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Karagiannis, Bridget
Curran, Brain Allen,
Mary Neely
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Draft Regulatory Guide: Release of Patients Administered Radioactive Material

Comment On: NRC-2023-0086-0001

Draft Regulatory Guide: Release of Patients Administered Radioactive Material; Extension of Comment Period

Document: NRC-2023-0086-DRAFT-0043

Comment on FR Doc # 2023-08418

Submitter Information

Email: mpeters@acr.org

Organization: American College of Radiology (ACR)

General Comment

Please see the attached comments to NRC on DG-8061 from the American College of Radiology (ACR) (Docket ID NRC-2023-0086).

Attachments

acr-comments_nrc-patient-release-dg-8061_8-20-2023

August 20, 2023

Submitted electronically via Regulations.gov

ATTN: Program Management, Announcements and Editing Staff
Office of Administration
Mail Stop: TWFN-7-A60M
U.S. Nuclear Regulatory Commission
Washington, DC 20555-0001

**Re: (Docket ID NRC-2023-0086) Draft Regulatory Guide: Release of Patients Administered Radioactive Material;
Comments of the American College of Radiology**

The American College of Radiology (ACR)—a professional association representing over 41,000 diagnostic radiologists, interventional radiologists, nuclear medicine physicians, radiation oncologists, and medical physicists—appreciates the opportunity to comment on the draft regulatory guide (DG), DG-8061, “Release of Patients Administered Radioactive Material,” noticed by the U.S. Nuclear Regulatory Commission (NRC) in the April 21, 2023, *Federal Register* (Docket ID NRC-2023-0086; 88 FR 24495). The ACR provides the following observations as expounded in the below comments/recommendations:

- NRC’s current “patient release” regulatory requirements conservatively protect public health and safety.
- The draft regulatory guide, if finalized, would unduly increase compliance burden and complexity.
- Key proposals in the draft are based predominantly on a non-peer-reviewed, NRC-contracted reference document rather than available standards and resources.
- NRC should retract and revise the proposed calculational methodologies with a focus on simplifying and clarifying compliance by I-131 therapy providers, the primary audience for this guidance.

Background

NRC regulations at 10 CFR 35.75, “*Release of individuals containing unsealed byproduct material or implants containing byproduct material*,” state patients can be released from licensee control if the total effective dose equivalent (TEDE) to any other individual from exposure to the released individual is not likely to exceed 5 mSv/0.5 rem. Patient instructions are required if the TEDE to any other individual is likely to exceed 1 mSv/0.1 rem, with additional instructions required if the TEDE to a nursing infant or child could exceed 1 mSv/0.1 rem assuming no interruption of breast-feeding.¹

NRC regulatory guidance, RG 8.39, “*Release of Patients Administered Radioactive Materials*,” provides agency-endorsed means of licensee compliance, including patient instructions content and calculational methodologies. The methodologies currently use conservative assumptions and values to enable generic applicability. Use of NRC guidance to demonstrate compliance with §35.75 is technically voluntary, though typically viewed as the lowest risk regulatory compliance option available to licensees. A large core audience for RG 8.39 includes licensees without full-time, onsite medical physicists able to develop and justify substitute compliance approaches to regulators.²

¹ <https://www.ecfr.gov/current/title-10/chapter-I/part-35/subpart-C/section-35.75>

² <https://www.nrc.gov/docs/ML1923/ML19232A081.pdf>

DG-8061, released for comment in 2023, is the “proposed Revision 2” of RG 8.39. It contains major calculational changes for patient release determinations. Licensees following DG-8061 methods would use patient-specific calculations with complex inputs and modifying factors whenever administered activity is higher than conservative basic threshold values. If such calculations indicate dose would exceed the limits, or if the licensee is unable to perform the calculations, the patient would either not receive treatment or would be held under licensee control to await decay.³

NRC and ACMUI Activities

The NRC Advisory Committee on the Medical Uses of Isotopes (ACMUI) 2017 report on the then-draft SECY-18-0015, “Staff Evaluation of the U.S. Nuclear Regulatory Commission’s Program Regulating Patient Release after Radioisotope Therapy,” as well as evidence gathered by NRC via the licensee survey, “Assessment of Where Patients Reside Immediately Following Their Release Report” and the literature review/model calculations, “Patient Release Following Radioiodine Therapy: A Review of the Technical Literature, Dose Calculations, and Recommendations,” validated the agency’s assumptions about negligible internal dose contribution from released patients who follow instructions.^{4 5} To address dose overestimations in anticipation of future therapeutic agents, ACMUI advised more realistic assumptions and flexibility in RG 8.39. Among its key recommendations, ACMUI offered the following:

“Other assumptions and methods in the relevant regulatory guidance are in general excessively conservative, tending to yield overestimates of the actual doses to family members and other individuals in most cases. The guidance should be sufficiently flexible to allow incorporation of more realistic assumptions for assessing patient releasability. NRC staff is encouraged to re-visit NCRP Report No 155, entitled, “Management of Radionuclide Therapy Patients,” dated December 11, 2006. This report includes a flexible, generally applicable algorithm for determining the releasability of therapy patients and the duration of post-release precautions; an EXCEL™ file for practical implementation of this algorithm is available from the NCRP.”⁶

In 2018, the NRC staff stated in the final SECY-18-0015, “Staff Evaluation of the U.S. Nuclear Regulatory Commission’s Program Regulating Patient Release After Radioisotope Therapy,” the following:

*“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. . .”⁷*

The NRC subsequently made revisions to patient instructions and other content in RG 8.39 “Revision 1,” then provided to ACMUI a preliminary draft of its calculation methodology proposals intended for “Revision 2.” In its January 21, 2022, final report on the “draft phase 2 revision” of RG 8.39, the ACMUI described concerns with the unrealistic, complex, and more conservative assumptions in the proposal that appear contradictory to the simplification and clarification policy goals described in SECY-18-0015. Most notably, NRC proposed use of an occupancy factor of 1.0 instead of the current 0.25, effectively assuming a patient is perpetually within 1 meter of another person for 24 hours per day every day throughout decay, despite being provided §35.75(b) instructions. This change would create unrealistic default activity and dose rate values, effectively obligating licensees to use patient-specific calculations with modifying factors for certain therapies or to hold their patients following those implicated therapies.

“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

³ <https://www.regulations.gov/document/NRC-2023-0086-0002>

⁴ <https://www.nrc.gov/docs/ML1727/ML17279B143.pdf>

⁵ <https://www.nrc.gov/docs/ML1727/ML17279B142.pdf>

⁶ <https://www.nrc.gov/docs/ML1728/ML17281A000.pdf>

⁷ <https://www.nrc.gov/docs/ML1727/ML17279B139.html>

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).⁸

I-131 Therapy Impacts

I-131 therapy is an effective, noninvasive treatment option for patients with hyperthyroidism as well as ablation of postoperative thyroid remnant and therapy of iodine-avid thyroid cancer. It is the most common and accessible \$35,300 unsealed radionuclide therapy in the U.S., with the greatest heterogeneity in terms of disparate types of clinical environments that can and do safely provide these therapies to patients. However, these common treatments typically use administration activity above the revised, ultra-conservative basic threshold values in DG-8061. Therefore, patient-specific calculations would be routinely implicated, necessitating resources such as full-time, onsite medical physicists to use the proposed calculational flexibility in DG-8061 to avoid routine holds that would likely impact care accessibility and reduce health and safety.

The ACR agrees with the concerns from ACMUI members and other stakeholders that routine hospitalization is generally not a practical option. To explore this further, the ACR Harvey L. Neiman Health Policy Institute⁹ compiled the below Medicare patient data from Centers for Medicare and Medicaid Services' (CMS) datasets over a three-year period. Note the COVID-19 public health emergency reduced the generalizability of post-2020 Medicare data. Total procedures are calculated using CMS' Medicare Physician/Supplier Procedure Summary (PSPS).¹⁰ Distinct counts of providers/facilities are calculated using CMS' Medicare 5% fee-for-service file as well as the Medicare Provider Practice and Specialty (MD-PPAS) file to identify those that performed these procedures.¹¹ Medicaid, TRICARE, VA, and private insurer data were not accessible to be included below, so bear in mind that this is an underrepresentation.

Table 1. I-131 Therapy, Medicare Procedures and Facilities

I-131 Therapy				
Year	Total Procedures	Distinct Providers	Distinct Facility	Distinct System
2019	2,099,029	20,756	4,999	2,710
2020	1,666,133	19,037	4,631	2,562
2021	1,746,094	*currently unavailable		
Avg	1,837,085	19,897	4,815	2,636

Comparable Medicare data on Lu-177 Dotatate (Table 2 below) demonstrate that relatively few licensed facilities are equipped to provide more advanced \$35,300 therapies to Medicare patients. We can assume that many of these institutions—e.g., academic medical centers and major institutions—have onsite medical physics (though not necessarily specialized nuclear medicine physicists), capabilities, and compliance resources to modify DG-8061 patient-specific calculations if they choose to use NRC's guidance. However, these types of licensees are not the core audience for NRC guidance.

Table 2. Lu-177 Dotatate, Medicare Procedures and Facilities

⁸ <https://www.nrc.gov/docs/ML2202/ML22021B300.pdf>

⁹ <https://www.neimanhpi.org/about/>

¹⁰ <https://www.cms.gov/research-statistics-data-systems/limited-data-set-lds-files/physician/supplier-procedure-summary-psps-limited-data-set-lds>

¹¹ <https://data.cms.gov/provider-summary-by-type-of-service/medicare-physician-other-practitioners>

Lu-177 Dotatate Therapy				
Year	Total Procedures	Distinct Providers	Distinct Facility	Distinct System
2019	60,332	271	154	63
2020	56,785	187	104	39
2021	78,120	*currently unavailable		
Avg	65,079	229	129	51

According to KFF (formerly known as the Kaiser Family Foundation) via data sourced from the 1999-2021 American Hospital Association (AHA) annual survey—which compiles adjusted expenses per inpatient day include expenses incurred for both inpatient and outpatient care (inpatient days are adjusted higher to reflect an estimate of the volume of outpatient services)—the average expense per day in the U.S. is **\$2,833**. Note, such expenses vary by state. For example, across NRC/Non-Agreement States (discounting U.S. territories due to dataset limitations), adjusted expenses per inpatient day range from **\$1,632** (South Dakota) to **\$3,974** (District of Columbia). These estimates do not substitute for actual charges or reimbursement for care provided. Uncertain coverage/payment policy for medically unnecessary holds in private rooms in the hospital would likely lead to unintended negative effects on patient access and cost.^{12 13}

Additionally, the availability of isolated beds and rooms within a given facility limits the licensee’s capability to routinely hospitalize such patients. Nurses and other non-AU-supervised staff working in hospitals, who do not have intrinsic radiation safety expertise, would need training to protect themselves and members of the public in the facility. Licensees will need to expand occupational dose monitoring programs to include non-AU-supervised staff. For patients, mandatory confinement under licensee control would involve separation from their homes and loved ones, medically unnecessary hospitalization costs, and the added risk of hospital-acquired infections. The September 25, 2017, study contracted by NRC and conducted by the Oak Ridge National Laboratory (ORNL), Center for Radiation Protection Knowledge, noted the following about the potential effects of routine holds of I-131 therapy patients on public safety as well as on patients:

“...The total dose received by any person during a period of time such as a year will likely be much higher for hospital staff than for any member of the general public. This is because, if patients are not released, hospital staff will be exposed repeatedly to all patients who are treated at that hospital during the year, and will be repeatedly exposed each year that they practice at the hospital. If patients are released, members of the general public are unlikely to be exposed for a significant duration of time to multiple patients and therefore are expected to receive a low dose. This is also most likely to be true for members of the patient’s family, who are likely to be exposed for longer durations than other members of the general public but usually only once, or a few times if the patient requires repeat treatments, in a lifetime. This is in addition to the other benefits of releasing patients, such as reduced medical costs, possibly increased patient comfort, potential availability of constant family support, and maybe improved patient psychological well-being during the therapy for those patients who prefer a home environment rather than a hospital setting.”¹⁴

Alternatives to routine holds or patient-specific calculations would be discontinuing to provide these treatments or using compliance methodologies other than NRC’s RG 8.39 Revision 2. The risk of the latter being that NRC/Agreement State investigators may find substitute methodologies unacceptable. It is therefore reasonable to assume that certain licensees may no longer provide I-131 or other implicated §35.300 therapies if DG-8061 were finalized.

ACR recommendation: Retract and revise RG 8.39.

To avoid impacts on patients and providers, the ACR recommends that NRC retract, reevaluate, and revise the draft calculational modifications in DG-8061 and reduce licensee compliance burden via more realistic baseline assumptions in the guidance that factor in the regulatory requirement for §35.75(b) instructions. For example, the ACMUI

¹² <https://www.kff.org/health-costs/state-indicator/expenses-per-inpatient-day/?currentTimeframe=0&selectedRows=%7B%22wrapups%22:%7B%22united-states%22:%7B%7D%7D%7D&sortModel=%7B%22colId%22:%22Location%22,%22sort%22:%22asc%22%7D>

¹³ <https://www.ahadata.com/aha-annual-survey-database>

¹⁴ <https://www.nrc.gov/docs/ML1726/ML17262A909.pdf>

recommended standards such as National Council on Radiation Protection and Measurements (NCRP) Report No. 155¹⁵ which provide simplified, peer-reviewed releasability/instruction determination models, are more realistic than NRC's current RG 8.39 as well as DG-8061, yet also maintain conservative generalizability that would be useful for achieving NRC's regulatory objectives. Also, a spreadsheet is available for calculation documentation, which could be readily employed as a template to update for radionuclides other than I-131 NaI.

Most of the available evidence points to RG 8.39 currently overestimating dose to members of the public from released therapy patients when instructions are followed. For example, employing the point source method overestimates the dose by at least a factor of 2, and potentially much higher. This has been substantiated in the literature, including:

Comparing Dose Rates Near a Radioactive Patient Evaluated Using Various Source Models.

Point, Line, Cylinder, and Anthropomorphic Phantoms. Liu, Yi-Ching; Lee, Kuo-Wei; Sheu, Rong-Jiun. *Health Physics* 109(1):p 69-77, July 2015

Comparison of Measured and Calculated Dose Rates Near Nuclear Medicine Patients. Yi, Y.; Stabin, M.G.; McKaskle, M.H.; Shone, M.D.; Johnson, A.B. *Health Physics* 105(2):p 187-191, August 2013

Correction Factors For More Accurate Estimates Of Exposure Rates Near Radioactive Patients: Experimental, Point, And Line Source Models. Willegaignon, J; Guimarães, Maria I. C.; Stabin, Michael G.; Sapienza, Marcelo T.; Malvestiti, Luiz F.; Marone, Marília M. S.; Sordi, Gian-Maria A. A. *Health Physics* 93(6):p 678-688, December 2007.

The Nuclear Medicine Patient as a Line Source: The Source Length Is Certainly Not the Patient Height, But It Is a Reasonable Approximation. Broggio, David. *Health Physics* 123(3):p 208-217, September 2022.

Calculating the Absorbed Dose from Radioactive Patients: The Line-Source Versus Point-Source Model. Jeffrey A. Siegel, Carol S. Marcus and Richard B. Sparks. *Journal of Nuclear Medicine* September 1, 2002, 43 (9) 1241-1244.

Assessment of the Point-Source Method for Estimating Dose Rates to Members of the Public from Exposure to Patients with 131I Thyroid Treatment. Dewji, Shaheen Azim; Bellamy, Michael; Hertel, Nolan; Leggett, Richard; Sherbini, Sami; Saba, Mohammad; Eckerman, Keith. *Health Physics* 109(3):p 233-241, September 2015.

Additionally, literature on measurements of family members demonstrate that regulatory limits are not exceeded in real-world practice.

Measurement of Radiation Exposure in Relatives of Thyroid Cancer Patients Treated With 131I. Ramírez-Garzón, Y.T.; Ávila, O.; Medina, L.A.; More. *Health Physics.* 107(5):410-416, November 2014.

Caregiver Exposure After 131I Therapy. *Journal Of Nuclear Medicine, Vol. 47, No. 9, 33N* September 2006

External Radiation Dose to Owners of Canines Treated with (117mSn) Radiosynoviorthesis for Osteoarthritis. Smith, Chad A.; Krimins, Rebecca A, *Health Physics.* 123(2):128-132, August 2022.

Recommended Restrictions After 131I Therapy: Measured Doses in Family Members Mathieu, Isabelle; Caussin, Jacques; Smeesters, Patrick. *Health Physics.* 76(2):129-136, February 1999.

ACR recommendation: RG 8.39 calculations should assume §35.75(b) instructions were provided and followed.

The ACR disagrees with the guidance's use of any default policy assumption that patients would ignore the §35.75(b) instructions, as this does not reflect expected behavior per the available evidence. §35.75(b) instructions have been shown by NRC and ORNL to be an effective risk mitigation that protects public health and safety and ensures the limit in §35.75(a) is unlikely to be exceeded in real-world scenarios.¹⁶

RG 8.39 Revision 2 should reflect the regulatory requirement that patient instructions are provided and that licensees generally ensure those instructions are understandable and practical per other subsections of RG 8.39. An area of

¹⁵ <https://ncrponline.org/publications/reports/ncrp-reports-155/>

¹⁶ <https://www.nrc.gov/docs/ML1726/ML17262A909.pdf>

needed improvement that was implicated in the ACMUI comments is patient instruction—i.e., making them clearer and assisting licensees in reinforcing them with the patient.

ACR recommendation: Reevaluate and incorporate ACMUI recommendations.

The ACR supports earlier ACMUI recommendations on the RG 8.39 revision process, particularly those from the committee’s 2022 report on the preliminary draft version. This valuable input, broadly representative of the licensee community’s concerns, has been mostly rejected by the NRC contractor and staff in DG-8061.¹⁷

For example, an occupancy factor of 1.0—which assumes 1 meter patient proximity to another individual for 24 hours per day—is unrealistic. §35.75(a) requires that TEDE to another individual from the released patient is not likely to exceed 5 mSv/0.5 rem, and the existing RG 8.39-leveraged occupancy factor of 0.25 conservatively provides reasonable assurance of compliance. The rationale for the extremely conservative 1.0 appears to be informed by hypothetical scenarios studied by NRC in 2017 that assume §35.75(b) violations by the licensee or negligence of instructions by the patient. However, in that same 2017 data collection effort, ORNL’s review of real-world external and internal dose data from family/caregivers demonstrated that the existing RG 8.39 occupancy factor of 0.25 is conservative when §35.75(b) instructions are followed:

“Nevertheless, family members of patients receiving the highest administered activities often show some of the lowest doses. This again points to the importance of behavior patterns and observation of ALARA guidance provided by the licensee. Nearly all of the recorded doses to the family members were below the NRC dose limit of 5 mSv (500 mrem) although a small percentage showed doses that exceeded that limit. The reasons for the high doses in these specific cases were not identified, but based on the patterns revealed by these studies, it is probable that not observing ALARA precautions must have been at least a major, if not the only, reason for the high doses. The availability of sufficient space for effective patient isolation at home also does not appear to play an important role as shown by some of the studies.”¹⁸

ACR recommendation: Use recognized standards instead of government-unique approaches to simplify and add flexibility.

SECY-18-0015 indicated that RG 8.39 updates would be based on “current scientific understanding,” which directly suggested incorporation of NCRP Report No. 155 standards to replace the older NCRP reference material upon which RG 8.39 was previously based. However, instead of using available NCRP resources or other standards, DG-8061 methodologies and appendices rely on a reference to NRC contractor-developed information contained in RCD Radiation Protection Associates, RCD-21-181-0, “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,” Corvallis, Oregon, June 30, 2021. (Agencywide Documents Access and Management System Accession No. ML21348A111).

The ACR cannot find evidence that this document was vetted and approved by ACMUI prior to its use as the foundation of the more controversial aspects of the proposed RG 8.39 Revision 2, **nor that the document underwent scientific peer review or public comment.** Moreover, verbal explanations of how to leverage the proposed modifying factors made by the contractor’s representative during the July 20, 2023, public meeting on DG-8061 indicate that incorrect assumptions were likely made during the creation of RCD-21-181-0/DG-8061 about the compliance capabilities of I-131 therapy providers in general—i.e., that medical physicists would be onsite in each of the ~4,800 U.S. facilities that perform these procedures to conduct patient-specific calculations enabling release.¹⁹ While this is likely accurate for larger institutions that provide the most advanced therapies (for example, those in Table 2 above that offer Lu-177 Dotatate therapy), this is mostly inaccurate for the majority of the ~4,800 provider facilities that provide I-131 therapies across the U.S.

¹⁷ NRC. ML23178A090, *Responses to ACMUI Recommendations on the Draft Proposed Revision 2 to RG 8.39*. July 10, 2023.

¹⁸ <https://www.nrc.gov/docs/ML1726/ML17262A909.pdf>

¹⁹ <https://adamswebsearch2.nrc.gov/webSearch2/main.jsp?AccessionNumber=ML23201A106>

While contracted experts can and do provide ACMUI and NRC staff with valued input to inform public policy recommendations, it is generally not regarded as good government practice to use agency-unique methodologies when there are available, peer-reviewed, and widely adopted national standards for meeting the government's objectives—in this case, ensuring that TEDE to another individual from the released patient is not likely to exceed 5 mSv/0.5 rem. NCRP resources are available on this topic and should be leveraged instead.

ACR Recommendation: Other/miscellaneous technical changes.

Please note the following areas of DG-8061 that need administrative or technical changes. The ACR recommends that the accuracy, precision, and editorial notes of all tables be reviewed and confirmed.

- Table 2, Patient Thresholds
 - Many values are below background or measuring precision.
 - Footnote e is not referenced in the table.
 - Footnote f discusses alpha-emitters yet is attached to positron-emitters in the table.
- Table 3, Breastfeeding
 - There are several errors due to inconsistent equivalents between GBq and mCi. For example, 2 GBq is given the equivalent of 40, 50, and 60 mCi.
 - Rather than providing true equivalent value there is an unclear rounding creating errors of around 10%. For example, 1000 mCi is stated as equivalent to 40 GBq when it is by definition 37 GBq. This is done throughout Table 3; however, entries in Table 4 are handled differently and with more numerical detail.
- Table 4, Breastfeeding Interruption
 - I-125 OIH and I-131 OIH are generally unavailable in practice.
 - The typical administered activity for I-123 NaI is 0.1-0.4 mCi.
 - The footnote and table values for I-125 may lead to confusion. I-125 NaI is not used for nuclear medicine purposes. The ACR assumes this is to account for contamination and we suggest clarification in the footnote via added language: "10% of the activity of I-123 that is administered (to consider contamination)."

The ACR welcomes further communications with NRC about this topic. Please contact Gloria Romanelli, JD, Senior Director, Legislative and Regulatory Relations and Legal Counsel, Quality and Safety, at gromanelli@acr.org; or Michael Peters, Senior Government Affairs Director, at mpeters@acr.org, with questions.

Sincerely,



Jacqueline A. Bello, MD, FACR
Chair, Board of Chancellors
American College of Radiology