isotopes

Subcommittee Review and Comments on

Draft Final Proposed Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials,"
Revision 1 (Phase 1) Issue Date: December 2019

Final Report
March 25, 2020

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Charge

During the September 20-21, 2018 ACMUI Meeting, ACMUI Chairman, Dr. Christopher Palestro, established a subcommittee to review the NRC staff's draft proposed revision to Regulatory Guide (RG) 8.39, "Release of Patients Administered Radioactive Materials."

Background

The NRC's current RG 8.39, Revision 0, was issued in April 1997, following the rule change in 10 CFR 35.75 to allow the release of patients administered radioactive material on a solely dose-based criteria. Since that time, there have been several challenges to the appropriateness of the release criteria and the associated precautions that are required to be provided to minimize radiation exposure to other individuals from the released patient. Over the past several years, the NRC staff has conducted an extensive evaluation, which included a review of published literature, and stakeholder engagement with licensees, patients, and Agreement States, to determine whether significant regulatory changes to the patient release program are warranted. A summary of this evaluation can be found in SECY-18-0015 "Staff Evaluation of the U.S. Nuclear Regulatory Commission's Program Regulation Patient Release After Radioisotope Therapy".[1] One of the recommendations was that the guidance in RG 8.39 should be updated, simplified, and made more clear and explicit.

RG 8.39 is currently being revised in two phases. Phase 1 revision of RG 8.39, updates the patient release guidance, including information for patient instructions and updates to Table 3, "Activities of Radiopharmaceuticals that Require Instructions and Records When Administered to Patients who are Breast-Feeding an Infant or Child." An initial proposed Revision 1 (Phase 1) to RG 8.39 was

issued in March 2019 and was reviewed by this ACMUI subcommittee, for which the comments and recommendations can be found in our previous subcommittee report.[2] The following Subcommittee comments and recommendations only pertain to the Final Draft Phase 1 revision, issued December 2019. In Phase 2 revision to RG 8.39, the dosimetric equations, methodologies, and tables used to calculate dose to members of the public from released patients will be updated. This Subcommittee will review those changes once they have been published.

Changes and Recommendations to Regulatory Guidance Considered by the Subcommittee

General Comment:

The Subcommittee commends the NRC efforts in updating the guidance to licensees on meeting the patient release criteria. The Subcommittee also acknowledges and appreciates that most of the recommendations from its previous report on the initial Phase 1 Revision of RG 8.39 have been incorporated, and we provide for your consideration, our specific comments and recommendations on this final draft Phase 1 Revision.

Summary of Recommendations

1. In the Patient Precautions and Instructions Sections, it should be emphasized that the major source of radiation dose to other individuals will be from external exposure from the patient. Therefore, the most important precautions to take are measures to reduce or avoid the external radiation exposure from the patient, especially in the early time period after administration of the radionuclide therapy. While the release instructions may also include measures to limit the transfer of radioactive contamination to others, they should not overshadow or detract from the external precautions, as the radiation doses from internal exposure have been demonstrated to be small or negligible.[3]

2. The patient instructions should be simple, clear, and concise. Consideration should be given to providing instructions at an 8th grade level of understanding, and given in the patient's native or primary language. Studies have shown that the primary factor for limiting radiation exposure to others is in influencing the patient's behavior.[3] As the IAEA noted[4], "The success of a patient release program is critically dependent on the quality and specificity of the information provided to the patient, the skill with which it is communicated, and whether or not the patient believes the information provided."

3. Discussions on the radionuclide therapy procedure and release instructions should also include a caregiver or family member, if possible.

4. Instructions should also be provided on how long the precautions should be followed. As a guideline, the licensee may consider using several (3-5) effective half-lives of the radionuclide therapy.

5. The Regulatory Guide should not include instructions that are excessive, likely to cause patient anxiety, and not likely to reduce public exposures, such as:
    a. Shower 2-3 times a day for the first two days.

b. Try to empty your bladder at least every hour for the first 8 hours. Empty bladder at least once during the first night.
c. After five days of use, replace the tooth brush. The old one is to be placed with the trash being held for a month prior to disposal.
d. Use a second rinse cycle when washing linen, personal clothing, and towels.
e. Instruction to "Drink plenty of liquids" should be deleted as it may conflict with the patient's medical condition. Excessive fluid intake has been reported to cause hyponatremia, which can cause seizures, coma, and even death.

6. Tables 1, 2, and A1 should be updated to include the new and potential radionuclides used in medicine listed below.

Radionuclide	**Half-Life (days)**	**Exposure Rate Constant (R/mCi-hr at 1 cm)**[5]
Ac-225	10	0.126
At-211	0.3	0.214
Cs-131 (implant)	9.7	0.679
Cu-67	2.58	0.574
F-18	0.076	5.68
Ga-68	0.047	5.43
I-124	4.2	6.59
Lu-177	6.7	0.181
Ra-223	11.4	0.77
Re-186	3.7	0.103
Re-188	0.71	0.316
Sm-153	1.93	0.481
Z-89	3.27	6.59

7. In Table 3. "Activities of Radiopharmaceuticals That Require Instructions and Records When Administered to Patients Who Are Breastfeeding an Infant or Child", the subcommittee supports the guidance for a standardized interruption time period of 24 hours for all Tc-99m radionuclides, and the recommended interruption period to limit the dose to the nursing infant to 1 mSv, and not the regulatory limit of 5 mSv.

8. In Phase 2 revision to RG 8.39, where the dosimetric equations, methodologies, and tables used to calculate dose to members of the public from released patients will be updated, the following issues should be considered:
   a. An occupancy factor of 0.75 to 1.0 is unrealistic and cannot be justified for routine application, even for radionuclides with a physical half-life less than one day. Dose calculations should be based on realistic assumptions, and not overly-cautious worst case scenarios.
   b. The dosimetric models and calculations must consider an option that uses the effective half-life and/or other patient specific factors for the radionuclide therapy.
   c. A dose based model should be developed to provide guidance on when precautions or restrictions would be appropriate following the death of a patient administered a therapeutic quantity of radioactive material.

Specific Comments:

Pg 1, Under "Purpose", last sentence: Add the words "activities and" before "dose rates that", and replace the word "should" with "may".

Pg 2, Under "Applicable Regulations", Delete the 4th bullet item (including sub bullets) and replace with:

- 10 CFR 35.75(c) requires the licensee to maintain a record of the basis for authorizing the release of an individual for 3 years after the date of release if the total effective dose equivalent is calculated by (1) using the retained activity rather than the activity administered, (2) using an occupancy factor less than 0.25 at 1 meter, (3) using the biological or effective half-life, or (4) considering the shielding by tissue.
- 10 CFR 35.75(d) requires the licensee to maintain a record for 3 years after the date of release that it provided instructions to a breastfeeding woman if the radiation dose to the infant or child from continued breastfeeding could result in a total effective dose equivalent that exceeds 5 mSv (0.5 rem)

Pg 5, Under "Background", 1st paragraph, 3rd sentence: Delete the words "a dose limit of 1 millisievert (mSv) (0.1 rem), or".

Pg 7, "Harmonization with International Standards": While this newly added section is an appropriate reference to the IAEA work and Report No. 63 "Release of Patients After Radionuclide Therapy", the subcommittee questions the use of the term "Harmonization" as the US patient release criteria is significantly different from the European release criteria.

Pg 8, Section 1.1 Release of Patients Based on the Administered Activity: Suggest moving the sentence "The total effective dose equivalent is approximately equal to external dose because the portion of the internal dose that contributes to the total external dose exposure is small or negligible (see Appendix B, Section B-3)" to after item "d" for better clarity.

Pg 9, Section 1.1 Release of Patients Based on the Administered Activity, last paragraph: Delete "and 2.3", as it does not pertain to breastfeeding infants or children.

Pg 9, Section 1.1 Release of Patients Based on the Administered Activity: Delete last sentence "If a record is required, the licensee may demonstrate compliance by using the records of dosage described in 35.40, "Written directives," which references 10 CFR 35.2040, "Records of written directives," and 35.2063, "Records of dosages of unsealed byproduct material for medical use." These dosage records are different from the record of patient instruction required by 35.75(d).

Pg 9, Table 1. Activities and Dose Rates for Authorizing Patient Release: This table should be updated to include the new and potential radionuclides used in medicine.

Pg 10, Section 2.1 "Activities and Dose Rates That Require Instructions", last sentence: Add "or Appendix B" after "using Equation 2 or 3," and before "as appropriate".

Pg 11, Table 2. Activities and Dose Rates above Which Instructions Should be Given When Authorizing Patient Release: This table should be updated to include the new and potential radionuclides used in medicine.

Pg 12, Table 3. "Activities of Radiopharmaceuticals That Require Instructions and Records When Administered to Patients Who Are Breastfeeding an Infant or Child": The subcommittee supports the guidance for a standardized interruption time period of 24 hours for all Tc-99m radionuclides, and the recommended interruption period to limit the dose to the nursing infant to 1 mSv, and not the regulatory limit of 5 mSv.

Pg 13, Table 3. "Activities of Radiopharmaceuticals That Require Instructions and Records When Administered to Patients Who Are Breastfeeding an Infant or Child", footnote b: Change the word "limit' to "constraint".

Pg 14, Section 2.3 Content of Instructions, 2nd paragraph: Add "currently" after "I-131 is".

Pg 14, Section 2.3 Content of Instructions, 2nd paragraph: Change the last sentence "The instructions should include the name of a knowledgeable person and his or her telephone number to contact if the patient has any questions." to read, "The instructions should include a telephone number for the patient to contact with any questions." Health care facilities establish an on-call number for emergent or after hours coverage. This may not be the same person responding to such a call every day.

Pg 14, Section 2.3.1 Pretreatment Discussions on the Administration of Radiopharmaceuticals, 1st sentence: Add "and caregiver or family member" after "Engaging the patient …" and add "or family member" after "familiarize the patient and caregiver…"

Pg 14, Section 2.3.1 Pretreatment Discussions on the Administration of Radiopharmaceuticals: Change Item a. to read "What type of post treatment lodging (e.g., single family home, group home, apartment, nursing home, hotel, detention facility) will the patient use? The use of hotels should be discouraged, if possible.

Pg 14, Section 2.3.1 Pretreatment Discussions on the Administration of Radiopharmaceuticals: Change Item b. (1) to read "Will the patient use a private vehicle, taxi service, ride-booking service, or public transportation (i.e., bus, train, or airplane)? The use of public transportation should be discouraged."

Pg 15, Section 2.3.1 Pretreatment Discussions on the Administration of Radiopharmaceuticals: Change Item f. to read "Can the patient take care of himself or herself, is he or she capable of complying with the release instructions.", and create a new item to read "Can the patient sleep alone in a separate bedroom or area?"

Pg 15, Section 2.3.1 Pretreatment Discussions on the Administration of Radiopharmaceuticals: Delete Item i. as this is already addressed in Item h.

Pg 15, Section 2.3.1 Pretreatment Discussions on the Administration of Radiopharmaceuticals: Delete Item j. as this question does not help in determining appropriate patient instructions.

Pg 15, Section 2.3.1 Pretreatment Discussions on the Administration of Radiopharmaceuticals: Change Item k. to read "Can the patient delay returning to work? What kind of work does the person do? For example, is the person a day care provider with significant exposure to young children?"

Pg 15, Section 2.3.2 Patient Precautions: Delete the wording in Item a. and replace with "The greatest radiation dose potential to other individuals from the released patient is from external exposure. Therefore, the most important precautions to take are measures to reduce or avoid the radiation exposure emanating from the patient, especially in the early time period after administration of the radiopharmaceutical therapy."

Pg 16, Section 2.3.2 Patient Precautions: After Item a. (1), add the following two precautions to minimize external exposures:

(2) If the patient is traveling with other individuals to the post treatment lodging location, emphasis should be made to minimize the number of traveling companions and to maximize the distance from the patient.

(3) Emphasize abstention from all forms of intimate contact.

Pg 16, Section 2.3.2 Patient Precautions: After Item a. (3), add a new Item b. to address the precautions to limit the spread of radioactive contamination and minimize internal exposures:

"b. The release instructions may include measures that are necessary to limit the transfer of radioactive contamination to others. The licensee should provide specific information on how to limit direct contact with others and on measures necessary to limit the contamination of objects, surfaces, and the spread of radioactive contamination. Patient education and awareness of how to minimize, isolate, and clean radioactive contamination is important in minimizing exposure to others."

Pg 16, Section 2.3.2 Patient Precautions: After new Item b., list the current precautions for (2), (3), (4), (5), (6) and (9). Delete Items (7) and (8). Advice on the recommended length of time before becoming pregnant is a medical issue to be discussed with a physician.

Pg 16, Section 2.3.2 Patient Precautions: Current Items a. (10) and Items b., c., and d. should be formatted as new paragraphs.

Pg 17, Section 2.3.2 Patient Precautions: Delete paragraph "The release instructions may include measures that are necessary to limit the transfer of radioactive contamination …" as this information was presented in Item b.

Pg 17, Section 2.3.3 Patient Instruction, 1st paragraph: In 3rd sentence, add "and/" after "At that point, the patient". Add the following sentence after the 4th sentence, "Consideration should be given to providing instructions at an 8th grade level of understanding, and with consideration given to native or primary language." Add the following sentence as the last sentence, "Instruction should

also be provided on how long the precautions should be followed. As a guideline, the licensee may consider using several (3-5) effective half-lives of the administered therapeutic radionuclide."

Pg 17, Section 2.3.3 Patient Instructions: The list of specific patient instructions should be simplified to read:

a. Minimize the amount of time in close proximity to other people, especially children and pregnant women.
b. Sleep alone in a separate bedroom.
c. Abstain from any intimate contact.
d. Avoid using public transportation.
e. Wash hands frequently and bath daily.
f. Wash laundry separately from others.
g. Use dedicated or disposable kitchen utensils, and do not share them with others.
h. Use a dedicated sole use bathroom, if possible. Always sit on the toilet. Flush the toilet twice after each use.
i. Use disposable gloves and flushable wipes when cleaning.
j. Discard trash separately and/or hold it to allow for radioactive decay.
k. Avoid preparing or sharing food with others.

Pg 17-18, Section 2.3.3 Patient Instructions: The following specific patient instructions should be deleted as they are excessive, difficult to comply with, and will likely cause patient anxiety:

e. Shower 2-3 times a day for the first two days.

f. Try to empty your bladder at least every hour for the first 8 hours. Empty bladder at least once during the first night.

i. After five days of use, replace the tooth brush. The old one is to be placed with the trash being held for a month prior to disposal.

p. Wash linen, personal clothing, towels, etc. separately from those used by family members. A second rinse cycle is recommended.

Patient instruction o. "Drink plenty of liquids (water, juice, tea, etc.)" should be deleted as it may conflict with the patient's medical condition. Excessive fluid intake has been reported to cause hyponatremia, which can cause seizures, coma, and even death.

Pg 19, Section 2.3.4 Patient Acknowledgment of Instructions, Item a: Add "prior to treatment" after "treatment process".

Pg 19, Section 2.3.4 Patient Acknowledgment of Instructions, Item c (6): Change wording to read "contact information if questions arise about the radiation safety instructions during the recovery period."

Pg 19, Section 2.4 Death of a Patient Following Radiopharmaceutical Administration or Implants, 1st sentence: Add the words "administration of" before "a therapeutic quantity" and delete the words "of administration" after "therapeutic quantity".

Pg 20, Section 2.4 Death of a Patient Following Radiopharmaceutical Administration or Implants, 5th paragraph, 1st sentence: Add the words "administration of" before "a therapeutic quantity" and delete the words "of administration" after "therapeutic quantity". Change the words "body contains therapeutic quantities" to "body contains residual quantities".

Pg 20, Section 2.4 Death of a Patient Following Radiopharmaceutical Administration or Implants, 6th paragraph: Move the first sentence to the last sentence in the paragraph.

References

1. NRC Policy Issue (Information) SECY-18-0015, "Staff Evaluation of the U.S. Nuclear Regulatory Commission's Program Regulation Patient Release After Radioisotope Therapy", January 29, 2018
2. ACMUI, Subcommittee Review and Comments on Draft Proposed Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials," Revision 1 (Phase 1) Final Report, June 19, 2019
3. NRC Publication, "Patient Release After Radionuclide Therapy – A review of the Technical Literature, Dose Calculations, and Recommendations", Reviewed by Shaheen Dewji and Nolan Hertel, September 25, 2017
4. IAEA Safety Reports Series No. 63, "Release of Patients after Radionuclide Therapy", International Atomic Energy Agency, 2009
5. Smith,DS, Stabin MG, "Exposure Rate Constants and Lead Shielding Values for Over 1,100 Radionuclides", Health Physics (102(3):271-291), 2012

The ACMUI unanimously approved this report, and the recommendations provided therein, during a public teleconference meeting on March 11, 2020.

Respectfully submitted on March 25, 2020,

Subcommittee on Regulatory Guide 8.39 Release of Patients Administered Radioactive Materials
Advisory Committee on the Medical Use of Isotopes (ACMUI)
U.S. Nuclear Regulatory Commission (NRC)