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Comment On: NRC-2023-0086-0001
Draft Regulatory Guide: Release of Patients Administered Radioactive Material; Extension of Comment Period

Document: NRC-2023-0086-DRAFT-0011
Comment on FR Doc # 2023-08418

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General Comment

The University of Virginia would like to formally submit our comments regarding Regulatory Guide 8.39 "Release of Patients Administered Radioactive Material". UVA disagrees with NRC's proposal of lowering the release criteria's and requiring the use of an occupancy factor of 1 for the release calculation.

On Page 9, under Section C.1, equation 1 uses the following assumption: "An occupancy of 100 percent at 1m is assumed". UVA is submitting the following comment on that assumption: "This assumption makes no sense when releasing a patient. No one person is around an individual within 1 m for 24 hours a day"

On Page 9, under Section C.1, the NRC states: "Equation 1 does not account for patient-specific information. The assumptions listed above are meant to be overly conservative to ensure compliance by avoiding the underestimation of dose in likely situations." UVA is submitting the following comment on that statement: "The equation needs to take into account patient uptake to be useful for a patient release. By using a patient's specific uptake fraction, you are providing the best and correct guidance to the patient. By using a non-specific uptake fraction, you are requiring the patient to be isolated beyond what is necessary which can be frustrating and upsetting to the patient.

On Pages 11-14 for Tables 1 and 2, the NRC has greatly reduced the values that licensees will be allowed to use when releasing patients. UVA is submitting the following comment for these tables: "By lowering the values for licensees, you will be requiring them to perform calculations for patient release when they were not needed previously. This will cause a great burden for some licensees who do not retain Certified Health Physicists or Medical Physicists to understand and perform the calculations. UVA believes the table values should not be lowered.

UVA is also recommending the NRC follow the comments and recommendations made by the Advisory Committee on the Medical Uses of Isotopes (ACMUI). I have attached the January 1, 2022 report.

I have also attached an article from the Journal of Nuclear Medicine, Vol. 42, No. 6 dated June 2001 titled: "Radiation Doses to Family Members, Rutar et al." which detailed that members of the public were not exposed to a dose greater than 500 mrem from released patients.

Lastly I have attached SECY-18-0015, in which data was provided to show that members of the public required to be near a released patient for a non-realistic time frame in order to exceed a dose of 500 mrem. The lowering of release limits seems to counter this finding.

Thank you for considering our comments.

Michael Welling
University of Virginia Radiation Safety Officer

Attachments

ML22021B300 2022 ACMUI comments on RG 8.39 Rev. 2

2001 patient release study with dosimetry

SEC-18-015 ML17279B140 I-131 patient release

U.S. Nuclear Regulatory Commission (NRC)
Advisory Committee on the Medical Uses of Isotopes (ACMUI)

Revision 2 to Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials"

Final Report
Submitted: January 21, 2022

Subcommittee Members:

Dr. Vasken Dilsizian
Dr. Hossein Jadvar
Mr. Josh Mailman
Ms. Melissa Martin
Ms. Megan Shober (Chair)

Consultant to Subcommittee: Mr. Michael Sheetz
NRC Staff Resource: Katherine Tapp, Ph.D.

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 revisions to Regulatory Guide (RG) 8.39, "Release of Patients Administered Radioactive Materials."

Background

The NRC's 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 clearer and more explicit.

The revision of RG 8.39 is being conducted in two phases. Phase 1 revision of RG 8.39, which was completed in April 2020, updated 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." This ACMUI subcommittee's review and recommendations for Phase 1 can be found in our previous subcommittee reports.[2,3] The following Subcommittee comments and recommendations pertain to the Draft Phase 2 revision to RG 8.39, which updates the dosimetric equations, methodologies, and tables used to calculate dose to members of the public from released patients.

General Comment:

The Subcommittee commends the NRC for their 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 two previous reports on the Phase 1 Revision of RG 8.39 have been incorporated. However, the draft Phase 2 Revision has made changes to the patient instructions, therefore, this content area will be included again in our comments and recommendations. The subcommittee recognizes that while this guidance document is primarily intended for licensees, it will also be viewed by patients, and their family and friends, so it is important for the content to be clear and easy to understand.

Summary of Recommendations

1. In the Content of Instructions Section (4.2), the subsections should be reordered to the original sequence: (1) Pretreatment Discussions on the Administration of Radiopharmaceuticals, (2) Patient Precautions, (3) Patient Instructions, (4) Patient Acknowledgement of Instructions. It is important to emphasize upfront 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. This is discussed in the Patient Precautions subsection and so it should precede the Patient Instruction subsection. While the release instructions may also include measures to limit the transfer of radioactive contamination to others, they should not overshadow or distract from the external precautions, nor should it cause patient anxiety, as the radiation doses from internal exposure have been demonstrated to be small or negligible.[4, 5] Suggested rewording of the patient instructions to make them more clear and easy to understand, and elimination of some precautions that have little effect in reducing bystander dose has been provided in the specific comments.

2. The basic administered activity thresholds in Table 1, and corresponding measured dose rates in Table 2, for the release of patients (and for providing instruction) were calculated assuming an occupancy factor of 100% at 1 meter. An occupancy factor of 1.0 is unrealistic and cannot be justified for routine application, even for radionuclides with a physical half-life less than one day. The corresponding activity and dose rate values are extremely conservative, and a factor of four lower than what is currently in RG 8.39 Revision 1. This will result in an increased need for licensees to perform patient specific dose calculations and provide patient instructions at activity levels much lower than previously required. This guidance is also not consistent with the record keeping requirement in 10 CFR 35.2075(a), which only requires a record of the release if using an occupancy factor less than 0.25 at 1 meter. It is recommended that the activity and dose rate values in Tables 1 and 2 be calculated with an occupancy factor of 0.25 at 1 meter, to be more realistic and compatible with 10 CFR 35.2075(a).

3. Sections 1.3 and 3.3 “Release of a Patient After a Hold Time” require the licensee to calculate the amount of time the patient release must be delayed for either radioactive decay or biological elimination to reduce the administered activity down to the threshold value in Table 1. Holding a patient after administration of a radiopharmaceutical to allow for some level of decay or biological elimination is not a current practice in the United States. Licensees will either use an effective half-life for a patient specific dose calculation or the measured exposure rate for release of the patient. This section should be removed as it is not

a practical option due to the length of holding time typicaly required to reduce the retained activity.

4. The Patient-Specific Modifying Factors and Methods presented in Appendix B, and Example Calcultions illustrated in Appendix C, are overly complex and require an unrealistic level of knowledge of extended patient behavior following release. While this calculational methodology is an admirable academic exercise, it is not practical for licensees to use for authorizing and documenting patient release using patient specific factors. Determining "Time Durations" for Travel, Instruction, and Afterward in units of effective half-lives, and the corresponding fraction of time a bystander spends in close contact with the patient during these periods would be unworkable. While the Geometric Modifying Factor accounts for varying bystander separation distances and source-receptor configurations, it again requires an unrealistic detailed knowledge of patient and bystander behavior following release. The Attenuation Modifying Factor tables account for photon scatter, buildup, and absorption at different patient tissue thicknesses, however, buildup is not applicable for distributed sources within the body and accurately determining the overlying tissue thickness would be much more challenging than simply measuring the dose rate from the patient after administration of the radiopharmaceutical. To be of practical operational value, the model needs to be simplified, such as that in the current RG 8.39 or the RADAR Patient Exposure Radiation Dose Calculator.[6] Consideration should be given to eliminating the geometric and attenuation modifying factors, keeping the biokinetic modifying factor (effective half-life) and simplifying the occcupancy modifying factor to single values of 0.5, 0.33, 0.25, 0.125, and 0.0625 for various patient/bystander conditions or situations. Examples of the possible occupancy conditions could be:
    a. Patient is unable or unwilling to follow any instructions (0.5)
    b. Patient requires significant medical care or living assistance (0.33)
    c. Patient will be around other members of the household and public but will follow instructions (0.25)
    d. Patient lives alone but will have potential contact with members of the public and will follow instructions (0.125)
    e. Patient lives alone and will not have any contact with others and will follow instructions (0.0625)

   Attachment 1 contains a sample patient questionnaire that could be used to ascertain the information to assign the appropriate occupancy factor.

5. In Section 6 "Material Separated from the Patient", it states that the dose limits in 10 CFR Part 20 apply to exposure from radioactive material separated from a released patient. The Subcommittee strongly disagrees with this position. Since the dose limits in 10 CFR Part 20 do not apply to radiation exposure from a patient released in accordance with 10 CFR 35.75, it is only reasonable that this would also apply to exposure from any radioactive material that the patient excretes or physically separates from the patient, with the exception of temporary implants. A licensee cannot practically control or predict, nor would they be able to know or evaluate if an event occured where radioactive material separated from a patient caused an exposure to a bystander. It is illogical and impractical for radioactive material that separates from a patient released in accordance with 10 CFR 35.75 to become "licensable" again under the licensee that administered it to the patient (with the exception of temporary implants which are still covered under the license even though the patient has been released).

6. In Section 4.3 "Death of a Patient Following Radiopharmaceutical Administration or Implants," the results of an analysis indicate that for several radionuclides, dose rates exceeding 0.02 mSv/h or total doses in excess of 1 mSv are possible if unexpected death were to occur within days of release and knowledge of the radioactive administration is not communicated. It should be noted that the analysis made very conservative assumptions. The dose rate was calculated only 6 hours after administration with no acccount for biological elimination, and the total dose was calculated for an exposure from hour 12 to 32 at a distance of 1 meter with full occupancy and no account for biological elimination. Therefore, the likelihood of these dose rates and integrated doses occurring from a decedent previously administered radionuclide therapy is exceedingly small. It would be helpful if a similar type of analysis were performed of the potential exposures from cremation of a body containing radioactive material, specifically, exposure to crematorium staff and exposure to the public from effluent releases.

Specific Comments:

Pg 1, Purpose: Continue the sentence "This RG also provides licensees with a methodology to modify the threshold …." in the first paragraph and start a new paragraph with the sentence "In addition, the RG provides licensees with instructions for patients…".

Pg 2, Applicable Regulations, 10 CFR 35.75(b): Change last sentence to read "If the dose to a breastfeeding infant or child could exceed an effective dose equivalent of 1 mSv (0.1 rem) without the patient's interruption of breastfeeding, written instructions must be given to the nursing mother on (1) guidance on the interruption or discontinuation of breastfeeding and (2) information on the potential adverse consequences if breastfeeding is not ceased or discontinued.

Pg 3, Table of Contents: Delete Section 3.3 Release of Patients After a Hold Time.

Pg 3, Table of Contents: 4.2 Content of Instructions, Reorder sequence of subsections to: (1) Pretreatment Discussions on the Administration of Radiopharmaceuticals, (2) Patient Precautions, (3) Patient Instructions, (4) Patient Acknowledgement of Instructions.

Pg 4, Background: In first sentence change 1979 to 1997.

Pg 5, Consideration of International Standards: Second paragraph, change (rem) to (tenths of rem).

Pg 7, Section 1 release Criteria: Consider using the exposure rate constant readily available in the literature[5,6] for Δ_{pr} instead of a calculated dose rate constant. It will be much simpler to obtain for new radionuclides and it does not differ significantly from the calculated dose rate constant.

Pg 8, Section 1, fourth paragraph: Delete the last sentence, "In addition, licensees may need to consider both internal and external exposure to a bystander from byproduct material which could have become separated or excreted from a patient…". It is impractical for a licensee to control or predict the exposure to a bystander from radioactive material separated (excreted) from a patient.

Pg 9, Table 1: The activity threshold for C-14 is unrealistically low due to its extremely long half-life and theoretical exposure from a patient.

Pgs 9, 11, and 14: Add Ac-225 to Tables 1, 2, and 3.

Pg 11, Table 2: The measurement thresholds for C-14, Ru-106, and Sr-90 are less than background levels (approximately 0.02 mR/hr) and cannot be accurately measured. A footnote should be added to state "Activity and dose rate limits do not apply to these radionuclides because of the minimal exposures to members of the public resulting from dosages normally administered for diagnostic or therapeutic purposes." Also, listing PET isotope measurement thresholds over 1 R/hr is imprudent.

Pg 12, Section 1.3 Release of a Patient After a Hold Time: This section should be deleted as it is not a practicle option due to the length of holding time for physical decay. Licensees will either use an effective half-life for a patient specific dose calculationor or the measured exposure rate for release of the patient.

Pg 13, Section 2 Breastfeeding Patients: First paragraph, 1st sentence, add the word "written" before "instructions and change the word "were" to "was". Second paragraph, 3rd sentence, Change the word "were" to "was".

Pg 14, Section 2, Table 3: Values in Column 1 and Column 2 that are less than 1 microcurie (or some similarly low value) should just be noted as record/instructions required. Listing nanocurie or lower values is not helpful with respect to medical use quantities.

Pg 15, Section 2, Table 4: For the very long recommended interruption times, it would be better for the guidance to say, "complete cessation for this child". Having a specific number 1400 hours vs. 1700 hours etc. is not practical for patients to follow. No nursing mother should be led to think that a 1400-hour interruption should be considered.

Pg 16, Section 3 Patient Specific Dose Calculations: First paragraph, in the sentence "In the basis, licensees must document any patient-specific modifying factors used in the calculation and a general description of how that information was acquired…", Change the word "must" to "should" as there is no regulatory requirement to document how patient specific information was obtained.

Pg 16, Section 3 Patient Specific Dose Calculations: First paragraph, Delete the sentence "Patient instructions must match or be more limiting than patient-specific factors used to release patients…" as there is no requirement to match patient instructions to patient specific dose calculations.

Pg 17, Section 3.1 Release of Patients Based on the Administered Activity: First sentence, "licensees may calculate patient-specific thresholds on a case-by-case basis." There should be an option to create a class or category of general patient specific factors applicable to multiple patients.

Pg 17, Section 3.1 Release of Patients Based on the Administered Activity: Second paragraph, delete "or based on a calculated hold time in Section 3.3".

Pg 17, Section 3.2 Release of Patients Based on the Measured Dose Rate: Delete "c. Calculate a hold time described in Section 3.3".

Pg 17, Section 3.3 Release of a Patient After a Hold Time: Delete section as it is not practical to hold a patient to allow for decay or biological elimination in order to allow for release.

Pg 20, Second paragraph: Delete the sentence "I-131 is currently the medical radioisotope of highest concern, as it is the most commonly used radionuclide in radiopharmaceutical therapy…"

as it will soon be surpassed by other radiopharmaceuticals and volatility is not an issue with I-131 inside a patient's body.

Pg 20, Second paragraph: Change second sentence to read "The regulations in 10 CFR 35.75 apply to all medical radioisotope therapies such as iodine (I)-131, yttrium (Y)-90, I-125, cesium (Cs)-131, lutetium (Lu)-177, radium (Ra)-223, and actinium (Ac)-225.

Pg 21, Under (3): Change second sentence to read "Patients who travel via motor vehicle, boat, or airplane through international border checkpoints are subject to screening for radiation.

Pg 21, Section 4.2.4 Patient Precautions should follow Section 4.2.1 Pretreatment Discussions on the Administration of Radiopharmaceuticals to place the emphasis on external exposures and precautions.

Pg 22, Third paragraph: Delete the sentences "To ensure dose limits are not likely to be exceeded, licensees must ensure patients can follow instructions if they are used to justify patient-specific modifying factors to demonstrate exposures will be less than 5 mSv (0.5 rem). Pre-treatment discussions with patients, or caregivers, such as those described in the section above, can help a licensee determine if a patient is able to follow the instructions and identify patients who cannot. If a patient is unable or unwilling to follow necessary instructions for release, they may need to be held longer than others with similar administrations." as it is redundant with what is stated in the previous paragraph.

Pg 22, Patient Instructions a-l: Suggest replacing the patient instructions a-l with the following to be more clear, concise, and consistent with the Patient Precaution section:

1. Minimize the time you spend in close contact with other individuals, especially pregnant women and young children (a general guideline is no closer than 3 feet for more than 1 hour per day). Try to maximize your distance from others as much as possible (6 feet).

2. Avoid direct contact or sharing of personal items which may result in the contamination of others with your body fluids (saliva, urine, sweat), especially pregnant women and young children.

3. Sleep alone in a separate bedroom. Avoid kissing or any intimate contact with another person.

4. If possible, have sole use of a bathroom (males should sit to urinate to avoid splashing).

5. Use good hygiene habits, wash your hands frequently. Use separate towels and washcloths.

6. Avoid handling or preparing food for others. Use separate dishes, cups, and eating utensils.

7. Avoid public facilities and the use of public transportation if possible.

8. Maintain good hydration, as directed by a physician.

9. If you need any medical care, the medical personnel should be informed about these instructions.

10. You should be aware that radiation detection devices used at border crossings, airports and federal facilities for homeland security purposes may be sensitive enough to detect the radioactivity levels in your body for up to several weeks. You should carry these instructions when you travel and provide them to law enforcement authorities if detained for triggering a radiation monitor.

Pg 23, First paragraph: Delete the sentence "The licensee should also inform the patient on how to clean up an area contaminated with body fluids (e.g., urine, vomit) and how to dispose of the cleaning materials." As it has been previously stated multiple times and the emphasis should be on external exposures.

Pg 23, Section 4.2.4 Patient Precautions, a. (1): Change first sentence to read "Emphasize the importance of keeping an adequate distance from others, especially children and pregnant women and to also minimize the time near others." Delete the sentences "Can arrangements be made for family members (including children and any pregnant household members) to lodge elsewhere temporarily? Or can another individual come and take care of the children and any pregnant household member in their home." The emphasis is simply to maintain an adequate distance from others, especially children and pregnant women.

Pg 24, Section 4.2.4 Patient Precautions, a. (3): Change sentence to read "Emphasize for the patient to sleep separately and abstain from all forms of intimate contact."

Pg 24, Section 4.2.4 Patient Precautions, b. (1): Change sentence to read "Encourage the patient not to prepare or share food with others and to use separate dishware and eating utensils."

Pg 24, Section 4.2.4 Patient Precautions, b.: Delete items (3), (4), and (5) as they are excessive, arbitrary, and not likely to reduce exposure to others.

Pg 25: Delete first full paragraph "The licensee may encourage patients to have available plastic bags, disposable gloves and wipes before treatment…." as this is redundant with the previous statement in this section.

Pg 25, Section 4.3 Death of a Patient Following Radiopharmaceutical Administration or Implants: It should be noted that the analysis made very conservative assumptions. The dose rate was calculated only 6 hours after administration with no acccount for biological elimination, and the total dose was calculated for an exposure from hour 12 to 32 at a distance of 1 meter with full occupancy and no account for biological elimination.

Pg 26, Section 4.3 Death of a Patient Following Radiopharmaceutical Administration or Implants: Change last sentence to read "The administering licensee should provide precautions to the funeral director for family members and the public to follow during visitation prior to burial or internment."

Pg 26, Records of Release: First paragraph, last sentence: Delete "or greater than 1" as this is unrealistic for exposures from a patient.

Pg 26, Records of Release: Delete "c. For Delayed Release of a Patient Based on a Radioactive Decay Calculation" as this is not used.

Pg 27, Section 6 Material Separated from the Patient: The dose limits in 10 CFR Part 20 do not apply to radiation exposure from a patient released in accordance with 10 CFR 35.75. This would also apply to exposure from any radioactive material that the patient excretes or physically separates from the patient, with the exception of temporary implants. A licensee cannot practically control or predict, nor would they be able to know or evaluate, if an event occured where radioactice material separated from a patient caused an exposure to a bystander. It is illogical and impractical for radioactive material that separates from a patient who has been released in accordance with 10 CFR 35.75 to become "licensable" again under the licensee that administered it to the patient (with the exception of temporay implants whcih are still covered under the license even though the patient has been released).

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. ACMUI, Subcommittee Review and Comments on Final Draft Proposed Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials," Revision 1 (Phase 1) Final Report, March 25, 2020
4. 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
5. RCD Radiation Protection Associates. "Activity Thresholds, Patient-Specific Modifying Factors, Breastfeeding Interruption Times, and Other Supporting Data," Research Information Letter Report for Phase 2 Revisions to Regulatory Guide 8.39: Release of Patients Administered Radioactive Material. RCD-21-181-0. Corvallis, OR. June 30, 2021. (ML21214A223)
6. RADAR Exposure and Dose Calculator (doseinfo-radar.com)
7. International Commission on Radiological Protection (ICRP). Nuclear Decay Data for Dosimetric Calculations. Annals of the ICRP. Publication 107. 38(3). 2008.
8. Smith, DS, Stabin MG, "Exposure Rate Constants and Lead Shielding Values for Over 1,100 Radionuclides", Health Physics (102(3):271-291), 2012

Respectfully submitted,

Subcommittee on Regulatory Guide 8.39 Release of Patients Administered Radioactive Materials,
Advisory Committee on the Medical Uses of Isotopes
U.S. Nuclear Regulatory Commission

The ACMUI unanimously approved this report as presented during its public teleconference meeting on December 15, 2021.

Attachment 1

PATIENT QUESTIONNAIRE FORTREATMENT WITH IODINE – 131

Patient Name: _____ Referring Physician: _____

MRN: _____ Patient Age: _____

1. **Confirmation that the patient is not pregnant (12-55 yrs.)**
   Date of negative pregnancy test: _____ (Must be within 24 hours of dosing)
   Other (Age, Tubal Ligation, or Hysterectomy): _____

2. **Is the patient breastfeeding? Yes _____ No _____**

3. **Where will the patient reside after administration of the therapeutic dose?**
   _____

4. **How will the patient travel to place of residence and who will be traveling with the patient?**

   _____

5. **List the age and relationship of all other household members who will be staying with the patient when they get dosed?**
   _____

   _____

6. **Will there be any young children (<10 yrs) or pregnant women at home when the patient returns after treatment? Yes _____ No _____**

7. **Will the patient be responsible for the primary care of any young children or individuals requiring living or medical assistance? Yes _____ No _____**

8. **Is the patient scheduled for travel or vacation for 2 wks after dosing?**
   Yes _____ No _____

9. **What is the patient's occupation and specific job duties?**
   _____

   _____

10. **Can the patient remain home from work for the recommended time?**
    Yes ___ No ___ NA ___

11. **Does the patient require any special medical care or living assistance? Yes ____ No _____**

12. **Is the patient incontinent or have any urinary bladder control problems? Yes ____ No____**

13. **Are there any other issues that would prevent the patient from being able to comply with radiation safety instructions? Yes _____ No _____**

    Explain: _____

Individual completing questionnaire: _____ Date: _____

Prescribed Dose:_____% Uptake: _____

Outpatient Treatment with ^{131}I-Anti-B1 Antibody: Radiation Exposure to Family Members

Frank J. Rutar, Samuel C. Augustine, David Colcher, Jeffry A. Siegel, David A. Jacobson, Margaret A. Tempero, Valorie J. Dukat, Maribeth A. Hohenstein, Lisa S. Gobar, and Julie M. Vose

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The Nuclear Regulatory Commission (NRC) regulations that govern release of patients administered radioactive material have been revised to include dose-based criteria in addition to the conventional activity-based criteria. A licensee may now release a patient if the total effective dose equivalent to another individual from exposure to the released patient is not likely to exceed 5 mSv (500 mrem). The result of this dose-based release limit is that now many patients given therapeutic amounts of radioactive material no longer require hospitalization. This article presents measured dose data for 26 family members exposed to 22 patients treated for non-Hodgkin's lymphoma with ^{131}I-anti-B1 antibody after their release according to the new NRC dose-based regulations. **Methods:** The patients received administered activities ranging from 0.94 to 4.77 GBq (25–129 mCi). Family members were provided with radiation monitoring devices (film badges, thermoluminescent or optically stimulated luminescent dosimeters, or electronic digital dosimeters). Radiation safety personnel instructed the family members on the proper wearing and use of the devices. Instruction was also provided on actions recommended to maintain doses to potentially exposed individuals as low as is reasonably achievable. **Results:** Family members wore the dosimeters for 2–17 d, with the range of measured dose values extending from 0.17 to 4.09 mSv (17–409 mrem). The average dose for infinite time based on dosimeter readings was 32% of the predicted doses projected to be received by the family members using the NRC method provided in regulatory guide 8.39. **Conclusion:** Therapy with ^{131}I-anti-B1 antibody can be conducted on an outpatient basis using the established recommended protocol. The patients can be released immediately with confidence that doses to other individuals will be below the 5-mSv (500 mrem) limit.

Key Words: release criteria; radionuclide therapy; radiation safety; monoclonal antibody therapy

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In 1997, the Nuclear Regulatory Commission (NRC) amended its regulations concerning criteria for the release of patients who have been administered radioactive material (*1*). The new criteria authorize patient release according to a dose-based limit (5 mSv to the maximally exposed individual) rather than the traditional activity-based limit ($<$1.11 GBq [30 mCi] or $<$0.05 mSv [5 mrem/h] at 1 m). The dose-based limit better expresses the primary concern of the NRC for public health and safety. This concern is reflected in a revised version of 10 Code of Federal Regulations (CFR) 35.75, which governs the release of patients containing radioactive materials; guidance is given in regulatory guide 8.39 (*2*). Compliance with this dose limit may be shown by licensees in 3 ways: use of a default table of administered activity, use of a default table of patient dose rates, or use of patient-specific dose calculations. A regulatory analysis (*3*) of the new dose-based limit concluded that the new standard is acceptable according to current radiation protection principles, resulting in fewer hospitalizations, and therefore significantly reduces national health care costs; in addition, earlier release benefits patients and their families personally and psychologically.

Before the NRC rule change, most radionuclide treatment protocols required extended patient hospitalization. This requirement, though intended to protect family members and others who would otherwise be in close contact with the patient, added to the effort, cost, and inconvenience of this treatment. In many cases, therapies were performed as inpatient solely to comply with regulations and not for medical reasons. In some instances, the previous limit coerced physicians to administer less radioactivity than they would have liked so that hospital stays could be avoided (*4*). Under the new regulations, many patients can now be immediately released from the hospital or clinic after therapy with radionuclides (*5–8*). Patient-specific calculations have indicated that all patients receiving ^{131}I-anti-B1 monoclonal antibody (Bexxar, tositumomab and ^{131}I-tositumomab; Corixa Corp., South San Francisco, CA), an investigational

new therapy for B-cell non-Hodgkin's lymphoma (*9–11*), are now releasable. Therefore, the new regulations permit ^{131}I-anti-B1 antibody therapy to be conducted on an outpatient basis using the established recommended protocol (*5*).

Although the patient who has received ^{131}I-anti-B1 antibody is releasable, it is important to determine whether other individuals exposed to the released patient are receiving doses < 5 mSv (500 mrem). Direct measurements are the best way to determine the dose any individual is likely to receive on the basis of the realities of daily living. In most cases, the maximally exposed individual will be a close family member. Generally, one must assume that such individuals will have little or no knowledge of radiation safety and thus require some instructions to limit their potential exposure. Although the NRC has provided patient release criteria (*2*), guidance on instructing these patients to keep the radiation dose to others as low as is reasonably achievable (ALARA) is limited. Recently, more guidance has been provided in the literature (*5,6,12,13*). Therefore, this study was conducted to determine the radiation doses received by maximally exposed members of the general public (e.g., family members) from patients who received therapeutic doses of ^{131}I-anti-B1 antibody as an outpatient treatment and to determine whether the instructions provided to maintain doses ALARA were adequate. The family members were provided with radiation monitoring devices (film badges, thermoluminescent or optically stimulated luminescent dosimeters (OSLs), or electronic digital dosimeters) to measure their radiation doses and also to confirm that these doses were below regulatory limits. Instructions were provided on actions recommended to keep doses to potentially exposed individuals ALARA. The dose measurement results of the radiation monitoring devices worn by the family members confirm the appropriateness of and patient compliance with the instructions provided.

MATERIALS AND METHODS

Patients

Twenty-two patients received intravenous radioimmunotherapy with ^{131}I-anti-B1 monoclonal antibody. Patients were administered a therapeutic amount calculated to deliver a nonmyeloablative total-body absorbed dose (30–75 cGy) as part of several different clinical research protocols. The administered therapy dose was based on the patient's total-body residence time, which was determined from an initial dosimetric study (*14*).

Patient-Specific Dose Calculation

According to the regulatory guidance, patients may be released on the basis of specific conditions. The following equations were used to calculate the total effective dose equivalent to individuals exposed to the patient for an infinite time (derivations of these equations are discussed in the Appendix):

On the basis of administered activity:

$$D(\infty) = Q_0[1.56 + 1.85\ T_{eff}]/3700. \quad \text{Eq. 1}$$

On the basis of the patient's dose rate:

$$D(\infty) = D_r[4.68 + 8.41\ T_{eff}] + (0.000143)Q_0, \quad \text{Eq. 2}$$

where $D(\infty)$ is the total effective dose equivalent (millisieverts) to the maximally exposed individual over an infinite time, Q_0 is the administered activity (megabecquerels), T_{eff} is the patient's total-body effective half-time (days) determined by measurements after a tracer dose, T_{eff} is $0.693 \times \tau$ (residence time) under the condition of modeling whole-body retention as a single exponential, and D_r is the dose rate (mSv/h) at 1 m from the patient immediately after therapeutic administration.

The release criteria calculated using the administered activity (Eq. 1) are more conservative than those calculated using the patient's dose rate (Eq. 2), because no attenuation of the radiation by the body is considered. With the release limit of $D(\infty) < 5$ mSv (500 mrem), Equations 1 and 2 can be rearranged as follows to determine maximum administered activity or patient dose rate for patient release (i.e., either Eq. 3 or Eq. 4 must be true to allow release):

$$Q_0 < 18{,}500/[1.56 + 1.85\ T_{eff}] \quad \text{Eq. 3}$$

$$D_r < [5 - (0.000143)(Q_0)]/[4.68 + 8.41\ T_{eff}]. \quad \text{Eq. 4}$$

These calculations take into account internal dose contribution and are based on conservative assumptions given in regulatory guide 8.39 (*2*). For example, regulatory guide 8.39 assumes that for the first 8 h after administration of radioiodine, 80% of the radioactivity is not voided from the urinary bladder (e.g., eliminated solely by the 8-d physical decay of ^{131}I) and that the occupancy factor (the fraction of time that the maximally exposed individual is within 1 m of the patient) is 0.75 for this initial period.

If the actual administered activity is less than the activity determined according to Equation 3, then the patient is releasable according to the new NRC regulations. Equation 3 involves the use of only a single patient-specific factor (i.e., effective half-time), which must be included in the patient's record at the time of release. Equation 4 was also used to determine the releasibility of the patient. In this case, a second patient-specific factor, the patient's dose rate at 1 m, which accounts for attenuation, must also be included in the patient's record at the time of release. The dose rate is measured after the therapeutic administration. All the calculations assume the use of an occupancy factor of 0.25 after the initial 8-h nonvoiding period. The occupancy factor is the fraction of time that an individual is assumed to be 1 m away from the released patient. If there is justification for using a lower occupancy factor of 0.125, or if a higher occupancy factor of 0.5 or more is indicated, then the calculated values must be changed accordingly (*5,7*).

For the ^{131}I-anti-B1 antibody protocol, data indicate that a more appropriate assumption is that an initial nonvoiding period of 3 h can be used, instead of the 8-h period suggested by the NRC. A 3-h period is more appropriate because it has been shown to be a conservative estimate for the time of the first voiding of the urinary bladder (*15*) and because it is consistent with the analysis performed on 109 ^{131}I-anti-B1 antibody patient studies (*6*). The conservative nature of this 3-h assumption is further supported by the fact that ^{131}I-anti-B1 antibody is absorbed instantaneously because of its intravenous administration, whereas regulatory guide 8.39 assumed oral administration. Additionally, for this initial nonvoiding period, it makes sense to account for 100% of the administered activity and not the 80% recommended in regulatory guide 8.39.

Using these assumptions and the fact that $R/h = \Gamma Q_0/r^2$, the dose over an infinite time to the exposed individual becomes:

$$D(\infty) = D_r[2.24 + 8.56\ T_{eff}]. \quad \text{Eq. 5}$$

This equation was also used to project the dose for infinite time in this study.

Guidelines

If the calculations indicate that the patient is releasable, one then determines whether the patient can actually be released. Patients containing >1.22 GBq (33 mCi) ^{131}I (or with a dose rate > 0.07 mSv/h [7 mrem/h] at 1 m) can be released if one can show that no individual who comes into contact with the patient is likely to receive a dose > 5 mSv. The release is dependent on the circumstances of each patient. Interviewing the patient and using that information to determine whether the patient may be released are essential. Factors to consider include the patient's ability to understand and willingness to follow written instructions, the patient's ability to care for himself or herself, the patient's ability to refrain from returning to work if necessary, the patient's exposure to others while returning home after treatment, and the presence of urinary incontinence. The form that we used to interview patients is shown in Figure 1. Once the patient interview is completed, the responsible physician or radiation safety officer evaluates whether the patient can be released. If the determination is affirmative, discharge instructions are given to the patient.

Instructions to Patients and Caregivers

Once the release has been determined, the patient must be provided with written instructions to comply with the provisions of 10 CFR 35.75(b). The instructions and all related discussions must be in a simple and clear format so that the patient can understand their importance. Specific instructions were developed to address the unique requirements of patients treated with the ^{131}I-anti-B1 antibody to maintain exposures ALARA to other individuals.

Patient discharge instructions for various activities (e.g., using public transportation, attending to personal hygiene, and maintaining distance from others) were developed using exposure data obtained from patients who had been treated with ^{131}I-anti-B1 antibody and confined under the old release regulations and by making assumptions about the distances at which individuals typically interact with each other in various social situations. A diary was kept by the maximally exposed individual to record the times that the radiation monitoring device was worn and the interactions with the patient.

The radiation safety discharge instructions were provided to and discussed with the patients and caregivers (if possible) by the nuclear medicine physician or radiation safety personnel before the release of the patient. Any questions about radiation safety issues were answered at that time. One copy of these written instructions was provided to the patient, and a second copy was maintained in the patient's files.

Radiation Monitoring

Family members received film badges, thermoluminescent dosimeters (TLDs), OSLs, or electronic digital dosimeters. In most cases, the caregiver was given more than a single type of device. Radiation safety personnel taught the caregivers how to wear and use the devices. The caregivers were also asked to log their activities and resultant exposures to verify the appropriateness of the discharge instructions and to confirm that the radiation doses to the family members were below the regulatory limits. The readings were also compared with the theoretic doses over an infinite time predicted by the patient-specific calculations.

Data Analysis

All radiation monitoring devices were processed on return. Diaries of the direct-reading dosimeters were reviewed, and the readings were transferred to spreadsheets for subsequent analyses. The final dosimeter reading was used to calculate the predicted dose over an infinite time based to the maximally exposed individual using the following equation:

$$D(\infty) = \frac{\text{final dosimeter reading}}{[1 - \exp(-N/(1.443 \times T_{eff}))]}, \quad \text{Eq. 6}$$

where $D(\infty)$ is the total effective dose equivalent (millisieverts) to the maximally exposed individual and N is the number of days the individual was monitored. This "measured" dose for infinite time was compared with the doses for infinite time predicted by Equations 1, 2, and 5.

RESULTS

Twenty-two non-Hodgkin's lymphoma patients were entered into several dose-escalating radioimmunotherapy clinical trials, some of which included chemotherapy and bone marrow transplantation. These patients received therapeutic doses of ^{131}I-anti-B1 antibody ranging from 0.94 to 4.77 GBq (25–129 mCi), resulting in total-body absorbed doses of 30–75 cGy (30–75 rad). The effective half-life of total-body clearance as determined from the dosimetry study ranged from 46 to 85 h. The dose rates at 1 m before patient discharge after the therapeutic administration ranged from 0.03 to 0.18 mSv/h (3–18 mrem/h) (Table 1). All but 1 patient were found to be immediately releasable on the basis of administered activity or dose rate. On the basis of the measured dose rate and application of Equation 4, patient 22 was told to remain in the clinic for 1 h before release. This patient would have been immediately releasable using Equation 5 (using a 3-h nonvoiding period). The radiation doses to family members ranged from 0.17 to 4.09 mSv (17–409 mrem) for indirect-reading dosimeters (e.g., TLDs and OSLs), with monitoring periods ranging from 3 to 17 d (mean, 8.2 d). Direct-reading dosimeter exposures ranged from 0.10 to 3.54 mSv (10–354 mrem), with monitoring periods ranging from 2.1 to 17 d (mean, 6.5 d).

The predicted doses for infinite time from these patients were calculated using Equations 1, 2, and 5 (Table 2). The predicted dose for infinite time using the maximum dosimeter reading for a family member was also calculated using Equation 6. All the doses over an infinite time based on dosimeter readings using Equation 6 (measured doses for infinite time) were below the 5-mSv (500 mrem) regulatory limit. Table 3 summarizes the predicted versus measured doses for infinite time. The average measured dose for infinite time was found to be 1.68 mSv (168 mrem), with an SD of 1.08 mSv. The median was 1.51 mSv (151 mrem).

Patient Information and Release Determination

B1 Monoclonal Antibody Therapy

I. Patient Information

1. Patient Identifier: _____ 2. Date: _____ 3. Administered Activity: _____ mCi
4. Patient Residence Time: _____ hrs. 5. Release Criteria from Radiation Safety Office: _____
6. Sex: Male ☐ Female ☐ 7. Pregnant? Yes ☐ No ☐ 8. Breast-feeding? Yes ☐ No ☐
9. Person Interviewed: Patient ☐ Guardian ☐ Other _____

II. Dwelling Information For Two Weeks After Treatment

1. Type of Dwelling: Single-Family ☐ Multi-Family ☐ Apartment ☐ Other_____
   If not single-family, possible proximity to neighbors: _____ feet
2. Household Members: Sex: a. _____ b. _____ c. _____ d. _____
   Age: a. _____ b. _____ c. _____ d. _____

III. Patient Release Determination (Occupancy Factor = 0.25)

Interview the patient to determine if the patient can accept the following actions based on the activity given:

Action	All Doses	Circle One
1. Sleep alone for:	3 nights	Yes No
2. Return to work (if others are in close proximity) for:	1 day	Yes No
3. Maintain a prudent distance (>9 ft) from others for:	4 day	Yes No
4. Avoid prolonged close contact with children and pregnant women for:	10 days	Yes No
5. Maintain sole use of the bathroom for _____. If not possible, keep the toilet especially clean by flushing 3 times after each use. Men should also sit during urination.	2 days	Yes No
6. Refrain from traveling by airplane or mass transportation for:	4 day	Yes No
7. Refrain from traveling on a prolonged automobile trip (> 6 hrs) with others for:	7 day	Yes No
8. Drink plenty of fluids for:	2 days	Yes No
9. Washing clothing and eating utensils separately for:	2 days	Yes No

The patient is releasable if all answers are "Yes". If any answer is "No", the patient must be hospitalized. (Proceed to Section VI)

IV. Instructions

1. Ensure patient receives, understands, and is willing to follow instructions.
2. Discuss procedures in case of emergency medical care.

V. Release Record

This patient was released according to federal and state guidelines regarding immediate release based on patient-specific calculations.

These calculations are maintained in the Radiation Safety Office. The release criteria for this patient is given above in Section I. If the patient is released by dose rate:

_____	_____	_____ mrem/hr	_____
Instrument	*S/N*	*Dose rate at 1 meter*	*Name of Individual Performing Survey*

VI. Signature

☐ This patient was not releasable and therefore hospitalized.

☐ This patient has reviewed all requirements for patient release, was given written instructions and released.

Signature: _____ Date: _____
(Individual completing form)

FIGURE 1. Form used to determine whether patient can be released from hospital after radioimmunotherapy with ^{131}I-anti-B1 antibody. S/N = serial number.

TABLE 1
Patient Data

Patient no.	Total body dose (cGy)	Administered activity (GBq)	T_{eff} (tracer) (h)	Initial patient dose rate (mSv/h)	Dosimeter* readings (mSv)			
					Direct reading	Days	TLD or OSL	Days
1	65	3.85	54.8	0.14	0.37	3.8	0.70	12.3
2	45	1.67	72.1	NA	0.61	9	0.50	9
3	65	1.48	85.2	NA	—	—	1.70	17
4	30	1.54	63.6	0.09	1.46	7	1.20	8
5	30	1.14	71.0	0.06	0.38	6	0.39	6
6	30	1.26	64.0	0.04	0.79	6.2	1.05	11
7	75	3.06	75.6	0.14	1.31	4.2	1.71	6
8	75	4.25	56.3	0.14	1.68	7	2.35	7
9	45	2.15	62.9	0.05	0.51	5.1	0.71	5.1
10	45	2.70	52.9	0.08	0.10	3.1	0.17	3.1
11	45	0.94	80.3	0.03	0.68	3	0.79	3
12	60	1.74	71.3	0.09	1.27	9	—	—
13	60	2.27	62.5	0.09	0.56	5.8	—	—
14†	60	3.26	67.6	0.14	2.28	5.9	3.45	5.9
15†	60	2.24	69.4	0.08	3.54	17	4.09	17
16	60	3.57	59.4	0.18	1.21	5	1.31	5
17	60	2.48	62.0	0.11	0.51	5	—	—
18	75	3.92	67.0	0.12	1.21	6.3	—	—
19	75	3.86	45.5	0.10	0.80	2.1	—	—
20	75	1.76	77.4	0.08	2.17	13	—	—
21	75	3.58	73.0	0.13	1.81	7	—	—
22	75	4.77	67.9	0.16	1.15	6	—	—
High	75	4.77	85	0.18	3.54	17	4.09	17
Low	30	0.94	46	0.03	0.10	2.1	0.17	3
Average	58	2.61	66	0.10	1.16	6.5	1.44	8.2

*MyDose electronic pocket dosimeter (Aloka Co., Ltd., Tokyo, Japan) used for direct readings. Film badge, TLD, or OSL dosimeter used for verification.

†Radiation badge shared by >1 individual (e.g., family member) to conservatively determine radiation dose to maximally exposed individual.

NA = patients who were released on basis of administered activity (no dose rates were recorded); — = dosimeter was not provided.

The measured doses for infinite time as a percentage of the predicted doses for infinite time based on Equations 1, 2, and 5 for all patients were found to average 32%, 47%, and 58%, respectively (Table 4). Results are also summarized in Tables 3 and 4 for the 7 patients receiving a 75-cGy total-body dose, because this is the expected treatment dose for this protocol. For the patients receiving 75 cGy, the average measured dose for infinite time was found to be 2.02 mSv (202 mrem), with a median of 2.27 mSv (227 mrem). The measured doses for infinite time as a percentage of the predicted doses for infinite time based on Equations 1, 2, and 5 were found to be significantly lower, averaging 35%, 53%, and 67%, respectively (Table 4).

DISCUSSION

The early release of these patients should lower health care costs and provide emotional benefits to the patients and their families and may improve outcome and lead to more effective health care. Health care professionals caring for patients in hospitals (e.g., the nursing staff) will receive a much lower radiation dose because of their decreased exposure to this type of patient. A potential disadvantage to releasing patients is that certain individuals exposed to them could receive a higher dose than if the patient remained hospitalized longer; however, if the patient is given appropriate instructions, that dose should be modest and below the limit set by the NRC. The 20 NRC states are governed by the new regulations. However, the 30 agreement states are not required to follow these recommendations and would therefore have to amend their regulations to release patients on the basis of these new criteria. To date, at least 20 of the 30 agreement states have already amended their regulations or granted individual institutions variances that permit outpatient release.

The fact that the new regulations are dose-based rather than activity-based is an advantage because this change standardizes the dose for release among different radionuclides, each of which is characterized by a different half-life and spectrum of emissions. Patients can now be released regardless of how much administered activity they received, as long as the total dose to any individual is not likely to exceed 5 mSv (500 mrem), which is approximately 1.5

TABLE 2
Predicted vs. Measured Dose over an Infinite Time

Patient no.	Predicted dose for infinite time			Measured dose for infinite time based on dosimeter readings (Eq. 6)
	Using Equation 1 (administered activity)	Using Equation 2 (patient dose rate and 8-h nonvoiding)	Using Equation 5 (patient dose rate and 3-h nonvoiding)	
1	6.02	3.89	3.05	0.72
2	3.20	NA	NA	0.70
3	3.25	NA	NA	1.76
4	2.68	2.65	2.24	1.74
5	2.17	1.94	1.65	0.52
6	2.21	1.21	0.95	1.11
7	6.11	4.80	4.09	2.33
8	6.77	4.03	3.12	2.69
9	3.72	1.54	1.14	0.96
10	4.11	2.13	1.58	0.27
11	1.97	1.22	1.02	1.71
12	3.32	2.77	2.35	1.45
13	3.92	2.64	2.13	0.71
14	5.96	4.44	3.69	4.51*
15	4.19	2.64	2.16	4.16*
16	5.92	4.97	4.10	1.74
17	4.25	3.26	2.68	0.60
18	7.13	3.94	3.14	1.53
19	5.29	2.62	1.85	1.49
20	3.57	2.80	2.39	2.31
21	6.96	4.45	3.68	2.27
22†	8.76	5.24	4.23	1.49

*Radiation badge shared by >1 family member to conservatively determine radiation dose to maximally exposed individual.
†Patient remained in clinic for 1 h before release.
NA = patients who were released on basis of administered activity (no dose rates were recorded).
Data are in millisieverts.

times the exposure the average American receives annually from natural background radiation.

The preference for this dose-based approach for patient release was expressed more than 30 y ago, as indicated by the following statement in NCRP report 37, from 1970 (*16*): "Since the exposure rates and half-lives of various radionuclides differ greatly, a more meaningful basis for release from the hospital is the possible exposure to other individuals with whom the patients are likely to associate."

When the predicted dose for infinite time to the maximally exposed individual is calculated, Equation 1 (administered activity) will always yield a greater dose than Equation 2 (patient dose rate) because Equation 1 conservatively assumes a point source geometry with no consideration for body attenuation. Likewise, Equation 2 will yield a more conservative dose for infinite time than Equation 5 because of the differences in the initial nonvoiding period. Although less conservative, Equation 5 should be used in predicting

TABLE 3
Summary of Predicted and Measured Doses for Infinite Time

Group	Dose for infinite time	High	Low	Average	Median
All patients	Predicted using Equation 1	8.76	1.97	4.61	4.15
	Predicted using Equation 2	5.24	1.21	3.12	2.78
	Predicted using Equation 5	4.23	0.95	2.54	2.37
	Based on measurements	4.51	0.27	1.68	1.51
75-cGy patients	Predicted using Equation 1	8.76	3.57	6.37	6.77
	Predicted using Equation 2	5.24	2.62	3.98	4.03
	Predicted using Equation 5	4.23	1.85	3.21	3.14
	Based on measurements	2.69	1.49	2.02	2.27

Data are in millisieverts.

TABLE 4
Comparison of Measured Dose for Infinite Time vs. Predicted Dose for Infinite Time

Group	Comparison of measured vs. predicted doses for infinite time	High	Low	Average
All patients	Using Equation 1	98	4	32
	Using Equation 2	155	8	47
	Using Equation 5	189	47	58
75-cGy patients	Using Equation 1	65	17	35
	Using Equation 2	83	29	53
	Using Equation 5	97	35	67

Data are percentages calculated by dividing measured dose for infinite time by predicted dose for infinite time and multiplying by 100.

dose for infinite time for 2 reasons: first, because the initial 3-h nonvoiding period is a more appropriate model for this protocol and, second, because our results show that the measured dose for infinite time will be considerably less than the predicted dose for infinite time the maximally exposed individual will receive (e.g., measured dose was 33% less than predicted dose for the patients receiving 75 cGy).

For patients 14 and 15, who had the highest measured dose for infinite time to the maximally exposed individual, the monitoring was shared by more than a single person. On the basis of these patients' travel and housing situations (i.e., exposure to various individuals), we determined that having more than a single person use the dosimeter would better approximate the dose to the maximally exposed individual. In both cases, the measured dose for infinite time was less than the 5-mSv limit.

For patient 11, the monitoring period was only 3 d. The monitored individual received 0.79 mSv during this period; however, projected out to infinite time, the resulting dose is 1.71 mSv. This dose is higher than what Equation 2 (1.22 mSv) or Equation 5 (1.02 mSv) predicts. This patient was to receive conventional chemotherapy shortly after the therapeutic administration, and in this situation the patient and caregiver spent more time together than usual during this short time.

CONCLUSION

Twenty-two patients were treated for non-Hodgkin's lymphoma using ^{131}I-anti-B1 antibody. After release of the patients, 26 family members were monitored for radiation exposure. All radiation doses received by these nonoccupational caregivers were below the regulatory limit of 5 mSv (500 mrem). These results indicate that the written instructions and the radiation safety counseling were effective in keeping exposures ALARA. Therefore, treatment with ^{131}I-anti-B1 antibody for non-Hodgkin's lymphoma can be performed on an outpatient basis.

APPENDIX

NRC Default Tables and Patient-Specific Calculations

Regulatory guide 8.39 (*2*) provides default tables with values authorizing patient release based on administered activities or 1-m patient dose rates for a variety of radionuclides. The values calculated for both tables are based solely on the physical half-life of the radionuclide (i.e., no biologic elimination is assumed). The equation used to calculate these release values is essentially the same as introduced in 1970 by National Council on Radiation Protection and Measurements report no. 37 (*16*) with the exception of the occupancy factor. The selection of an occupancy factor of 0.25 at 1 m for estimating the ^{131}I dose to an individual from exposure to a released patient is based on the professional judgment of time–distance combinations that are likely after instructions to minimize time near the patient.

Use of the physical half-life, not the effective half-life, of the radionuclide assumes that the body retains the radionuclide (e.g., ^{131}I) until it is fully decayed and that none is cleared through biologic processes. Clearly, this is not true: biologic processes do affect the clearance of radionuclides. Patients receiving ^{131}I therapy do not retain radioactivity for the physical half-life of the radionuclide. Rather, patients eliminate ^{131}I more quickly because of biologic elimination. As a result, the patient-specific dose calculations, which take into account both the physical and the biologic half-life (i.e., the effective half-life) of the radionuclide, are more complete and appropriate than the NRC default tables in calculating the dose an individual will likely receive if exposed to a patient treated with ^{131}I (*7*). Because the default tables do not take into account the biologic elimination of the radionuclide, their use will overestimate the dose an individual would receive if exposed to a patient treated with ^{131}I. Using a patient-specific dose calculation provides a more complete and appropriate estimation of dose.

Direct measurements are the best way to obtain the dose any individual is likely to receive under realistic exposure conditions. Three previous studies (*17–19*) measured doses to family members from patients who were released after treatment of thyroid cancer or hyperthyroidism with $<$1.11 GBq (30 mCi) ^{131}I. These studies showed that use of only the physical half-life in calculations will overestimate radiation doses received by family members and suggested that the patient-specific dose calculation will be conservative. These data are summarized in Table 1A. On the basis of these 3 studies, a regulatory analysis (*3*) concluded that the revised NRC patient-release rule provides an adequate level of protection, with a significant margin of safety for patients who make a reasonable effort to follow instructions. Therefore, both professional judgment and empiric measurements support the validity of using the patient-specific dose calculation in determining the maximum likely radiation dose to another individual. The radiation dose predicted by the calculation is usually significantly higher than the dose

TABLE 1A
Comparison of Measured Dose with Dose Predicted Using Physical Half-Life and Biologic Elimination

Study	% of measured doses < predicted doses	
	Using physical half-life	Using biologic elimination
Buchan and Brindle (*17*)	72	57
Harbert and Wells (*18*)	100	86
Jacobson et al. (*19*)	90	90

obtained by direct measurements with film badges or TLDs worn by the family members of the patients.

Regulatory guide 8.39 allows the licensee to release patients on the basis of patient-specific calculations, including using the biologic or effective half-life. The procedure for calculating doses based on patient-specific factors is given in Appendix B of the regulatory guide. To account for the time for ^{131}I to be absorbed from the stomach and the holdup of iodine in the urine while in the bladder, the regulatory guide conservatively makes the following assumptions: during the first 8 h after administration, 80% of the ^{131}I is removed from the body by only the physical decay of ^{131}I, and the occupancy factor for this 8-h nonvoiding period is assumed to be 0.75 (0.25 after this period).

The University of Nebraska Medical Center has performed several ^{131}I-anti-B1 antibody therapies since late 1996. In all cases, a monoexponential clearance rate has been observed. Using the assumptions of the regulatory guide for the initial 8-h period and a monoexponential clearance after this nonvoiding period, and taking into account the internal dose contribution from ^{131}I (Eq. B-6 in the regulatory guide), the following equation based on a point source geometry determines the dose for infinite time to the maximally exposed individual:

$$D(\infty) = Q_0\left(\frac{34.6\Gamma}{10{,}000\ \text{cm}^2}\right) \times \left[E_1 T_p(0.8)\left(1 - e^{\frac{(-0.693)(0.33)}{T_p}}\right) + 0.972E_2\, T_{eff}\right] + 0.000143Q_0, \quad \text{Eq. 1A}$$

where $D(\infty)$ is the dose for an infinite time to the maximally exposed individual (millisieverts); Q_0 is the administered activity (megabecquerels); 34.6 is a conversion factor of 24 h/d divided by ln2 (resulting from integration); Γ is the γ-ray constant, which is 0.595 mSv-cm^2/MBq-h for ^{131}I; E_1 is the occupancy factor for the first 8 h, or 0.75; E_2 is the occupancy factor after 8 h, or 0.25; T_p is 8.04 d; T_{eff} is the effective half-life (days) based on the patient's dosimetric dose (e.g., the initial 185-MBq [5 mCi] dose administered to calculate the activity required for that patient's therapy); and 0.000143 is a factor derived from regulatory guide 8.39. When multiplied by Q_0, this factor gives the internal dose contribution in millisieverts. On simplification, the equation for dose for infinite time becomes:

$$D(\infty) = Q_0[1.56 + 1.85\ T_{eff}]/3700. \quad \text{Eq. 2A}$$

Using the patient dose rate at 1 m (D_r), the equation for dose for infinite time becomes:

$$D(\infty) = D_r[4.68 + 8.41\ T_{eff}] + (0.000143)Q_0, \quad \text{Eq. 3A}$$

where D_r is the patient dose rate at 1 m (mSv/h). The administered activity and dose rate at which the patient may be released can be determined by setting the dose for infinite time in Equations 2A and 3A to 5 mSv (500 mrem) and solving for the corresponding parameter as follows:

$$Q_0 = 18{,}500/[1.56 + 1.85\ T_{eff}] \quad \text{Eq. 4A}$$

$$D_r = [5 - (0.000143)\ Q_0]/[4.68 + 8.41\ T_{eff}]. \quad \text{Eq. 5A}$$

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REFERENCES

1. United States Nuclear Regulatory Commission. *Criteria for the Release of Individuals Administered Radioactive Material.* Washington, DC: Office of the Federal Register; 1997.10 CFR parts 20 and 35:62 FR 4120.
2. United States Nuclear Regulatory Commission. *Release of Patients Administered Radioactive Materials.* Washington, DC: United States Nuclear Regulatory Commission; 1997. Regulatory guide 8.39.
3. Schneider S, McGuire SA. *Regulatory Analysis on Criteria for the Release of Patients Administered Radioactive Material.* Washington, DC: United States Nuclear Regulatory Commission; 1996. NUREG-1492 (final report).
4. Saenger EL, Kereiakes JG. Reflections on cancer treatment and the federal agency regulations. *Radiology.* 1980;137:865–866.
5. Siegel JA. Revised Nuclear Regulatory Commission regulations for release of patients administered radioactive materials: outpatient iodine-131 anti-B1 therapy. *J Nucl Med.* 1998;39(suppl):28S–33S.
6. Gates VL, Carey JE, Siegel JA, et al. Nonmyeloablative iodine-131 anti-B1 radioimmunotherapy as an outpatient therapy. *J Nucl Med.* 1998;39:1230–1236.
7. Siegel JA. Outpatient radionuclide therapy. In: *Radiation Protection in Medicine: Contemporary Issues—Proceeding of the Thirty-Fifth Annual Meeting of the National Council on Radiation Protection and Measurements.* Bethesda, MD: National Council on Radiation Protection and Measurements; 1999:187–199. Proceeding no. 21.
8. Caldwell CB, Ehrlich LE. Outpatient treatment of thyroid cancer using high doses of iodine 131. *Can Assoc Radiol J.* 1999;50:331–336.
9. Kaminski MS, Zasadny KR, Francis IR, et al. Radioimmunotherapy of B-cell lymphoma with [^{131}I]anti-B1 (anti-CD-20) antibody. *N Engl J Med.* 1993;329:459–465.
10. Kaminski MS, Zasadny KR, Francis IR, et al. Iodine-131-anti-B1 radioimmunotherapy for B-cell lymphoma. *J Clin Oncol.* 1996;14:1974–1981.
11. Kaminski MS, Fig LM, Zasadny KR, et al. Imaging, dosimetry, and radioimmunotherapy with iodine 131-labeled anti-CD37 antibody in B-cell lymphoma. *J Clin Oncol.* 1992;10:1696–1711.
12. Barrington S, Kettle A, O'Doherty M, et al. Radiation dose rates from patients receiving iodine-131 therapy for carcinoma of the thyroid. *Eur J Nucl Med.* 1996;23:123–130.
13. Zanzonico PB, Siegel JA, St Germain J. A generalized algorithm for determining the time of release and the duration of post-release radiation precautions following radionuclide therapy. *Health Phys.* 2000;78:648–659.
14. Wahl RL, Kroll S, Zasadny KR. Patient-specific whole-body dosimetry: principles and a simplified method for clinical implementation. *J Nucl Med.* 1998; 39(suppl):14S–20S.

15. Thomas SR, Stabin MG, Chen CT, Samaratunga RC. MIRD pamphlet no. 14: a dynamic urinary bladder model for radiation dose calculations. *J Nucl Med.* 1992;33:783–802.
16. National Council on Radiation Protection and Measurements. *Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides*. Bethesda, MD: National Council on Radiation Protection and Measurements; 1970. NCRP report 37.
17. Buchan RCT, Brindle JM. Radioiodine therapy to out-patients: the radiation hazard. *Br J Radiol.* 1971;44:973–975.
18. Harbert JC, Wells N. Radiation exposure to the family of radioactive patients. *J Nucl Med.* 1974;15:887–888.
19. Jacobson AP, Plato PA, Toeroek D. Contamination of the home environment by patients treated with iodine-131: initial results. *Am J Public Health*. 1978;68: 225–230.

POLICY ISSUE
(Information)

January 29, 2018 SECY-18-0015

FOR: The Commissioners

FROM: Marc L. Dapas, Director
Office of Nuclear Material Safety and Safeguards

SUBJECT: STAFF EVALUATION OF THE U.S. NUCLEAR REGULATORY COMMISSION'S PROGRAM REGULATING PATIENT RELEASE AFTER RADIOISOTOPE THERAPY

PURPOSE:

The purpose of this paper is to provide the Commission with the results of the U.S. Nuclear Regulatory Commission (NRC) staff's evaluation of the NRC's program for regulating patient release after radioisotope therapy (patient release). The evaluation was conducted in response to Staff Requirements Memorandum (SRM) SRM-12-0011, "Data Collection Regarding Patient Release," dated January 25, 2012 (Agencywide Documents Access and Management System (ADAMS) Accession No. ML121000248), and SRM-COMAMM-14-0001/COMWDM-14-0001, "Background and Proposed Direction to NRC Staff to Verify Assumptions made Concerning Patient Release Guidance" dated April 28, 2014 (ADAMS Accession No. ML14118A387). This paper also presents the results from revised dose modeling calculations, reviews of published literature, and extensive stakeholder engagement that included outreach to licensees, patients, Agreement States, and the Advisory Committee on Medical Uses of Isotopes (ACMUI).

SUMMARY:

As directed by the Commission, the NRC staff conducted an evaluation of whether significant regulatory changes to the patient release program are warranted. This evaluation was based on information from computational dose modeling calculations, including state of the art virtual simulations; published data, including scientific literature; and extensive stakeholder

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outreach. As part of stakeholder outreach, the NRC staff issued two *Federal Register* notices (FRNs) and held subsequent public meetings soliciting comments on patient release instructions for keeping public doses as low as reasonably achievable (ALARA) and on whether alternate criteria to clarify patient release regulations should be developed. The NRC staff also issued a licensee questionnaire on where patients reside following treatment, considered stakeholder letters to the Commission, and coordinated with Agreement States and the ACMUI. Documentation in support of these efforts is provided in the following four enclosures: (1) summary of patient release after radioiodine therapy research review, (2) summary of the draft pilot study on the assessment of where patients reside immediately following their release report, (3) summary of public comments regarding the patient release program, and (4) ACMUI comments on the draft SECY paper.

BACKGROUND:

In SRM-COMGBJ-11-0003, "Data Collection Regarding Patient Release," dated June 23, 2011 (ADAMS Accession No. ML111741188), the Commission directed the staff to evaluate whether there are gaps in the available data regarding the doses received by members of the public from released patients. The NRC staff responded to the SRM in SECY-12-0011, "Data Collection Regarding Patient Release," dated January 25, 2012 (ADAMS Accession No. ML112630115), identifying gaps related to (1) internal doses to members of the public from close physical contact with patients or radioactive contamination from bodily fluids, and (2) internal and external doses to members of the public from patients released to locations other than their primary residences (e.g., public transportation, hotels, nursing homes).

In the SRM for SECY-12-0011, the Commission directed the NRC staff to revisit patient release calculations and methods described in agency guidance and conduct additional analytical and empirical data collection. The staff coordinated with the Office of Research to analyze and collect data and perform associated evaluations. This led to the issuance of two reports: "Patient Release after Radioiodine Therapy: A Review of the Technical Literature, Dose Calculations, and Recommendations" (literature review); and "Assessment of Where Patients Reside Immediately Following Their Release." (Enclosures 1 and 2 summarize these reports).

In SRM-COMAMM-14-0001/COMWDM-14-0001, the Commission directed the NRC staff to complete four tasks associated with the consistency and usefulness of the instructions that Iodine-131 (I-131) patients are given before being released, and whether those instructions are consistently followed. The staff completed the first three tasks. The first task involved the development of a standardized set of guidelines that licensees can use to provide instructions to patients. In addressing this task, the staff published an Information Notice (IN) 2017-02, "Best Practice Concepts for Patient Release," dated May 17, 2017.

The second task involved the development of a Web page that provides information and links to relevant medical organizations and patient advocacy groups to enable patient access to accurate information. The staff launched a Web page on March 31, 2016, which provides information for patients administered I-131 that is consistent with information from professional medical organizations and patient advocacy groups. The Web page can be accessed at the following link: https://www.nrc.gov/materials/miau/patient-release.html.

With respect to the third task, the Commission directed the staff to evaluate whether significant regulatory changes to the patient release program are warranted. This paper provides the

results of that evaluation. In terms of the fourth task, the Commission directed the staff to revise Regulatory Guide (RG) 8.39 "Release of Patients Administered Radioactive Material," dated April 1997, and subsequently NUREG-1556, Volume 9, "Consolidated Guidance About Materials Licenses: Program-Specific Guidance About Medical Use Licenses," to specify guidelines for patient information and instructions. Based on the staff's work completed in response to SRM-12-0011 and the results of the staff's evaluation pertaining to the third task, the staff determined (as discussed in this paper) that a more comprehensive update to the guidance in RG 8.39 is warranted than was directed by the Commission in connection with this fourth task. As it updates NUREG-1556, Volume 9, the staff plans to refer to RG 8.39 to remove duplicative patient release guidance and avoid inconsistencies between the two documents.

DISCUSSION:

Title 10 of the *Code of Federal Regulations* (10 CFR) 35.75, "Release of individuals containing unsealed byproduct material or implants containing byproduct material," often referred to as the "Patient Release Rule," was promulgated in 1997. The NRC developed the subject regulation because the revision of 10 CFR Part 20 in 1991, which revised the dose limits for members of the general public in 10 CFR 20.1301, did not address exposure from the release of patients. The NRC determined that while doses should be maintained ALARA, a dose limit of 1 millisievert (mSv) (0.1 rem), or a dose limit of 5 mSv (0.5 rem) in certain circumstances, provides adequate protection. The "Patient Release Rule" allows a licensee to authorize the release of a patient from its control if the total effective dose equivalent (TEDE) to any other individual, from exposure to the released patient, is not likely to exceed 5 mSv (0.5 rem).

In addition, 10 CFR 35.75 requires that a licensee provide the released individual, or the patient's family or other caregivers, with appropriate instructions, including written instructions, on recommended actions to maintain doses to other individuals ALARA if the TEDE to any other individual is likely to exceed 1 mSv (0.1 rem).

In addressing the third task in SRM-COMAMM-14-0001/COMWDM-14-0001, the NRC staff evaluated estimated radiation doses to members of the public from released patients by performing a data analysis of peer-reviewed scientific articles; evaluating models and calculations to estimate radiation doses to members of the public who are exposed through contact with released patients, such as hotel workers; and evaluating information obtained from licensee questionnaire responses to identify patient destinations after treatments.

The staff studied patients treated for hyperthyroidism and thyroid cancer and focused on exposure from I-131 given its potential for a higher external exposure to members of the public. While 10 CFR 35.75 applies to other medical radioisotope therapies such as Phosphorus-32, Strontium-89, Yttrium-90, Lutetium-177, and Radium-223, none of these radioisotopes have the high energy gamma emission and volatility of I-131, and thus, they present a lower external radiation hazard than I-131.

Based on the results of the literature review (ADAMS Accession No. ML17262A909) summarized in Enclosure 1, the staff identified that the dominant factor in determining both internal and external doses to members of the public is based on the behavior of the patient after release. Patient behavior was a more important factor than the activity, at the time of patient release, of the I-131 that had been administered to the patient. From the literature review, the staff also identified potential enhancements to the calculations, methodologies, and tables provided in RG 8.39, that are used to estimate radiation dose to members of the public

from released patients. Specifically, the existing methods could result in underestimating radiation dose in certain situations if patients do not follow the provided instructions. The literature review also indicated that radiation contamination in the home is not a significant cause of radioiodine uptake. For such uptake to occur, close contact with the released patient is necessary. The literature included reports of thyroid doses of 0.04–13.3 mSv (4–1330 mrem) to members of the public from iodine uptake. All cases involved close contact with the patient, mostly in a child-parent relationship. The results of the literature review show that the internal dose is generally small compared to the potential external dose caused by contact with patients who were administered I-131. From the literature, the staff noted that internal doses were small when the patient avoided close contact with others and followed ALARA principles and instructions. Likewise, nearly all of the recorded external doses to the family members were below the patient release limit of 5 mSv (0.5 rem). In the few instances where the dose to another individual exceeded 5 mSv (0.5 rem), not observing ALARA principles and patient instructions contributed to the higher doses to other individuals. A more detailed discussion of the internal and external exposure insights from the literature review can be found in Enclosure 1.

To evaluate exposure to members of the public, such as hotel workers and individuals exposed during public transportation, the NRC staff contracted with Oak Ridge National Laboratory to calculate the external doses received by members of the public in a variety of scenarios and geometries (hotels, nursing homes, public transportation) using a phantom model. The staff concluded that the calculations performed by licensees to determine whether the patient meets regulatory release criteria may underestimate doses to members of the public. The calculations assume hypothetical behavioral conditions by the patient and apply standard conditions for distance of 1 meter and an occupancy factor of 0.25 in the default calculations. Significant deviations from one or more of these assumptions can result in substantially different doses to members of the public than the calculated values would indicate. This highlights the importance of patient discussions and instructions by the licensee to inform the patient on how best to limit the dose to family members, hotel workers, people on buses, people in nursing homes, and others. The summary of the phantom model dose estimates are as follows:

Hotel Worker Models:

- To exceed an external dose of 1 mSv (0.1 rem), the hotel check-in staff would need to be exposed to a newly released thyroid cancer patient at 1 meter for approximately 4 hours.
- To exceed the patient release dose limit of 5 mSv (0.5 rem), the hotel check-in staff would need to be exposed to a newly released thyroid cancer patient at 1 meter for approximately 23 hours.
- The internal dose received by a hotel cleaning staff person would be approximately 1.5 microsievert (μSv) (0.15 mrem) for cleaning a newly released I-131 thyroid cancer patient's room and 0.7 μSv (0.07 mrem) for cleaning a newly released I-131 hyperthyroidism patient's room.

Consequently, the NRC staff concluded that a hotel cleaning staff person would need to clean approximately 670 rooms of newly released thyroid cancer patients to exceed 1 mSv (0.1 rem), and 3,300 rooms of newly released patients to exceed the patient release limit of 5 mSv (0.5 rem).

Public Transportation Model:

- This model, using conservative assumptions, shows that a newly released thyroid cancer patient could expose a member of the public to an external dose of greater than 5 mSv (0.5 rem) if the patient, shortly after being released, got on a public transportation system and was face-to-face with a member of the public for 3.8 hours or seated in front of someone for 13 hours.

In 2015, the staff sent a questionnaire to a limited number of licensees who administer I-131 treatments. The purpose of the questionnaire was to obtain information on where patients go immediately following treatment, and to assess the number of patients who go to locations other than their private residences. The questionnaire responses indicate that the majority of patients went home; however, about 5 to 10 percent went to other locations. A more detailed analysis and discussion of the responses to the questionnaire is provided in Enclosure 2.

The staff published a FRN (80 FR 70,843, November 16, 2015) to solicit comments from the medical community and other stakeholders on patient release instructions. The staff assessed the stakeholder responses to identify best practices, based on well-established radiation safety concepts, with respect to I-131 patient release instructions and published these best practices in IN 2017-02, “Best Practice Concepts for Patient Release,” dated May 17, 2017 (ADAMS Accession No. ML17101A560). The comments informed the staff’s evaluation of when is it best to provide the patient with instructions in meeting the 10 CFR 35.75 regulation.

In addition, to further obtain stakeholder input on the patient release matter, the staff published an FRN (82 FR 17,465, April 11, 2017) to solicit comments on whether additional or alternate criteria for patient release are needed and whether to clarify the NRC's current patient release program requirements. Specifically, the FRN asked members of the public to comment on six questions regarding the patient release program. The staff asked for comments on changing 10 CFR 35.75 to require an activity-based threshold for release; whether release limits are per year or per treatment; whether the release limit should remain above the general public limit (1 mSv (0.1 rem)); and on whether other requirements should be developed for pregnant women and children exposed to released patients. The staff also asked for comment on patient isolation and the timing of when instructions should be given to patients or caregivers. The staff held two public meetings during the public comment period. Meeting summaries are available in ADAMS at Accession Nos. ML17157B387 and ML17284A358. The full transcripts for the meetings are available in ADAMS at Accession Nos. ML17157B388 and ML17284A169. The NRC received 132 responses from 128 public stakeholders and 4 Agreement States. The specific list of questions and a summary of stakeholder comments associated with each question is contained in Enclosure 3.

The responses from medical stakeholders (including licensees, professional organizations, and medical practitioners) indicated that they strongly disagreed with any patient release rulemaking, and that the current regulations are sufficient to protect members of the public from exposure to released patients. The medical stakeholders further stated that there is no data from reputable sources that indicate that an exposure of 500 mrem causes any statistically significant increase in risk. Medical stakeholders generally supported updating NRC guidance such as RG 8.39.

Many patients responded with testimonials communicating their strong preference to have the option of being isolated in a hospital for a few days after treatment before being released. Some patients support the former activity-based rule since that rule would have required hospitalization following some I-131 treatments. Other patients who had been treated and

released under the current dose-based rule, cited their increased stress and anxiety in trying to isolate themselves from other family members, and expressed their concerns about exposing their families to radiation and contaminating their living spaces.

Patient Release Program Evaluation:

In its evaluation of the patient release program regulations, the NRC staff considered the feasibility and technical merit of rule changes and guidance updates. Specifically, the staff evaluated whether there were benefits to revisiting an activity-based limit, establishing different dose limits for different groups, clarifying a time limit for exposure, and prescribing the time frame for giving patients instructions. The staff also considered enhancements to existing guidance.

Rulemaking to change patient release criteria to an activity-based limit

Prior to the 1997 rulemaking, patient release regulations were based on retained activity in the patient and the dose rate measured at one meter from the patient. The 1997 rule changed the patient release criteria to a limit based on TEDE to any other individual regardless of the administered activity.

Benefits of returning to an activity-based rule include the use of a measurable quantity of I-131 that ensures consistent patient release practices by all licensees. An activity-based rule also would reduce reliance on assumptions about patient behavior, as well as remove the need for licensee consideration of any special circumstances associated with patient release, such as patient plans to use public transportation following treatment or to isolate themselves at locations other than at home, such as hotels.

The NRC staff determined that development of an activity-based, patient release threshold under which patients would be required to remain in a clinic-sponsored facility until the standard for release is met, is not warranted. An activity-based rule does not reduce dose to other individuals below the current dose limit, as other factors, such as biological half-life and proximity of other individuals to patients, also affect public dose. An activity-based rule could result in different exposures under seemingly identical exposure conditions for the different radionuclides, or radiopharmaceuticals with the same nuclide, because biological or radiological half-lives can be significantly different.

The broad consensus from the staff's stakeholder outreach is that the existing dose limits, and therefore the risk-informed, performance-based patient release requirements in 10 CFR 35.75, sufficiently protect public health and safety. In addition, there is no substantial benefit to using an activity-based standard instead of allowing licensees to make informed decisions based on patient circumstances. Mandatory hospitalization of otherwise healthy patients could introduce additional negative consequences, such as an increased risk of hospital-acquired infections for patients, additional patient anxiety and apprehension about the procedure, fewer healthcare facilities providing I-131 therapy, and insurance coverage and healthcare cost concerns. The staff concluded that the current dose-based release criteria provides adequate protection of the public by basing patient release decisions on the dose, directly related to the potential radiation hazard from the radiopharmaceutical administered to the patient, rather than on an activity that is at best, only indirectly related to this potential hazard.

Rulemaking to create different dose limits for different members of the public exposed to radiation from released individuals who have been administered unsealed byproduct material or implants containing byproduct material.

The provisions in 10 CFR 35.75 apply equally to all members of the public. A rulemaking to reduce the dose limit for pregnant women and children would require licensees to assume all members of the public who are not known to the patient are pregnant women or children. It is difficult for licensees to determine when and where a released patient would come into contact with a pregnant woman or child not known to the patient. This uncertainty could require licensees to hospitalize patients, which may increase the associated cost of treatment.

The 5 mSv (0.5 rem) TEDE limit for exposure from a released individual who has been administered a radiopharmaceutical, applies to any individual, including family members, young children, pregnant women, caregivers, hotel workers, and other members of the public. The 5 mSv (0.5 rem) limit is safe and reasonable under the circumstance of medical benefit. There is no evidence that the higher dose limit for those individuals exposed to the released patient, 5 mSv (0.5 rem) instead of 1 mSv (0.1 rem) for the general public, has put any individual at undue risk. The NRC staff therefore determined that changing the dose limit to members of the public who are exposed to released patients is not warranted.

The staff acknowledges that children and fetuses/embryos may be more susceptible than adults to some health effects attributable to ionizing radiation exposure, as described by the International Commission on Radiological Protection (ICRP) in Publication 94, “Release of Patients after Therapy with Unsealed Radionuclides.” However, based on the staff’s evaluation, there is no increased risk at the 5 mSv (0.5 rem) TEDE limit. The staff therefore concludes that the current regulations in 10 CFR 35.75 are adequately protective of all members of the public. In addition, 10 CFR 35.75 requires that if a patient could cause a dose to an individual in excess of 1 mSv (0.1 rem), the licensee is required to give the patient instructions on actions recommended to maintain doses to other individuals ALARA. The staff provided guidance on this topic in Regulatory Issue Summary 2008-11, “Precautions to Protect Children who may come in contact with Patients Released after Therapeutic Administration of Iodine-131.”

From the literature review, the staff noted that numerous publications discuss the radiation exposure to other individuals from I-131 patient therapy and reported that doses typically did not exceed 1 mSv (0.1 rem). Several of the publications included in the literature review contained findings that adhering to simple instructions, such as keeping an “arms-length” distance from other individuals whenever possible, is adequate to keep exposures ALARA. The consensus from the staff’s stakeholder outreach indicates the current NRC regulations, coupled with guidance, address concerns about exposures to women and children without the need for additional rulemaking. The licensee is required to provide written instructions on actions recommended to maintain doses to other individuals ALARA if the dose limit is likely to exceed 1 mSv (0.1 rem). These instructions should include information on the potential increased risks associated with exposing young children and pregnant women, including instructions to avoid close proximity to anyone for a specified period of time following treatment.

Rulemaking to change the 5 mSv (0.5 rem) limit for members of the public who are exposed by released patients from a per-release limit to a per-year limit.

The provisions in 10 CFR 35.75(a) authorize the licensee to release from its control patients who have been administered radioactive material if the TEDE to another individual from the patient does not exceed 5 mSv (0.5 rem). The Statements of Consideration for the 1997 rule

provide the clarification that the 5 mSv (0.5 rem) TEDE limit to an individual from exposure to the released patient is for each patient treatment. The broad consensus from the extensive stakeholder outreach conducted for the patient release evaluation is that the 1997 rule intended the limit to be applied on a per patient release basis. The NRC staff reaffirmed its determination that the limit for releasing patients who have been administered radioactive material applies to each individual treatment, and that based on the stakeholder feedback, rulemaking to make this clarification is not warranted. Some stakeholders suggested the limit should be an annual limit because the dose limits in 10 CFR Part 20 and the National Council on Radiation Protection and ICRP standards are annualized.

Rulemaking to require the 5 mSv (0.5 rem) limit to be a per-year limit ensures licensees track released patients throughout the year to reduce the possibility that a member of the public would receive a collective dose of more than 5 mSv (0.5 rem) per year from multiple patients, to the extent that the licensee has records that exposed individuals are common from different treatments. Rulemaking to require a per year dose limit is consistent with both occupational and public dose limits in 10 CFR Part 20 as well as national and international standards. Rulemaking would also reduce the possibility that a member of the public would receive a dose that is greater than 5 mSv (0.5 rem) in a year from a patient who receives multiple treatments or from multiple patients, to the extent that such information is available to the licensee.

However, rulemaking to require dose limits on a per-year basis could cause licensees and patients to postpone treatments that would otherwise be administered in a given year. In addition, rulemaking to require per-year limits would likely lead to inconsistencies in an otherwise standard set of patient instructions used nationwide based upon potential previous exposures to others.

Rulemaking to require licensees to conduct radiation safety discussions and provide written instructions with sufficient time prior to the administration

The provisions in 10 CFR 35.75(b) require a licensee to provide the released patient, or the patient's parent or guardian, instructions, including written instructions, on actions recommended to maintain public doses ALARA, if the dose to a member of the public is likely to exceed 1 mSv (0.1 rem). This regulation, however, does not specify that instructions need to be given before treatment.

Rulemaking to require licensees to conduct discussions with, and provide instructions to, the patient in a timely manner before the treatment could allow patients sufficient time to plan their actions following release (such as finding child care if necessary). Early discussions with the patient also allow licensees time to perform patient-specific calculations based on the patient's planned actions, and if necessary, arrange for the patient to be hospitalized. However, rulemaking to specify the timing of these discussions and when the instructions need to be provided to the patient before treatment could impede on the practice of medicine. Under the current regulations, if the licensee does not give patients adequate time to make arrangements for isolation, it will either have to wait to treat the patient until arrangements are made or make arrangements itself to hospitalize the patient; otherwise, the licensee would be in violation of the NRC's regulations.

The results of the literature review and dose calculations indicate that the dominant factor in determining both internal and external doses to members of the public from a released patient is the behavior of the patient once they have been released. This highlights the central

importance of instructions. The consensus from the stakeholder engagement indicates that a prescriptive regulatory requirement on when safety instructions must be provided to a radionuclide therapy patient or the patient's guardian is not warranted. The NRC staff determined that timely and adequate patient discussions should be addressed in guidance and not specified in regulations because there is much variability between treatment procedures and patient situations. Thus, when to provide required instructions is a "practice of medicine" decision.

Update to guidance associated with the patient release program

RG 8.39 was issued in April 1997 and provides guidance to licensees on determining when they should authorize patient release per 10 CFR 35.75(a) and when instructions to patients are required by 10 CFR 35.75(b).

The NRC staff identified that the guidance in RG 8.39 is out-of-date and could result in the underestimation of exposure if licensees use the default assumptions in the guidance when calculating the potential dose to other individuals, especially when a patient uses public transportation following release. The equations provided in RG 8.39 should not be used as an unjustified default in any particular case, but if the licensee chooses to use them, then the default assumptions need to be justified based on the licensee's assessment of the patient's likely behavior after release. The decision to release the patient should be reviewed before starting treatment to determine the conditions under which the patient is expected to be released, and whether the living arrangements, modes of transportation, and staying at a hotel are such that releasing the patient is unlikely to result in doses above 5 mSv (0.5 rem). The staff determined that the guidance in RG 8.39, as well as the equations and parameters contained/referenced in the guide, should be updated, simplified, and made more clear and explicit. A comprehensive update incorporating current scientific knowledge and patient instruction enhancements would lead to a more accurate estimate of public doses from released patients, resulting in better licensee decisions regarding when it may release patients following radioactive material administrations, as well as enhancing the patient's understanding of how their behavior, including following the provided instructions, affects the radiation exposure to other individuals.

Agreement State Coordination

The NRC staff received comments from five Agreement States and the Organization of Agreement States (OAS) board on the NRC staff's evaluation of the patient release program/regulations. The OAS board and the five Agreement States all support the staff's conclusion that updates to NRC guidance regarding calculations, methods, tables, and standard patient instructions would enhance the patient release program. In addition, the OAS board and two Agreement States are supportive of a limited rulemaking to require licensees to conduct radiation safety discussions and provide written instructions in a timely manner before radioisotope treatments.

Advisory Committee on Medical Uses of Isotopes Coordination

ACMUI agrees with the NRC staff's conclusions with respect to the patient release program. (Enclosure 4). The ACMUI also recommended specific changes in NRC guidance. The staff will consider these specific changes in updating RG 8.39.

CONCLUSION

From its evaluation, the NRC staff concluded that the current patient release regulations are protective of public health and safety, and that rulemaking to change the release criteria is not warranted. However, the staff determined that a comprehensive update to the NRC's patient release guidance, including incorporation of guidance currently provided in generic communications, as well as updates to the equations and methodologies described in the NRC guidance for calculating dose to members of the public from released patients, is warranted. Updating the NRC guidance with current scientific knowledge would lead to more accurate estimates of public doses from released patients, resulting in better licensee decisions regarding the timing, circumstances, and risks associated with patient release following byproduct material administration.

The staff is planning a phased approach to comprehensively update RG 8.39. Phase 1 would include incorporation of guidance currently provided in generic communications and patient instructions. Phase 2 would update the dosimetric equations, methodologies, and tables used to calculate dose to members of the public from released patients. A detailed breakdown of estimated resources for Phase 1 and Phase 2 is provided in Enclosure 5, "Resource Estimates."

COORDINATION:

The Office of the General Counsel has reviewed this paper and has no legal objections. The Office of the Chief Financial Officer has also reviewed this paper for resource implications and has no objections.

/RA/
Marc L. Dapas, Director
Office of Nuclear Material Safety
and Safeguards

Enclosures:
1. Summary of Patient Release after Radioiodine Therapy Research Review
2. Summary of Assessment of Where Patients Reside Immediately Following Their Release Report
3. Summary of Public Comments Regarding the Patient Release Program
4. Advisory Committee on the Medical Uses of Isotopes Comments on the Patient Release Draft SECY Paper Subcommittee Final Report
5. Resource Estimates (non-public)
6. NRC Form 757, "Non-Concurrence Process" (non-public)

SUBJECT: STAFF RECOMMENDATIONS FOR REVISIONS TO THE PATIENT RELEASE PROGRAM

ML17279B139

OFC	NMSS/MSTR	NMSS/MSTR	NMSS/MSTR	NMSS/MSTR	RES	OGC
NAME	KTapp	DBHowe NC*	LDimmick	DBollock	RTadesse	MSpencer
DATE	10/17/17	12/18/17	10/18/17	10/18/17	12/5/17	12/6/17
OFC	OCFO	NMSS/MSTR	Tech Ed	NMSS/MSTR	NMSS	
NAME	RAllwein	CEinberg for DCollins	WMoore	KWilliams	MDapas	
DATE	12/4/17	11/15/17	12/8/17	12/8/17	1/29/18	

OFFICIAL RECORD COPY
Non-Concurrence* Supporting documents attached