Advisory Committee on the Medical Uses of Isotopes

Public Teleconference Meeting December 15, 2021

Meeting Handout

TELECONFERENCE MEETING AGENDA
Advisory Committee on The Medical Uses Of Isotopes

December 15, 2021
2:00 PM – 4:00 PM EST

OPEN SESSION

1. **Opening Statements** — **C. Einberg, NRC**
   Mr. Chris Einberg will formally open the meeting.

2. **Alpha Dart Licensing Guidance** — **R. Ennis, M.D., ACMUI**
   Dr. Ronald Ennis will present the ACMUI Subcommittee on Alpha Dart draft report on the NRC staff's draft licensing guidance.

3. **CivaDerm** — **M. Shober, ACMUI**
   Ms. Megan Shober will present the ACMUI Subcommittee on Civaderm draft report on the NRC staff's additional considerations memo for CivaDerm.

4. **Revision to Regulatory Guide 8.39** — **M. Shober, ACMUI**
   Ms. Megan Shober will present the ACMUI Subcommittee on Regulatory Guide 8.39, "Release of Patients Administered Radioactive Material" draft report on the NRC staff's draft revision of the regulatory guide.

5. **Closing and Adjournment** — **D. Metter, M.D., ACMUI**
   Dr. Darlene Metter will close the meeting.

U.S.NRC
United States Nuclear Regulatory Commission
Protecting People and the Environment

Report of Subcommittee on Alpha Tau Alpha DaRT™ Manual Brachytherapy Licensing Guidance

Ronald Ennis, MD

December 15, 2021

Subcommittee Members

- Becky Allen
- Ronald Ennis, M.D.
- Hossein Jadvar, M.D., Ph.D
- Zoubir Ouhib
- Michael O'Hara, Ph.D
- Megan Shober
- Consultant: Michael Sheetz
- NRC Staff Resource: Katherine Tapp, Ph.D.

Subcommittee Charge

- Comment on Draft Licensing Guidance for Alpha Tau AlphaDaRT™ brachytherapy source

Licensing under 35.1000

- The subcommittee agrees with licensing AlphaDart™ under 35.1000 rather than 35.400 or 35.300.
- The source has both similarities to and differences from a sealed brachytherapy source and an unsealed. radiopharmaceutical. So, a licensing guidance that is unique but draws from 35.300 and 35.400 is appropriate.

Roles of Authorized Medical Physicist

- The subcommittee does not believe acceptance testing of treatment planning software requires an AMP but rather should be done by a qualified medical physicist.
- The subcommittee does not believe the AMP has a role in training the RSO for this source. Training of an RSO should come from the vendor or an RSO who has previously been trained in this source.

Role of Nuclear Pharmacist

- The subcommittee does not see any role for a nuclear pharmacist. This source is not provided in a pill or liquid form and is not ingested or delivered intravenously.

Assessment of Leakage

- The subcommittee does not believe there is a role for an assessment of patient surface contamination/leakage. Radioactive particles are diffusing through tissue in all directions, including toward the body surface. There is no way to distinguish radioactivity at the patient surface that would be expected as part of a superficial application of the source vs. surface contamination.
- In addition, the Ra-224 is not encapsulated but rather is adherent to the surface of the source from which Rn-220 gas and its daughter particles diffuse into tissue. As such the notion of assuring there in not leakage from the source itself also does not apply.

Integrity of source seal

The subcommittee does not think this is necessary since even if the seal were broken and equilibrium were not reach inside the applicator, dose delivery would not be affected.

Contamination of procedure room

- Because Ra-224 is adherent to the surface, if the source were to come into contact with any surfaces in the procedure room or operating room during an application, there is the possibility of contamination. Therefore, the subcommittee recommends that in the event such contact occurs, the licensee be required to follow the contamination guidance in NUREG 1556 Volume 9.
- The subcommittee recommends changing the phrase “survey instrument used” to “radiation detection instrument” to keep this more generic.

Patient release

- The subcommittee recommends the following modification: Change requirement that patient should not be released if it is "*possible* under normal circumstances for a seed or a seal to become dislodged" to "*likely* under normal circumstances…
- Stating possible is too vague-anything is possible

Medical Event

- The subcommittee agrees with the proposed definition of ME for temporary implants. However, if the manufacturer obtains approval for permanent implantation, the subcommittee recommends that in that circumstance the definition of ME be the same as for other permanent brachytherapy applications.
- NB: The draft guidance states that no modifications are anticipated if permanent applications are used in the future. Therefore, we recommend including the definition of ME in the setting of permanent implantation in the current licensing guidance in anticipation of that eventuality.

Documentation of patient location

- The subcommittee does not believe documentation of the location(s) where the patient anticipates to spend significant time adds and safety benefit. Therefore, we do not support a requirement of document this.

Acronyms

- AMP-Authorized Medical Physicist
- RSO-Radiation Safety Officer

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

Subcommittee Review and Comments on

Draft Licensing Guidance Alpha Tau Alpha DaRT™ Manual Brachytherapy

Draft Report
Submitted: November 29, 2021

Subcommittee Members:

Becky Allen
Ronald Ennis, M.D. (chair)
Hossein Jadvar, M.D., Ph.D.
Zoubir Ouhib
Michael O'Hara, Ph.D.
Megan Shober

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

The subcommittee thanks the NRC for the opportunity to comment of the Alpha Tau Alpha DaRT™ Manual Brachytherapy Licensing Guidance. All mentions of section numbers refer to this document as shared with the subcommittee.

The subcommittee supports the licensing of Alpha DaRT™ under 35.1000. The diffusion of radioactive particles into the interstitial tissues and blood circulation make this device significantly different from brachytherapy sources such that licensing it under 35.400 would be inappropriate. Similarly, Alpha DaRT™'s delivery via a source placed into tissue differentiates it substantially from radiopharmaceuticals to support not licensing it under 35.300. The subcommittee believes it is appropriate to draw on requirements of 35.400 regarding aspects of Alpha DaRT™ that are similar to brachytherapy and requirements of 35.300 for aspects similar to radiopharmaceuticals.

The subcommittee does not support any specified role for an authorized medical physicist (AMP) in acceptance testing of software for treatment planning (section 6.3). This opinion aligns Alpha Dart™ with brachytherapy treatment planning software requirements in 35.400. However, it should be noted that the subcommittee believes strongly that rigorous acceptance testing of any new software system or modification of existing software system, such as the addition of a new source, be performed by a qualified medical physicist prior to clinical use.

Similarly, the subcommittee does not believe an AMP has any role in training RSOs (section 5.2.2). RSO training should come from the vendor or an RSO already trained in Alpha DaRT™.

Finally, the subcommittee sees no role for an authorized nuclear pharmacist for this device (section 5.2.2). There is no liquid or pill for a pharmacist to manage.

The subcommittee does not support an assessment to assure the sources are not leaking outside the body (section 6.1, 6.5). Since the radioactive particles are traveling through tissue in all directions, it is impossible to assess leakage as opposed to intended radiation distribution from treatment. The concept of leakage does not apply since Alpha DaRT™ is not a sealed source, rather the Ra-224 is adherent to the surface of the source with the Rn-220 gas and subsequent daughters readily diffusing off the device.

Regarding the required surveys required by 10 CFR 35.70 and 35.404 (section 6.5), the subcommittee notes that unlike sealed source brachytherapy, there is a potential of room contamination after the procedure due to the fact that sources are not sealed, but rather, the radioactivity is adherent to the surface of the source and the daughter products diffuse from the source. These two features create the possibility of contamination in the procedure room. Following both the ambient radiation level and contamination survey guidance in NUREG 1556 Volume 9 is recommended. In addition, the subcommittee recommends changing the phrase "survey instrument used" to "radiation detection instrument" to keep this more generic.

The subcommittee does not support assessing the integrity of the source seal (section 6.7). In the subcommittee's opinion, even if the integrity were broken and equilibrium were not reached, the dose delivery would not be affected.

Regarding patient release (section 7.3), the subcommittee recommends changing the following language. Patients should not be released from the licensed facility "if it is *possible* under normal conditions for a seed or seal has a potential to become dislodged" to "if it is *likely* under normal conditions for a seed or seal to become dislodged."

The subcommittee agrees with the definition of Medical Event (section 6.2) for temporary applications of Alpha Dart™. However, if in the future permanent implants are performed, the subcommittee recommends the definition of Medical Event for that application be defined like other permanent brachytherapy as stated in 10 CFR 35.3045.

The requirement that locations where the patient will spend significant time be documented (section 7.4) does add any clear safety benefit. It is unclear what the clinical and safety team at the treating facility will do with this information to enhance radiation safety. The subcommittee recommends removal of the requirement.

Respectfully submitted on November 29, 2021,

Subcommittee on Alpha DaRT™ Manual Brachytherapy,
Advisory Committee on the Medical Uses of Isotopes,
U.S. Nuclear Regulatory Commission

Alpha Tau Alpha Dart™ Manual Brachytherapy Licensing Guidance

XXXX, 2021

NRC Contact
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Table of Contents

1 10 CFR 35.1000 Use

Alpha DaRT™ (Diffusing Alpha-emitters Radiation Therapy) are manual brachytherapy sources, with many unique properties that merit radiation safety considerations other than those required by Title 10 of the Code of Federal Regulations (CFR) Part 35, Subpart F, "Manual Brachytherapy." These unique properties include the release of radon-220 (Rn-220) in tissue, an alpha emitting noble gas from the radium-224 (Ra-224) source. As a result, Alpha DaRT™ is regulated under 10 CFR 35.1000, "Other Medical Uses of Byproduct Material or Radiation from Byproduct Material."

2 Device description

The Alpha DaRT™ device is a source and applicator designed for manual brachytherapy. The Alpha DaRT™ source are Ra-224 seeds which are implanted into the tumor using an Alpha DaRT™ applicator. Inside the tumor, the Ra-224 decays by alpha emission and the seeds release Rn-220 by recoil. Rn-220 is a noble gas and will diffuse in the extra- and intra-cellular space near the seed, occasionally entering and leaving the porous network of tumor blood vessels. Irradiation of tissue continues through beta and alpha emissions throughout the remainder of the decay chain. The seeds are made of a stainless steel with layer of Ra-224 affixed to the surface of the tube.

In the Alpha DaRT treatment, a number of Alpha DaRT seeds are inserted into the tumor via the Alpha DaRT applicator according to a pre-determined plan.

The applicator comprises two major components:

1. A needle or catheter with the Alpha DaRT seeds placed in it. The Alpha DaRT seeds are stringed on a biocompatible suture and loaded inside a rigid needle or flexible catheter and sealed inside with glycerin.
2. A stylet (plunger) inserted into the needle cannula (or catheter), reaching the back end of the Alpha DaRT seeds. During administration, the strung seeds are pushed through the glycerin into the tumor volume via the plunger.

In addition, there are two auxiliary components of the applicator:

1. A protective cap is attached to the needle or catheter to prevent inadvertent damage during transportation.
2. A safety screw, which secures the needle and the stylet firmly together.

More information about the device can be found in its sealed source and device registry, MA-1426-D-101-S.

Alpha Tau Medical, Inc. Model Alpha DaRT™ series device was conditionally approved by the U.S. Food and Drug Administration (FDA) in Investigational Device Exemption number G180076, dated May 10, 2018, for temporary implant therapy. No change in this guidance is expected should the FDA permit the device for permanent implant therapy.

3 Licensing Guidance

The applicant must submit the information required to meet 10 CFR 30.33, "General Requirements for issuance of specific licenses," and 35.12, "Application for license, amendment, and renewal", as described below. Applicants should refer to NUREG-1556, Volume 9, Revision 3, "Consolidated Guidance About Material Licenses: Program-Specific Guidance about Medical Use Licenses," as it provides overall licensing guidance for all medical uses of byproduct material. Guidance and license conditions specific for the use of Alpha DaRT™ under 10 CFR 35.1000, "Other medical uses of byproduct material or radiation from byproduct material" are contained herein. The guidance and license conditions listed in this document provide applicants with the acceptable means in satisfying the requirements for a license for the use of Alpha DaRT™. This information is not intended to be the only means of satisfying the requirements for a license. The applicant should submit additional information and commitments requested below or may, unless the information is specifically required by regulation, submit alternative information and commitments for review by the NRC staff to make a licensing determination. The commitments incorporated into the license by license condition will be reviewed during routine inspections. If an applicant commits to the guidance provided below, the applicant is committing to follow commitments described with the use of the word "should."

4 Requirements not Specific to 10 CFR 35.1000 Use

Applicants must commit to meet the general requirements in 10 CFR Part 35, Subpart A, "General Information;" Subpart B, "General Administrative Requirements;" Subpart C, "General Technical Requirements;" Subpart L, "Records;" and Subpart M, "Reports," except as specified in this guidance. Additionally, applicants must meet applicable requirements of 10 CFR Parts 19, "Notices, Instructions and Reports to Workers: Inspection and Investigations;" Part 20, "Standards for Protection Against Radiation;" and Part 30, "Rules of General Applicability to Domestic Licensing of Byproduct Material."

5 Specific Licensing Guidance for Alpha DaRT™

5.1 Radionuclides, Form, Possession Limits, and Purpose of Use

The information in the table below provides the suggested format for completing Item 5 (Radioactive Material) and Item 6 (Purpose of Use) on the NRC Form 313, "Application for Materials License."

Radionuclides (NRC Form 313 Item 5a)	Radium-224 permitted by 10 CFR 35.1000
Chemical/Physical Form (NRC Form 313 Item 5b)	Sealed sources (Manufacturer Alpha Tau Medical, Inc., Model No. _____)
Maximum Possession Limit (NRC Form 313 Item 5c)	___ mCi
Purpose of Use (NRC Form 313 Item 6)	Diffusing alpha emitting brachytherapy procedure permitted by 10 CFR 35.1000.

5.2 Training and Experience

Licensees must have at least one Authorized User (AU) and Radiation Safety Officer (RSO) for Alpha DaRT before the source can be added to the license. NRC staff have determined the following training and experience (T&E) criteria is appropriate to authorize AUs and RSOs for Alpha Dart. Applicants may submit documentation showing this criteria is met or may submit alternative T&E commitments to be reviewed on a case-by-case basis by NRC staff. The alternative T&E commitments should include an explanation of why the applicant believes the alternative T&E commitments demonstrate that the individuals are qualified to be an AU.

5.2.1 Authorized Users

NRC has determined that individuals meeting the Authorized User (AU) training and experience (T&E) criteria A, and B, provided below can be authorized for the use of Alpha DaRT.

A.

1. Is identified as an AU for medical use in 10 CFR 35.1000 for Alpha DaRT or 10 CFR 35.400, "Use of sources for manual brachytherapy;" or

2. Meets the training and experience requirements of 10 CFR 35.490, "Training for use of manual brachytherapy sources," including a written attestation when necessary.

And

B.

Has successfully completed training in delivery, safety procedures, and clinical use for Alpha DaRT. This requirement may be satisfied by completing a training program provided by the vendor for new users or by receiving training supervised by an AU who is authorized for Alpha DaRT. Safety procedures and clinical use training should include preparing, implanting, and removing the seeds; using administrative controls to prevent a medical event; and using procedures to control contamination and proper decontamination. The applicant should have a written attestation that the AU has satisfactorily completed these requirements and is able to independently fulfill the radiation safety-related duties as an AU for use of Alpha DaRT brachytherapy.

***5.2.2** Radiation Safety Officer*

The Radiation Safety Officer (RSO) must have training as specified in 10 CFR 35.50, "Training for Radiation Safety Officer and Associate Radiation Safety Officer", including training in radiation safety, regulatory issues, and emergency procedures for Alpha DaRT. This training requirement may be satisfied by completing training that is supervised by an RSO, an Associate RSO, authorized medical physicist, authorized nuclear pharmacist, or authorized user, as appropriate, who is authorized for Alpha DaRT. In addition, RSO's should be aware of conditions and procedures specific to the individual license.

6. License Conditions

The applicant shall commit to follow all applicable requirements in 10 CFR Part 35 for brachytherapy sources and manual brachytherapy use, except as specified in the following licensing commitments. The table contained in the appendix provides more details on applicable 10 CFR Part 35 requirements.

6.1 Procedures for Administration

The licensee must have procedures for administration requiring a written directive as specified in 10 CFR 35.41,"Procedures for administrations requiring a written directive," specifically to ensure high confidence that the patient's or human research subject's identity is verified before each administration and each administration is in accordance with the written directive. In addition to requirements in 10 CFR 35.41, licensees shall commit to include verification that seeds are fully contained without leakage outside the patient's body after administration. In addition, licensees shall commit to evaluating the location of the seeds prior to removal for temporary use to determine if the seeds moved during treatment to determine if a medical event occurred. Similar to 10 CFR 35.2041, "Records for procedures for administrations requiring a written directive," licensees shall retain a copy of these procedures for the duration of the license. See NUREG-1556, Volume 9, Revision 3, Section 8.10.13, "Procedures for Administration when a Written Directive is Required," and NUREG-1556, Volume 9, Revision 3, Appendix S for more information.

6.2 Medical Event Reporting

Licensees are required to report medical events in accordance with 10 CFR 35.3045, "Medical event reporting" with the exceptions listed below.

- Licensees will not be required to report a medical event caused by a leaking source in accordance with 10 CFR 35.3045(a)(1)(ii)(e) or 10 CFR 35.3045 (2)(iii)(D) as AlphaDart seeds are not a sealed source.
- Licensee shall commit to report any event in which the seed is planted directly into a location discontiguous from the treatment site, as documented in the post-implantation portion of the written directive. As stated above, total source strength only needs to include radium-224 activity.
- Licensees shall commit to report any discovered event where the dose to the skin or an organ or tissue other than the treatment site that exceeds by 0.5 Sv (50 rem) or more the expected dose to that site from the procedure if the administration had been given in accordance with the written directive prepared or revised before administration; and 50 percent or more the expected dose to that site from the procedure if the administration had been given in accordance with the written directive prepared or revised before administration..

6.3 Therapy-related computer systems

The licensee must complete acceptance testing on the treatment planning system of therapy-related computer systems in accordance with 10 CFR 35.457, "Therapy-related computer systems." The licensee shall commit to having an authorized medical physicist perform additional acceptance testing on any modifications to a treatment planning system specifically made for Alpha DaRT therapy to ensure accuracy of dose; graphic displays, as needed for treatment planning; and software used to determine sealed source positions from radiographic images.

6.4 Labeling

Labeling requirements in 10 CFR 35.69, "Labeling of vials and syringes," are not required for Alpha DaRT seeds. The seeds are not a radioactive drug. Licensees shall commit to keep the applicator in its labeled container (i.e. sterilized bag) provided by the manufacturer until its needed for use or conditions in 10 CFR 35.92, "Decay-in-storage," are met.

6.5 Surveys

In addition to area surveys required by 10 CFR Part 20 and 10 CFR 35.70, “Release of individuals containing unsealed byproduct material or implants containing byproduct material“, a licensee shall commit to survey with a radiation detection survey instrument after each administration of Alpha DaRT seeds where prepared for use or administered. Similar to 10 CFR 35.2070, “Records of surveys for ambient radiation exposure rate”, licensees shall retain a record of the surveys after each administration for 3 years. The record must include the date of the survey, the results of the survey, the instrument used to make the survey, and the name of the individual who performed the survey. See NUREG-1556, Volume 9, Revision 3, Section 8.10.12, “Area Surveys” and Appendix R, “Model Procedures for Area Surveys” for more information regarding surveys.

In addition to surveys required by 10 CFR 35.404,“Surveys after source implant and removal”, licensees shall commit to perform a removable contamination survey of the patient to ensure no contamination or leakage prior to patient release. Similar to 10 CFR 35.2404, “Records of surveys after source implant and removal,” shall maintain a record of these surveys for 3 years. Each record must include the date and results of the survey, the survey instrument used, and the name of the individual who made the survey. Licensees shall commit to file a report within 5 days if this survey reveals the presence of 185 Bq (0.005 µCi) or more of removable contamination similar to reports required per 10 CFR 35.2067, “Records of leaks tests and inventory of sealed sources and brachytherapy sources.” The report must be filed with the appropriate NRC Regional Office listed in 10 CFR 30.6 of this chapter, by an appropriate method listed in 10 CFR 30.6(a) of this chapter, with a copy to the Director, Office of Nuclear Material Safety and Safeguards. The written report must include the type of applicator and lot number, if assigned; the radionuclide and its estimated activity; the results of the test; the date of the test; and the action taken.

6.7 Calibration

As Alpha DaRT is a brachytherapy device, licensees do not need to determine unsealed byproduct activity in accordance with 10 CFR 35.63, “Determination of dosages of unsealed byproduct material for medical use”. Licensees shall commit to following 10 CFR 35.432, “Calibration measurements of brachytherapy sources”, and 10 CFR 35.2432, “Records of calibration measurements of brachytherapy sources,” for calibration and recordkeeping. In accordance with 10 CFR 35.432, licensees may use measurements provided by the source manufacturer instead of making their own measurements. However, there is a potential that radon-220 could leak from the applicator, which would mean equilibrium with decay products would not be present during administration as anticipate. Therefore, licensees shall commit to ensure the integrity of the applicator seal prior to administering seeds to a patient to verify that leakage has not occurred. This could be completed by performing a survey of the sterilization bag after the applicator has been removed, but prior to administration, to ensure no leakage. Similar to 10 CFR 35.3432, licensees shall retain a record of their validation of the integrity of the applicator seal for 3 years after its use.

6.8 Radiation Protection Program Changes

This guidance may be revised as additional experience is gained regarding the medical use of Alpha DaRT. An applicant initially applying for authorization for the medical use of Alpha DaRT may request to incorporate into its license a change process similar to 10 CFR 35.26. Such a change process can allow some future changes to radiation safety programs without a license

amendment provided that the change process requires the following conditions to be met for revisions to the radiation safety program:

1. the revision is in compliance with the regulations; and
2. the revision is based upon NRC's current 10 CFR 35.1000 use guidance for Alpha DaRT posted on the NRC's Medical Uses Licensee Toolkit Web site; and
3. the revision has been reviewed and approved by the licensee's RSO and licensee's management; and
4. the affected individuals are instructed on the revised program before the change is implemented; and
5. the licensee will retain a record of each change for five years; and
6. the record will include a copy of the appropriate website guidance, the old procedure, the new procedure, the effective date of the change, and the signature of the licensee management that reviewed and approved the change.

7. Notes to Licensees

7.1 Change in Physical Conditions of Use

If the physical conditions of use differ from those reported in the Sealed Source and Device (SSD) certificate, the limited specific medical use licensee shall request an amendment for the new conditions, and a broad scope licensee shall perform its own engineering and radiation safety evaluation addressing those differences.

7.2 Written Directives

The licensee must complete a written directive in accordance with 10 CFR 35.40, "Written directives". When total source strength is required to be recorded on the written directive, only radium-224 activity needs to be included. The licensee shall retain a copy of the written directive in accordance with 10 CFR 35.2040, "Records of written directives."

7.3 Patient Release

The licensee should develop procedures that describe measures taken to ensure that radiation emissions from each patient or human research subject permits his or her release in accordance with 10 CFR 35.75, "Release of individuals containing unsealed byproduct material or implants containing byproduct material." Licensees should note temporary use affixed by sutures which protrude outside of the body have a potential to become dislodged or allow for gaseous release. Patients should not be released from the licensed facility if it is possible under normal conditions for a seed or seal has a potential to become dislodged and potentially cause public dose limits to be exceeded. If there is a potential for a seed or seal to become dislodged under unique situations, licensees must have preventative measures in place to ensure public dose limits are not exceeded. Licensees must report lost sources in accordance with 10 CFR 20.2201 if a seed becomes dislodged lost and is not recovered or if temporary implants issued to a patient are not returned to the licensee. Additional guidance for release of patients or human research subjects following administration of radioactive materials may be found in Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials."

7.4 Brachytherapy Source Accountability

Licensees shall maintain accountability at all times for all brachytherapy sources in storage or use in accordance with 10 CFR 35.406, “Brachytherapy sources accountability”. In addition, licensees shall maintain records of brachytherapy sources accountability in accordance with 10 CFR 35.2406, “Records of brachytherapy source accountability.” Licensees should document the location which the patient plans to reside and spend a significant period of time (i.e. such as work) as locations of use when used as a temporary implant on an outpatient basis. Licensees should also have patient contact information and provide the patient with instructions on actions to take if source is dislodged during treatment.

8. Notes to Regulators

8.1 Inspection Frequency

Licenses authorizing Alpha DaRT should be inspected every two years. Per Enclosure 1 to Inspection Manual Chapter 2800, licenses authorizing emerging technology under 10 CFR 35.1000 are assigned a Priority 2 inspection code.

8.2 Program Code

The NRC regions should use program code 02240.

9. Paperwork Reduction Act Statement

This Licensing Guidance provides voluntary guidance for implementing the mandatory information collections in 10 CFR Parts 30 and 35 that are subject to the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 et. seq.). These information collection were approved by the Office of Management and Budget (OMB), approval numbers 3150-0017 and 3150-0010. Send comments regarding this information collection to the Information Services Branch (T6-A10M), U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001, or by e-mail to Infocollects.Resource@nrc.gov, and to the OMB reviewer at: OMB Office of Information and Regulatory Affairs (3150-0017, 3150-0010), Attn: Desk Officer for the Nuclear Regulatory Commission, 725 17th Street, NW Washington, DC 20503;
e-mail: oira_submission@omb.eop.gov.

10. Public Protection Notification

The NRC may not conduct or sponsor, and a person is not required to respond to, a collection of information unless the document requesting or requiring the collection displays a currently valid OMB control number.

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United States Nuclear Regulatory Commission
Protecting People and the Environment

Comments on Licensing Guidance for CivaDerm™

Megan Shober

Advisory Committee on the Medical Uses of Isotopes

December 15, 2021

Subcommittee Members

- Vasken Dilsizian, M.D.
- Hossein Jadvar, M.D., Ph.D.
- Josh Mailman
- Melissa Martin
- Megan Shober (Chair)
- Consultant to Subcommittee: Michael Sheetz
- NRC Staff Resource: Katherine Tapp, Ph.D.

Charge

- Review the draft CivaDerm™ licensing guidance with regard to patient release.

Background

- Sealed palladium-103 sources
- Temporary brachytherapy
- Primary intended use—superficial application

- NRC determined CivaDerm™ will be licensed under 10 CFR 35.400 (Manual Brachytherapy)

Questions

- What is the potential for the sources to become dislodged from the patient?
- Does the increased risk of dislodgement warrant additional patient release considerations?

Recommendations

- The Subcommittee agrees that CivaDerm™ should be licensed under 10 CFR 35.400 as it does not present any unique radiation safety issues not already covered by Part 35.
- The Subcommittee recommends developing shorter guidance, focusing on the consequences of loose or dislodged sources.

Recommendations

- The Subcommittee believes it is highly unlikely for public dose limits to be exceeded in the case of a dislodged palladium-103 source.
  - Low-energy gamma (mean energy 21 keV)
  - Public dose limits are based on effective dose equivalent

Recommendations

- The Subcommittee recognizes that other temporary brachytherapy sources (i.e., eye plaques) have similar risks of becoming loose or dislodged.
- The Subcommittee made a number of editorial recommendations to shorten the draft document.

Questions?

Abbreviations

- keV: kiloelectron volts

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

Subcommittee Review and Comments on

Draft Licensing Guidance for Superficial Manual Brachytherapy CivaDerm Device

Draft Report
Submitted: December 1, 2021

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

In October 2021, the ACMUI Chairman, Dr. Darlene Metter, charged the Regulatory Guide 8.39 Subcommittee to review the draft CivaDerm™ licensing guidance with regard to patient release.

Background

The CivaTech Oncology CivaDerm™ manual brachytherapy device (CivaDerm) contains sealed palladium-103 seeds and is FDA-approved for use as an interoperative or superficial temporary brachytherapy source to treat skin cancer or other lesions. The primary intended use is superficial application.

Following evaluation, NRC staff determined the use of CivaDerm will be licensed under 10 CFR 35.400, "Manual Brachytherapy" because radiation protection concerns for this device are adequately covered under existing regulations in 10 CFR 35, Subpart F. However, NRC Staff determined additional guidance is needed regarding patient release as sources have the potential to become dislodged. NRC staff have added a relevant section in draft Regulatory Guide 8.39 (Section 6, "Material Separated from the Patient"); however, as the Regulatory Guide will take time to finalize and CivaDerm is already approved by the FDA for use, NRC decided to prepare separate guidance for CivaDerm at this time.

General Comments:

1. The Subcommittee agrees that CivaDerm should be licensed under 10 CFR 35.400 as it does not present any unique radiation safety issues not already covered by Part 35.

2. The subcommittee strongly disagreed with newly proposed Regulatory Guide 8.39, Section 6 "Material Separated from the Patient", that stated the dose limits in 10 CFR Part 20 apply to exposure from radioactive material separated from a released patient, with the exception

of temporary implants. While the CivaDerm device may have a higher potential for the source(s) to become dislodged from a patient due to its superficial application than with previous manual brachytherapy devices, the potential is not high enough to warrant specific consideration for patient release in Regulatory Guide 8.39. Other temporary implants such as eye plaques also have the potential for becoming dislodged or lost. Regulations and licensing guidance already exist that require licensees to develop, implement, and maintain written procedures to provide high confidence that each administration is in accordance with the written directive.

3. Since NRC determined that CivaDerm may be licensed under 10 CFR 35, Subpart F, the Subcommittee recommends developing shorter guidance, more consistent with past examples[1]. The guidance should focus on the specific radiation safety challenge, rather than providing comprehensive considerations for use.
4. The Subcommittee notes that it would be highly unlikely for a member of the public to exceed the public dose limits in 10 CFR 20.1301 due to exposure from a palladium-103 source no longer affixed to a released patient. Although Table 1, Column 2 in draft Regulatory Guide 8.39 indicates that an implant containing 2.1 mCi of Pd-103 can lead to a 100 mrem total effective dose equivalent to a bystander, this assumes an occupancy factor of 1 at a distance of 1 meter until the source physically decays away. With a 17-day half-life, a bystander would need to be continuously near the Pd-103 source for over 3 months. This is unrealistic. Also, the low energy photons from Pd-103 do not result in a whole body effective dose equivalent, based on the exposure rate constant as do higher energy photon emitters, due to tissue shielding of the exposed individual[2].

Specific Comments:

1. Background section, 1st paragraph: the guidance should also acknowledge that CivaDerm may be used intraoperatively.

2. Background section, 2nd paragraph: Remove sentence, "In accordance with 10 CFR 35.400, the Pd-103 sources must be listed on a Sealed Source and Device Registry (SSDR) for manual brachytherapy and used in accordance with the radiation safety conditions and limitations described in that SSDR or in research under an active Investigational Device Exemption as described in 10 CFR 35.400(b)."

3. Background section, 3rd paragraph: Remove sentence, "The manufacturer states the Civaderm sources can be affixed to a patient's skin by a variety of means, such as staples, glue, tape, sutures, or cast."

4. Procedures for Administration section:
    a. Remove sentence, "If a Civaderm source becomes loose or dislodged, it is likely the administration would not go in accordance with the written directive and result in a medical event as defined in 10 CFR 35.3045, "Reports and notification of a medical event." This is a negative, what if, worst case scenario that is not appropriate for an introductory sentence.

[1] Licensing of Lutetium-177, June 1, 2018. ML18136A824.
[2] Boyce DE and Sheetz, MA, "Patient Release Criteria for Low Dose Rate Brachytherapy Implants", Health Physics (104(4):413-418), 2013

b. Remove phrase, “to ensure high confidence the procedure will be in accordance with the written directive. In addition, licensees must have procedures to determine if a medical event has occurred in accordance with 10 CFR 35.41.” It is not necessary to describe the regulations.
c. Remove sentence, “If the NRC becomes aware of future developments related to the production, distribution, or medical use of the Civaderm that may negatively impact radiation safety, the NRC staff will revisit this licensing decision for any additional actions.”

5. Patient Release Considerations section:
    a. First paragraph, remove “unsealed byproduct material or.” This phrase is not relevant for CivaDerm use.
    b. Remove sentence, “As members of the public could be exposed to the hot side of the source, it is possible that public dose limits could be exceeded if the source becomes loose. Therefore, licensees must ensure that the Civaderm sources are affixed to the patient so that they are highly unlikely to become loose or dislodged.”
    c. Remove sentences, “As described in 10 CFR 20.1003, public dose limits in 10 CFR Part 20 do not apply to exposure to individuals released under 10 CFR 35.75. However, public dose limits would apply if the source became dislodged or separated from the patient, as Part 20 does not exclude exposure from sources which are no longer affixed to a patient.”

6. Source accountability section:
    a. First paragraph, remove last sentence. The Subcommittee believes that licensees should only be held accountable for locations of use prior to patient release.
    b. Change the second paragraph to read, in its entirety: “If a licensee is unable to retrieve the source from the patient following treatment for whatever reason such as the source fell off or the patient does not return, the source would be considered lost or missing and would need to be reported in accordance with 10 CFR 20.2201 “Reports of theft of loss of licensed material.” It is highly unlikely that a Pd-103 brachytherapy implant would exceed the activity threshold (100 mCi) requiring immediate reporting; however, 30-day notification is required for aggregated activities exceeding 1 mCi which have not been found.”

Respectfully submitted on December 1, 2021,

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

UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

DRAFT LICENSING GUIDANCE FOR SUPERFICIAL MANUAL BRACHYTHERAPY CIVADERM DEVICE

Purpose: To provide the Advisory Committee of Medical Uses of Isotopes an opportunity to comment on the additional licensing guidance for a new manual brachytherapy device known as Civaderm.

Background: On September 20, 2019, CivaTech Oncology Inc. received 510(k) clearance for Civaderm from the U.S. Food and Drug Administration for use as a superficial temporary brachytherapy source. Civaderm is a sealed palladium-103 (Pd-103) planar brachytherapy source inside a polymer shell. The source has both a hot and cold side. The cold side is made utilizing a thick gold layer placed inside the polymer shell and serves as a radio-opaque shell. Due to the proposed use of superficial application of a brachytherapy source, the U.S. Nuclear Regulatory Commission (NRC) staff received questions and carefully reviewed the safety aspects of the medical use of the Civaderm to determine if it should be licensed under Title 10 of the *Code of Federal Regulations* (10 CFR) Part 35, Subpart F, "Manual Brachytherapy" or 10 CFR Part 35, Subpart K, "Other Medical uses of Byproduct Material or Radiation From Byproduct Material."

Following its evaluation, the NRC staff recommended that Civaderm be licensed under 10 CFR 35, Subpart F, "Manual Brachytherapy" to the NRC/Organization of Agreement States (OAS) Standing Committee of Emerging Medical Technologies. The staff made this recommendation as it found the use of Civaderm is addressed in regulations contained in 10 CFR 35, Subpart F and has radiation safety concerns similar to other temporary brachytherapy devices used in manual brachytherapy as shown in the attached table. The standing committee agreed with the staff's recommendation and determined Civaderm should be licensed under 10 CFR 35.400. In accordance with 10 CFR 35.400, the Pd-103 sources must be listed on a Sealed Source and Device Registry (SSDR) for manual brachytherapy and used in accordance with the radiation safety conditions and limitations described in that SSDR or in research under an active Investigational Device Exemption as described in 10 CFR 35.400(b).

As Civaderm will be licensed under Subpart F, NUREG-1556, Volume 9, "Consolidated Guidance About Materials Licenses: Program-Specific Guidance About Medical Use Licenses," provides the necessary guidance for licensing. However, the Standing Committee recommended NRC staff provide additional guidance for patient release considerations as Civaderm is affixed superficially. The manufacturer states the Civaderm sources can be affixed to a patient's skin by a variety of means, such as staples, glue, tape, sutures, or cast. As application is superficial, there is a higher potential for the source to become dislodged from a patient than with previous brachytherapy therapies. The NRC staff identified several focus areas with regards to the licensing and oversight of Civaderm sources and has drafted additional guidance to address potential concerns and ensure controls in these key areas. The draft

guidance for your review and comment is provided below. Once finalized, we will provide this guidance to the NRC regions and the Agreement States.

Draft Licensing Guidance

Procedures for Administration

If a Civaderm source becomes loose or dislodged, it is likely the administration would not go in accordance with the written directive and result in a medical event as defined in 10 CFR 35.3045, "Reports and notification of a medical event." In accordance with 10 CFR 35.41, "Procedures for administration requiring a written directive", licensees must develop, implement, and maintain written procedures to provide high confidence that each administration is in accordance with the written directive. This written procedure must contain necessary affixation processes to ensure the source will not become loose or dislodged from the patient under normal conditions to ensure high confidence the procedure will be in accordance with the written directive. In addition, licensees must have written procedures to determine if a medical event has occurred in accordance with 10 CFR 35.41. If a patient is released in accordance with 10 CFR 35.75 while treatment is ongoing, these procedures need to include how a licensee will determine if the source moved or became dislodged to determine if a medical event occurred. If the NRC becomes aware of future developments related to the production, distribution, or medical use of the Civaderm that may negatively impact radiation safety, the NRC staff will revisit this licensing decision for any additional actions.

Patient Release Considerations

Regulations in 10 CFR 35.75 permit licensees to authorize the release of any individual from its control who has been administered unsealed byproduct material or implants containing byproduct material if the total effective dose equivalent (TEDE) to any other individual from exposure to the released individual is not likely to exceed 5 millisieverts (mSv) (0.5 rem). As members of the public could be exposed to the hot side of the source, it is possible that public dose limits could be exceeded if the source becomes loose. Therefore, licensees must ensure that the Civaderm sources are affixed to the patient so that they are highly unlikely to become loose or dislodged. Patients must not be released from the licensed facility if it is possible that the Civaderm sources could become loose or dislodged from the patient under normal conditions.

As described in 10 CFR 20.1003, public dose limits[1] in 10 CFR Part 20 do not apply to exposure to individuals released under 10 CFR 35.75. However, public dose limits would apply if the source becomes dislodged or separated from the patient, as Part 20 does not exclude exposure from sources which are no longer affixed to a patient. If there is a potential for a source to become dislodged under unique situations, licensees must have preventative measures in place to ensure these public dose limits are not exceeded. Preventative measures include providing licensees with a shielded container to place the source if it becomes dislodged. In addition, licensees should provide patients emergency contact information with 24-hour a day coverage and instructions to contact the licensee immediately if a source becomes loose or after the source is secured if it becomes dislodged. If a licensee discovers a member of the public

1 Public dose limits in Part 20 are provided in 10 CFR 20.1301, "Dose limits for individual members of the public" and are 0.1 rem in a year and 0.002 mrem in any one hour.

exceeds the public dose limits in 10 CFR 20.1301 due to exposure from a source no longer affixed to a released patient, licensees must report the event in accordance with 10 CFR 20.2203, “Reports of exposures, radiation levels, and concentrations of radioactive material exceeding the constraints or limits.”

Source Accountability

Licensees must maintain accountability at all times for Civaderm brachytherapy sources in storage or use in accordance with 10 CFR 35.406, “Brachytherapy sources accountability”. In addition, licensees must also maintain records of Civaderm source accountability, in accordance with 10 CFR 35.2406, “Records of brachytherapy source accountability.” Specifically, the records of source accountability for temporary implants should include the location of use. For Civaderm sources used on an outpatient basis, locations of use should include the patient’s residence or locations where the patient will spend a significant period of time (i.e., work place).

If a licensee is unable to retrieve the source from the patient following treatment for whatever reason such as the source fell off or the patient does not return, the source would be considered lost or missing. Regulations in 10 CFR 20.2201, “Reports of theft or loss of licensed material,” require a licensee report any lost, stolen, or missing source. For Pd-103, if the activity of the aggregated activity of the source is over 100 mCi, the licensee would need to make an immediate telephone report accordance with 10 CFR 20.2201(a)(1)(i). If the aggregated activity is over 10 mCi, the licensee would need to make a 30 day telephone report in accordance with 10 CFR 20.2201(a)(1)(ii). The licensee shall also provide a written report within 30 days of making the telephone report, in accordance with 10 CFR 20.2201(b). The written report shall contain a description of the licensed material involved, including kind, quantity, and chemical and physical form; a description of the circumstances under which the loss or theft occurred; a statement of disposition, or probable disposition, of the licensed material involved; exposures of individuals to radiation, circumstances under which the exposures occurred, and the possible total effective dose equivalent to persons in unrestricted areas; actions that have been taken, or will be taken, to recover the material; and procedures or measures that have been, or will be, adopted to ensure against a recurrence of the loss or theft of licensed material.

Discussion: We appreciate your review and comments of this draft licensing guidance. The draft licensing guidance is also being transmitted to the Organization of Agreement States and the NRC regions for review and comment at the same time. Following resolution of comments, the NRC staff intends to issue this licensing guidance on the NRC’s medical toolkit website as well as send them to the Agreement States and regions. Note comments of an editorial nature will be considered; however, the draft text may undergo additional technical editing and formatting by the NRC prior to publication.

U.S.NRC
United States Nuclear Regulatory Commission
Protecting People and the Environment

Regulatory Guide 8.39, Revision 2 Subcommittee Draft Report

Megan Shober

Advisory Committee on the Medical Uses of Isotopes

December 15, 2021

Subcommittee Members

- Vasken Dilsizian, M.D.
- Hossein Jadvar, M.D., Ph.D.
- Josh Mailman
- Melissa Martin
- Megan Shober (Chair)

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

Subcommittee Charge

To review draft proposed revisions to Regulatory Guide 8.39, “Release of Patients Administered Radioactive Materials” and provide feedback and recommendations (RG 8.39).

Background

- Initial RG 8.39 issued in 1997 following rulemaking change on patient release.
- NRC conducted extensive evaluation to determine whether significant regulatory changes to the patient release program are warranted.
- Phase 1 revision, completed in April 2020, updated the patient release guidance.
- Draft Phase 2 revision updates the dosimetric equations and methodologies used to calculate dose to members of the public from the released patient.

General Comments

- Draft Phase 2 Revision also made changes to the patient instructions; therefore, this content area will again be included in the subcommittee review.
- Important for content of guidance to be clear and easy to understand as it will also be viewed by patients and general public.

Recommendations

- Section 4.2 “Content of Instructions” should be reordered to the original sequence
  - Important to emphasize upfront the major source of radiation dose to other individuals will be from external exposure from the patient
  - The most important precautions to take are measures to reduce or avoid external radiation exposure from the patient, especially in the early time period after administration of the radionuclide therapy.
  - Measures to limit the transfer of radioactive contamination to others should not overshadow or distract from the external precautions, nor cause patient anxiety.

Recommendations

- Activity and dose rate values in Tables 1 and 2 should be calculated with an occupancy factor of 0.25 at 1 meter
  - Occupancy factor of 1.0 is unrealistic and cannot be justified for routine application
  - Will result in increased work for licensees to perform patient specific dose calculations and provide patient instructions at activity levels much lower than previously required
  - Draft RG 8.39 is not consistent with record keeping requirement in 10 CFR 35.2075(a)

Recommendations

- Sections 1.3 and 3.3 “Release of a Patient After a Hold Time” should be removed.
  - Holding a patient after radiopharmaceutical administration to allow for decay or biological elimination is not practical.
  - Licensees will use an effective half-life for patient-specific dose calculation or measured exposure rate for release of patient.

Recommendations

- Patient-Specific Modifying Factors and Methods (Appendix B) and Example Calculations (Appendix C) are overly complex and need to be simplified.
  - Determining the amount of time a bystander spends in close contact with the patient for “travel”, “instruction”, and “afterward” time periods requires an unrealistic level of knowledge of extended patient behavior.
  - The Attenuation and Geometric Modifying Factors should be eliminated.
  - Consideration should be given to simplifying the occupancy factors to single values for various patient/bystander conditions.

Recommendations

- Section 6 “Material Separated from the Patient” should be deleted.
  - Subcommittee disagrees with position that dose limits in 10 CFR Part 20 apply to exposure from radioactive material separated from a released patient (except for temporary implants).
  - Licensee cannot practically control or predict if an event occurred where radioactive material separated from a patient caused an exposure to a bystander.

Recommendations

- Section 4.3 “Death of a Patient Following Radiopharmaceutical Administration or Implants”
  - Should note that analysis for dose rates exceeding 0.02 mSv/h or total doses in excess of 1 mSv used very conservative assumptions.
  - Recommend analysis be performed of potential exposures from cremation of a body containing radioactive material.

Specific Comments

- Subcommittee report also provided additional edits and directed changes to make content clearer and easier to understand.

Questions?

Abbreviations

- mSv: milliSievert
- RG: Regulatory Guide

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

Subcommittee Review and Comments on

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

Draft Report
Submitted: December 1, 2021

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 methodolgy 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 on December 1, 2021,

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

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: _____

U.S. NUCLEAR REGULATORY COMMISSION

DRAFT REGULATORY GUIDE DG-8061

Proposed Revision 2 to Regulatory Guide 8.39

Issue Date: Month 2021
Technical Lead: Vered Shaffer

RELEASE OF PATIENTS ADMINISTERED RADIOACTIVE MATERIAL

A. INTRODUCTION

Purpose

This regulatory guide (RG) provides methods that are acceptable to the U.S. Nuclear Regulatory Commission (NRC) staff for release of patients after a medical procedure involving the administration of unsealed byproduct material, such as radiopharmaceuticals, or implants that contain radioactive material. The RG provides tables of an activity threshold and dose rate that may be used by licensees for the release of the patients and meeting NRC regulatory requirements.

This RG also provides licensees with a methodology to modify the threshold and dose rate values on a patient-specific basis. In addition, the RG provides licensees with instructions for patients before and after they are administered radioactive material, as well as requirements for recordkeeping.

Applicability

This RG applies to all NRC medical use licensees subject to Title 10 of the *Code of Federal Regulations* (10 CFR) Part 35, "Medical Use of Byproduct Material," Section 35.75, "Release of Individuals Containing Unsealed Byproduct Material or Implants Containing Byproduct Material" (Ref. 1).

Applicable Regulations

- 10 CFR Part 35 provides requirements and provisions for the radiation safety of workers, the general public, patients, and human research subjects.
    - 10 CFR 35.75(a) permits the licensee to authorize the release of any individual from its control who has been administered unsealed byproduct material or implants containing byproduct material if the total effective dose equivalent (TEDE) to any other individual from exposure to the released individual is not likely to exceed 5 millisieverts (mSv) (0.5 rem).
    - 10 CFR 35.75(b) requires the licensee to provide the released individual or the individual's parent or guardian with instructions, including written instructions, on actions recommended to maintain doses to other individuals as low as is reasonably achievable (ALARA) if the TEDE to any other individual is likely to exceed 1 mSv (0.1 rem). If the dose to a breastfeeding infant or child could exceed 1 mSv (0.1 rem) without the patient's interruption of breastfeeding, the instructions shall also include (1) guidance on the interruption or discontinuation of breastfeeding and (2) information on the potential consequences of failure to follow the guidance.

- 10 CFR 35.75(c) and 35.2075(a) require the licensee to maintain a record of the basis for authorizing the release of an individual for 3 years after the date of release if the TEDE to any other individual from exposure to the released individual is calculated by using the retained activity rather than the activity administered, using an occupancy factor less than 0.25 at 1 meter, using the biological or effective half-life, or considering the shielding by tissue.

- 10 CFR 35.75(d) and 35.2075(b) require the licensee to maintain a record of instructions provided to a breastfeeding female for 3 years after the date of release if the TEDE to a nursing infant or child is likely to exceed 5 mSv (0.5 rem) without breastfeeding interruption.

Related Guidance

- Current version of NUREG-1556, "Consolidated Guidance about Materials Licenses: Program-Specific Guidance about Medical Use Licenses," Volume 9 (Ref. 2).

Purpose of Regulatory Guides

The NRC issues RGs to describe to the public methods that the staff considers acceptable for use in implementing specific parts of the agency's regulations, to explain techniques that the staff uses in evaluating specific problems or postulated events, and to provide guidance to licensees. Regulatory guides are not substitutes for regulations, and compliance with them is not required. Methods and solutions that differ from those set forth in RGs will be deemed acceptable if they provide a basis for the findings required for the issuance or continuance of a permit or license by the Commission.

Paperwork Reduction Act

This RG provides voluntary guidance for implementing the mandatory information collections in 10 CFR Part 35 that is subject to the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 et. seq.). These information collections were approved by the Office of Management and Budget (OMB), approval number 3150-0010. Send comments regarding this information collection to the FOIA, Library, and Information Collections Branch (T6-A10M), U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001, or by e-mail to Infocollects.Resource@nrc.gov, and to the OMB reviewer at: OMB Office of Information and Regulatory Affairs (3150-0010), Attn: Desk Officer for the Nuclear Regulatory Commission, 725 17th Street, NW Washington, DC 20503; e-mail: oira_submission@omb.eop.gov.

Public Protection Notification

The NRC may not conduct or sponsor, and a person is not required to respond to, a collection of information unless the document requesting or requiring the collection displays a currently valid OMB control number.

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B. DISCUSSION

Reason for Revision

This revision of RG 8.39 (Revision 2) provides updated guidance to calculate basic release thresholds for patient release after they have been administered radioactive material. In this revision, threshold calculations assume unity for the occupancy factor in threshold calculations when patient specific information is not known to avoid underestimating exposure when patients have close contact with individuals, referred to as bystanders. Updated thresholds for administered activity and measured dose-rates are tabulated for individual radionuclides. Updated activity thresholds for radiopharmaceuticals are also presented for patients who may continue breastfeeding an infant or child after administration, and breastfeeding interruption times are recommended for example administered activities.

This revision also provides an acceptable methodology for patient release when patient-specific information is considered. This methodology includes factors for biokinetics, occupancy, geometry, and attenuation based on patient-specific information. Additionally, the calculational methodology in this RG provides flexibility to accommodate new radiopharmaceuticals that could be used for diagnostic or therapeutic purposes. Therefore, revision 2 incorporates current scientific knowledge that 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.

Background

Title 10 of the *Code of Federal Regulations* (10 CFR) 35.75, "Release of individuals containing unsealed byproduct material or implants containing byproduct material," was revised in the 1979 rule often referred to as the "Patient Release Rule." It was revised because the 1991 revision of 10 CFR Part 20 revised the dose limits for members of the general public in 10 CFR 20.1301, but did not clarify how the new public dose limit was related to the release of patients. NRC determined that while doses should be maintained ALARA, the new public dose limit did not apply to radiation exposure from a patient and that a dose limit of 5 mSv (0.5 rem) provides adequate protection. The "new" 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).

The Commission directed the NRC staff in Staff Requirements Memorandum-COMAMM-14-0001/COMWDM-14-0001, "Background and Proposed Direction to NRC Staff to Verify Assumptions Made Concerning Patient Release Guidance," to "Revise Regulatory Guide 8.39, and subsequently NUREG-1556, Volume 9, to specify guidelines for patient information and instructional guidance." NRC staff responded to Staff Requirements Memorandum-COMAMM-14-0001/COMWDM-14-0001in SECY-18-0015, "Staff Evaluation of the U.S. Nuclear Regulatory Commission's Program Regulating Patient Release after Radioisotope Therapy." In SECY-18-0015, the NRC staff concluded that the current patient release regulations are protective for 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. NRC staff updated NUREG-1556, Volume 9, Rev. 3, to refer to this RG to remove duplicative patient release guidance and avoid inconsistencies.

Following up on the determination for a comprehensive update to the NRC's patient release guidance, the staff has developed Revision 2 to RG 8.39 to provide a methodology for licensees to determine when it is appropriate to release a patient from their control and when instructions or records are required. Per 10 CFR 35.75, licensees can authorize release of an individual, referred to as the patient in this RG, from its control if the TEDE to any other individual from exposure to the released individual is not likely to exceed 5 mSv. To ensure compliance with this regulation, licensees must ensure dose to all other individuals other than the patient is likely to be below this limit based on the amount of activity retained in the patient at the time of release and expected patient interactions with others. Individuals being exposed to the patient are referred to as bystanders in this guidance. Bystanders are all members of the public, including family members and caregivers. This guidance provides administered activity and measured dose rate thresholds to demonstrate compliance for commonly used and emerging radiopharmaceuticals. Seldom used radionuclides listed in the original RG are retained in this revision to address the potential for their return to usage in future radiopharmaceuticals. This guidance offers calculational methodologies to accommodate threshold modifications for patient-specific exposure situations. This is accomplished with patient-specific modifying factors for biokinetics, occupancy, geometry, and attenuation based on patient-specific information. In addition, this guidance provides activity thresholds for radiopharmaceuticals for patients who may continue breastfeeding an infant or child after administration, and breastfeeding interruption times recommended for example medical dosages.

Implementing fundamentals outlined in the National Council on Radiation Protection and Measurements (NCRP) Report No. 155, "Management of Radionuclide Therapy Patients" (Ref. 3), and NCRP Report No. 37, "Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides" (Ref. 4), this RG is structured so that licensees can satisfy requirements for patient release, issuing instructions, or maintaining records. For a majority of clinical procedures, a simple comparison of the administered activity to conservative basic thresholds is sufficient to reach patient release conclusions without invoking the patient-specific modifying factors. Licensees are guided to consider the patient-specific modifying factors when the administration activity is above the basic threshold values. Determining these factors yields modified, patient-specific thresholds that are more realistic for a particular patient. If calculations show radiation dose could exceed the limits, an administrative hold of the patient in the medical facility may be appropriate, and this guidance provides a methodology to calculate the hold time. NUREG-1556 Vol. 9 provides guidance on controls needed for patients who cannot be released in accordance with 10 CFR 35.75. Instructions for the patient, unexpected death of the patient, maintaining records, and radioactive material separated from the patient are also addressed.

Consideration of International Standards

The International Atomic Energy Agency (IAEA) works with member states and other partners to promote the safe, secure, and peaceful use of nuclear technologies. The IAEA develops Safety Requirements and Safety Guides for protecting people and the environment from harmful effects of ionizing radiation. This system of safety fundamentals, safety requirements, safety guides, and other relevant reports, reflects an international perspective on what constitutes a high level of safety. The NRC considered IAEA Safety Requirements and Safety Guides pursuant to the Commission's "International Policy Statement," published in the *Federal Register* on July 10, 2014 (Ref. 5), and Management Directive 6.6, "Regulatory Guides" dated May 2, 2016 (Ref. 6).

The IAEA (Ref. 7) provides guidance for releasing patients after radioactive material administration that is related to the basic safety principles considered in developing this RG. The instructions to patients included in the IAEA report are also similar to the instructions listed in this RG. The IAEA guidance is based on retained activity in the patient such that doses to a bystander would not exceed a few mSv (rem).

IAEA recommends special considerations for patients who are or may become pregnant, patients who are breastfeeding children, as well as patients who unexpectedly die soon after treatment. The NRC notes that the U.S. dose limits in 10 CFR Part 35 differ from many international regulatory requirements.

C. STAFF REGULATORY GUIDANCE

This section describes in detail the methods, approaches, and data that the NRC staff considers acceptable for meeting the requirements of the applicable regulations cited in the introduction.

1. Release Criteria

Fundamental Dose Equation for Patient Release

Radioactive material activities administered to patients qualifying for patient release were calculated with updated parameters that implement fundamentals outlined in the National Council on Radiation Protection and Measurements (NCRP) Report No. 155, "Management of Radionuclide Therapy Patients" (Ref. 3) and NCRP Report No. 37, "Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides" (Ref. 4). Radiological exposure of a bystander to radioactive material in the released patient is estimated in a two-tiered approach.

In the first tier, a basic dose assessment is performed using generic, conservative assumptions.

$$D = 1.44 \cdot T_r \cdot \Delta_{pr} \cdot A_0 \qquad \text{(Equation 1)}$$

where

D	=	External dose equivalent, mSv
1.44	=	Constant for reciprocal of the natural logarithm of 2
T_r	=	Radiological (physical) half-life, h
Δ_{pr}	=	Dose-rate constant for a point source at 1 m, $\frac{\text{mSv}}{\text{GBq h}}$
A_0	=	Activity of the radionuclide administered to the patient, GBq

Equation 1 is used to calculate the administered activity below which patients may be released without patient-specific information. These basic activity thresholds include several general assumptions:

- external dose equivalent to a point in tissue is calculated from the photon emissions (including electron bremsstrahlung) of a point source surrounded by an infinitely thin sphere of tissue;
- dose rate is calculated at a distance of 1 m;
- radionuclide loss from the patient only includes physical decay;
- external dose begins immediately after administration and lasts through infinity, i.e., total decay;
- an occupancy of 100% at 1 meter is assumed; and
- implants are encapsulated in 50 μm of titanium.

As Equation 1 does not account for patient-specific information, these assumptions are meant to be overly conservatism to avoid underestimation of dose in likely situations. Conservative assumptions include assuming full occupancy and not including biological loss. Through the use of these conservative generic assumptions, this basic equation can demonstrate compliance with 10 CFR Part 35 for many lower activity and external dose-rate procedures without detailed patient-specific information. The second tier can be used when increased realism with patient-specific information is necessary to provide a basis for

release and demonstrate compliance with 10 CFR 35.75 (refer to Section 3).

The external dose pathway is considered to be dominant, and internal dose pathways are not included. Dose implications from potential intakes by household members and members of the public have been shown to be small (less than a few percent) relative to external doses (Refs. 7, 8, 9 and 10). When internal dose pathways are negligible, TEDE equals the accumulated external dose equivalent D, and the basic activity threshold Q is calculated by replacing A_0 with Q:

$$Q = \frac{D}{1.44 \cdot T_r \cdot \Delta_{pr}} \quad \text{(Equation 2)}$$

where

Q = Basic activity threshold, GBq
D = TEDE limit, mSv

Licensees are authorized to release the patient when TEDE to the maximally exposed bystander is not likely to exceed 5 mSv. Instructions to minimize dose to the bystander are required when TEDE is likely to exceed 1 mSv (0.1 rem). Basic activity thresholds for dose limits of 5 mSv for patient release and 1 mSv for issuing dose-minimizing instructions are denoted as Q_{rel} and Q_{ins}, respectively. At the standard measurement distance of 1 m, the basic measurement threshold M is closely related to the basic activity threshold Q

$$M = \Delta_{pr} \cdot Q \quad \text{(Equation 3)}$$

where

M = Basic measurement threshold at 1 m, $\frac{\text{mSv}}{\text{h}}$

Denoted by M_{rel} and M_{ins}, basic measurement thresholds are computed from Equation 3 for dose limits of 5 mSv (0.5 rem) for patient release and 1 mSv (0.1 rem) for issuing instructions, respectively. To avoid redundancy, equations in this section avoid the subscript notation. Compliance can be demonstrated by either (i) comparing the administered activity[1] to the basic activity threshold or (ii) comparing the measured dose rate at 1 m at the time of administration[1] to the basic measurement threshold. These thresholds are provided in Tables 1 and 2 in Sections 1.1 and 1.2, respectively. Licensees may use one of the following options discussed in Sections 1.1 – 1.4 to release a patient who has been administered radiopharmaceuticals or implants that contain radioactive material.

Equations 1 – 3 consider external exposure to the patient and do not include internal dose contributions. However, internal doses are important, and licensees must calculate internal dose for infants or children who continue to breastfeed to determine if instructions are needed in accordance with 10 CFR 35.75(b). Breastfeeding is considered in Section 2 of this guide. 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 for patient-specific situations described in Section 6 of this guide.

1.1 Release of Patients Based on the Administered Activity

Licensees can demonstrate compliance with the dose limit in 10 CFR 35.75(a) for releasing

[1] Activity retained in the patient at the time of release, as determined by the licensee, can replace the administered activity in comparisons to the basic activity threshold. The measured dose rate at the time of release can also be compared to the basic measurement threshold. These replacements are permitted because basic thresholds neglect biological clearance (i.e., F_B=1).

patients from licensee control if the administered activity is not greater than the basic activity threshold listed in Column 1 of Table 1. Basic activity thresholds in Column 1 of Table 1 were calculated using Equation 2 and are based on a TEDE to an individual of 5 mSv (0.5 rem) for the previously listed conservative assumptions. The basic activity thresholds do not include the dose from internal intake by household members and members of the public because internal dose from potential bystander intake is expected to be small for most radiopharmaceuticals (less than a few percent) relative to external dose.

When the activity administered, A_0 (GBq), is not greater than Q_{rel} (GBq) in Column 1 of Table 1 $(A_0 \leq Q_{rel})$, release of the patient is authorized and no record is required of the basis for authorizing release of the patient, unless the patient is breastfeeding an infant or child as discussed in Section 2.

Table 1. Basic Activity Thresholds for Radionuclides

RADIONUCLIDE	COLUMN 1 Patient Release Threshold Q_{rel}		COLUMN 2 Instruction Threshold Q_{ins}	
	(GBq)	(mCi)	(GBq)	(mCi)
Ag-111	4.4	120	0.88	24
At-211	17	460	3.3	89
Au-198	0.88	24	0.18	4.9
Bi-213	210	5,700	41	1,100
C-11	68	1,800	14	380
C-14[b]	0.0014	0.038	0.00028	0.0076
Cr-51	1.1	30	0.23	6.2
Cs-131	1.1	30	0.21	5.7
Cs-131 implant[a]	1.1	30	0.23	6.2
Cu-64	9.7	260	1.9	51
Cu-67	3.7	100	0.75	20
Dy-165	320	8,600	65	1,800
Er-169[b]	130	3,500	26	700
F-18	13	350	2.5	68
Ga-67	2.1	57	0.42	11
Ga-68	22	590	4.4	120
Ho-166[b]	26	700	5.2	140
I-123	6.7	180	1.3	35
I-124	0.20	5.4	0.041	1.1
I-125	0.074	2.0	0.015	0.41
I-125 implant[a]	0.084	2.3	0.017	0.46
I-131	0.32	8.6	0.063	1.7
In-111	0.64	17	0.13	3.5
Ir-192	0.015	0.41	0.0030	0.081
Ir-192 implant[a]	0.016	0.43	0.0033	0.089
Lu-177	4.1	110	0.82	22
N-13	140	3800	28	760
O-15	680	18,000	140	3,800
P-32[b]	9.2	250	1.8	49
P-33[b]	64	1,700	13	350
Pd-103	0.27	7.3	0.055	1.5
Pd-103 implant[a]	0.39	11	0.077	2.1
Ra-223	0.27	7.3	0.054	1.5

Rb-82	960	26,000	190	5,100
Re-186	6.2	170	1.2	32
Re-188[b]	16	430	3.1	84
Ru-106[b]	180	4,900	37	1,000
Ru-106[b] implant[a]	200	5,400	550	15,000
Sc-47	3.1	84	0.62	17
Se-75	0.0080	0.22	0.0016	0.043
Sm-153	6.8	180	1.4	38
Sn-117m	0.29	7.8	0.058	1.6
Sr-89[b]	3.3	89	0.66	18
Sr-90[b]	0.055	1.5	0.011	0.30
Tc-99m	30	810	6.1	160
Tl-201	1.2	32	0.23	6.2
Xe-127	0.073	2.0	0.015	0.41
Xe-133	2.1	57	0.42	11
Y-90[b]	34	920	6.8	180
Yb-169	0.094	2.5	0.019	0.51
Zr-89	0.21	5.7	0.042	1.1

a. Implants including eye plaques are assumed to be encapsulated in 50 μm of titanium.
b. Greater than 5% of Δ_{pr} due to bremsstrahlung production.

NOTE: Agreement State licensees should check their State regulations before using these values.

If the activity administered exceeds the activity in Column 1 of Table 1 $(A_0 > Q_{rel})$, the licensee may select one of the following options:

a. Consider releasing the patient according to measured dose rates as described in Section 1.2.

b. Release the patient when the activity retained in the patient has decreased to Q_{rel} (GBq) in Column 1 of Table 1. In this case, 10 CFR 35.75(c) and 35.2075(a)(1) require the licensee to maintain a record of the basis for authorizing the release because it is based on the retained activity instead of on the administered activity.

c. Consider patient-specific modification of the activity threshold as described in Section 3. In this case, 10 CFR 35.75(c) and 35.2075(a) require the licensee to maintain a record of the basis for authorizing the release when it incorporates an occupancy factor less than 0.25 at 1 meter, use of the biological or effective half-life, or includes shielding by tissue.

d. Calculate a hold time as described in Section 1.3. In this case, 10 CFR 35.75(c) and 35.2075(a)(1) require the licensee to maintain a record of the basis for authorizing the release because it is based on the retained activity instead of on the administered activity.

Radionuclide data used in the calculation of the basic thresholds are tabulated in Appendix A. If the licensee administers a radionuclide that is not listed in Table 1, it may demonstrate compliance with the regulation in 10 CFR 35.75 by maintaining a record of the calculation (for NRC inspection) of the release activity that corresponds to the dose limit of 5 mSv (0.5 rem).

Release activities in Column 1 of Table 1 do not consider the dose to a breastfeeding infant or child from the ingestion of radiopharmaceuticals contained in a patient's breast milk. When the patient is breastfeeding an infant or child, the activities in Column 1 of Table 1 do not apply to the infant or child.

More information regarding breastfeeding guidance can be found in Section 2.

1.2 Release of Patients Based on the Measured Dose Rate

Licensees may release patients administered radionuclides in amounts greater than the activities listed in Column 1 of Table 1 ($A_0 > Q_{rel}$) if the measured dose rate at 1 meter from the patient is no greater than the M_{rel} value in Column 1 of Table 2 for that radionuclide.

Table 2. Basic Measurement Thresholds for Radionuclides[d]

RADIONUCLIDE	COLUMN 1 Patient Release Threshold[c] M_{rel}		COLUMN 2 Instruction Threshold[c] M_{ins}	
	(mSv/h)	(mrem/h)	(mSv/h)	(mrem/h)
Ag-111	0.019	1.9	0.0039	0.39
At-211	0.49	49	0.096	9.6
Au-198	0.054	5.4	0.011	1.1
Bi-213	4.6	460	0.90	90
C-11	10	1000	2.1	210
C-14	0.000000070	0.0000070	0.000000014	0.0000014
Cr-51	0.0051	0.51	0.0011	0.11
Cs-131	0.015	1.5	0.0029	0.29
Cs-131 implant[a]	0.014	1.4	0.0030	0.30
Cu-64	0.27	27	0.053	5.3
Cu-67	0.056	5.6	0.011	1.1
Dy-165	1.5	150	0.30	30
Er-169[b]	0.016	1.6	0.0031	0.31
F-18	2.0	200	0.38	38
Ga-67	0.044	4.4	0.0088	0.88
Ga-68	3.1	310	0.62	62
Ho-166	0.13	13	0.026	2.6
I-123	0.26	26	0.051	5.1
I-124	0.034	3.4	0.0070	0.70
I-125	0.0024	0.24	0.00050	0.050
I-125 implant[a]	0.0024	0.24	0.00049	0.049
I-131	0.018	1.8	0.0036	0.36
In-111	0.051	5.1	0.010	1.0
Ir-192	0.0020	0.20	0.00039	0.039
Ir-192 implant[a]	0.0019	0.19	0.00040	0.040
Lu-177	0.022	2.2	0.0043	0.43
N-13	21	2,100	4.2	420
O-15	100	10,000	21	2,100
P-32[b]	0.010	1.0	0.0020	0.20
P-33[b]	0.0057	0.57	0.0012	0.12
Pd-103	0.0084	0.84	0.0017	0.17
Pd-103 implant[a]	0.0086	0.86	0.0017	0.17
Ra-223	0.013	1.3	0.0025	0.25
Rb-82	160	16,000	32	3,200
Re-186	0.039	3.9	0.0076	0.76
Re-188	0.21	21	0.040	4.0

Ru-106	0.00038	0.038	0.000078	0.0078
Ru-106 implant[a]	0.00038	0.038	0.000077	0.0077
Sc-47	0.043	4.3	0.0087	0.87
Se-75	0.0012	0.12	0.00024	0.024
Sm-153	0.075	7.5	0.015	1.5
Sn-117m	0.010	1.0	0.0021	0.21
Sr-89[b]	0.0029	0.29	0.00057	0.057
Sr-90[b]	0.000014	0.0014	0.0000028	0.00028
Tc-99m	0.57	57	0.12	12
Tl-201	0.049	4.9	0.0094	0.94
Xe-127	0.0039	0.39	0.00081	0.081
Xe-133	0.027	2.7	0.0055	0.55
Y-90[b]	0.054	5.4	0.011	1.1
Yb-169	0.0045	0.45	0.00091	0.091
Zr-89	0.044	4.4	0.0088	0.88

a. Implants including eye plaques assumed to be encapsulated in 50 µm of titanium
b. Greater than 5% of Δ_{pr} due to bremsstrahlung production
c. If the release is based on the dose rate at 1 meter in Column 2, the licensee must maintain a record as required by 10 CFR 35.75(c) and 35.2075(a)(4) because the measurement includes shielding by tissue. See Staff Regulatory Guidance 3.1, "Records of Release," for information on records.
d. Values listed in the table are calculated and shown for completeness. Values do not consider detection capabilities.

NOTE: Agreement State licensees should check their State regulations before using these values.

If the measured dose rate at 1 meter is greater than the M_{rel} value, licensees may choose to perform patient-specific release calculations as described in Section 3 or hold the patient for release as described in Section 1.3. Unlike activity thresholds, measured dose rates intrinsically include geometric radionuclide distribution within the patient's body and patient tissue attenuation effects. Measured dose rates at times after administration may also include some amount of biological clearance. Therefore, the regulation 10 CFR 35.75(c) and 35.2075(a) requires licensees to maintain a record of the basis for authorizing release as described in Section 5.

If a licensee administers a radionuclide not listed in Table 1 and chooses to release a patient based on the measured dose rate, the licensee must calculate a dose rate that corresponds to the 5 mSv (0.5 rem) dose limit to determine when a patient can be released per 10 CFR 35.75. Dose-rate constants are preferred over exposure rate constants because dose-rate constants are calculated for dose to tissue rather than exposure to air. For radionuclides not listed, an approach to determine dose-rate constants for new radionuclides is described, with supporting details (Ref. 9) that include a comparison of dose-rate constants to exposure-rate constants published by other researchers (e.g., Refs. 11 and 12).

1.3 Release of a Patient After a Hold Time

When the administered activity or measured dose rate at 1 m exceeds the basic activity or dose rate threshold for release, a licensee may choose to hold a patient until the threshold for release has been satisfied. A conservative administrative hold time can be calculated based on radioactive decay

$$t_{hold} = 1.44\, T_r \ln\left(\frac{A_0}{Q_{rel}}\right) \quad \text{(Equation 4)}$$

where hold times apply only when $A_0 > Q_{rel}$. More information regarding guidance and specific

regulations for in-patients can be found in NUREG-1556, Volume 9, Revision 3. A licensee may also choose to do a patient specific calculation as described in Section 3 to determine if the threshold for release is satisfied after justifying more realistic values of the modifying factors for the patient.

2. Breastfeeding Patients

10 CFR 35.75(b) states that a licensee will provide instruction regarding breastfeeding, including guidance on interruption or discontinuation of breastfeeding, if the TEDE to a nursing infant or child is likely to exceed 1 mSv (0.1 rem) assuming there were no interruption of breastfeeding following the release. To ensure compliance, licensees must determine a patient's breastfeeding status, as appropriate, prior to release if the dose to the infant or child could exceed 1 mSv (0.1 rem).

Breastfeeding activity thresholds were calculated for common radiopharmaceuticals that could lead to 5 mSv (0.5 rem) or 1 mSv (0.1 rem) to a nursing infant or child if there is no interruption in breastfeeding (Ref. 9). The thresholds for 1 mSv are listed in Column 2 of Table 3. If the patient could be breastfeeding an infant or child after release and if the patient were administered a radiopharmaceutical with an activity above the value stated in Column 2 of Table 3, additional breastfeeding instructions must be provided in accordance with 10 CFR 35.75(b). The instructions must include appropriate recommendations on whether and how long to interrupt breastfeeding. The instructions must inform the patient of the consequences of failure to follow the recommendation to interrupt or discontinue breastfeeding. The licensee should explain the consequence in a manner that will help the patient understand that, in some cases, breastfeeding after an administration of certain radionuclides should be avoided. For example, a consequence of procedures involving iodine (I)-131 is that continued breastfeeding could harm the infant's or child's thyroid.

The requirement in 10 CFR 35.2075(b) states that a licensee shall retain a record of instructions provided to the patient if the radiation dose to the infant or child from continued breastfeeding would likely result in a TEDE exceeding 5 mSv (0.5 rem). The breastfeeding activity thresholds that could result in 5 mSv (0.5 rem) to a nursing infant or child are listed in Column 1 of Table 3 and are further described in supporting documentation (Ref. 9). If the administered activity is above this threshold, a record of the instructions provided to the patient shall be maintained for 3 years after patient release.

Table 4 provides the recommended duration of interrupting (or discontinuation) of breastfeeding to minimize the dose to below 5 mSv (0.5 rem) and 1 mSv (0.1 rem) for typical administrations of certain radiopharmaceuticals (Ref. 9). When the biological half-time, T_b (h), of a radiopharmaceutical is known, effective half-life, T_e (h), can be calculated as

$$T_e = \frac{T_r \cdot T_b}{T_r + T_b} \qquad \text{(Equation 5)}$$

When breastmilk is pumped and discarded during interruption, the interruption time, τ (h), equals

$$\tau = 1.44 \cdot T_e \cdot \ln\left(\frac{A_0}{Q_{B|ins}}\right) \qquad \text{(Equation 6)}$$

where

$Q_{B|ins}$ = Breastfeeding activity threshold for instructions shown in Table 3.

For administrations of radiopharmaceuticals not listed in Tables 3 or 4 to a patient who could be breastfeeding, the licensee shall evaluate whether instructions or records (or both) are required. A method for calculating dose to the infant or child is documented separately (Ref. 9). Records of the calculation

shall be maintained and instructions on interrupting breastfeeding are expected if the dose to the nursing child or infant is likely to exceed 5 mSv (0.5 rem) without breastfeeding interruption.

Table 3. Breastfeeding Activity Thresholds Assuming No Breastfeeding Interruption

RADIO-NUCLIDE	PHARMA-CEUTICAL	COLUMN 1 5-mSv Breastfeeding Activity Requiring a Record $Q_{B\|rec}$ (GBq)	(mCi)	COLUMN 2 1-mSv Breastfeeding Activity Threshold for Instructions $Q_{B\|ins}$ (GBq)	(mCi)
C-11	choline	2	60	0.5	10
Cr-51	EDTA	30	800	6	200
F-18	FDG	1	30	0.2	6
Ga-67	citrate	0.08	2	0.02	0.4
Ga-68	octreotate	9	200	2	50
I-123	MIBG	1	40	0.3	8
	OIH	2	40	0.3	8
	NaI[a]	0.002	0.05	0.0004	0.01
I-124	NaI[a]	0.00003	0.0008	0.000006	0.0002
I-125	OIH	0.1	3	0.02	0.6
	NaI[a]	0.00007	0.002	0.00001	0.0004
I-131	OIH	0.08	2	0.02	0.4
	NaI[a]	0.000004	0.0001	0.0000009	0.00002
In-111	octreotate	0.9	30	0.2	5
	WBC	0.08	2	0.02	0.4
Lu-177	octreotate	0.4	10	0.08	2
N-13	Any	10	400	3	70
O-15	water	10	300	2	60
Ra-223	dichloride	0.000002	0.00005	0.0000004	0.00001
Rb-82	chloride	10	300	2	60
Tc-99m	DISIDA	0.2	6	0.05	1
	DTPA	50	1000	10	300
	DTPA aerosol	100	4000	30	700
	glucoheptonate	20	600	5	100
	HAM	0.2	7	0.05	1
	MAA	2	60	0.4	10
	MAG3	40	1000	8	200
	MDP	40	1000	9	200
	MIBI	30	800	6	200
	pertechnetate	0.5	10	0.1	3
	PYP	0.7	20	0.1	4
	RBC in vitro	50	1000	10	300
	RBC in vivo	40	1000	8	200
	sulfur colloid	0.5	10	0.1	3
	WBC	0.8	20	0.2	4
Tl-201	chloride	2	50	0.4	10
Zr-89	panitumumab	0.01	0.3	0.002	0.07

a. $Q_{B|rec}$ and $Q_{B|ins}$ based on thyroid dose equivalent to nursing child or infant after patient release.

NOTE: Agreement State licensees should check their State regulations before using these values.

Table 4. Recommended Breastfeeding Interruption Times for Radiopharmaceutical Administrations

RADIO-NUCLIDE	PHARMA-CEUTICAL	Example Administered Activity (GBq)	(mCi)	Interruption Time [h] for 5 mSv	for 1 mSv
C-11	any	0.925	25	-	-
Cr-51	EDTA	0.00185	0.05	-	-
F-18	FDG	0.74	20	-	3
Ga-67	citrate	0.333	9	120	250
Ga-68	octreotate	0.185	5	-	-
I-123	MIBG	0.37	10	-	4
	OIH	0.074	2	-	-
	NaI*(HYP)	0.185	0.01	78	110
I-124	NaI*(HYP)	0.074	2	620	750
I-125	OIH	0.00037	0.01	-	-
	NaI*(CA)	0.0185†	0.05	1,100	1,400
I-131	OIH	0.011	0.3	-	-
	NaI*(CA)	5.55	150	1,700	1,900
In-111	octreotate	0.185	5	-	-
	WBC	0.037	1	-	50
Lu-177	octreotate	7.8	210	350	540
N-13	any	0.925	25	-	-
O-15	water	1.85	50	-	-
Ra-223	dichloride	0.00385	0.1	1,400	1,700
Rb-82	chloride	1.85	50	-	-
Tc-99m^{+}	DISIDA	0.296	8	1	10
	DTPA	1.11	30	-	-
	DTPA aerosol	0.04	1	-	-
	glucoheptonate	0.74	20	-	-
	HAM	0.296	8	-	8
	MAA	0.151	4	-	-
	MAG3	0.37	10	-	-
	MDP	1.11	30	-	-
	MIBI	1.48	40	-	-
	pertechnetate	0.37	10	-	6
	PYP	0.555	15	-	7
	RBC in vitro	1.11	30	-	-
	RBC in vivo	1.11	30	-	-
	sulfur colloid	0.222	6	-	5
	WBC	0.37	10	-	5
Tl-201	chloride	0.148	4	-	-
Zr-89	panitumumab	0.075	2	140	270

* Interruption time based on most restrictive infant thyroid dose equivalent for mothers with hyperthyroidism (HYP) or thyroid cancer (CA).

† 10% of the activity administered as I-123 (to consider nuclide contamination).

$^{+}$ 24-hour interruption is generally applied to Tc-99m pharmaceuticals.

A dash (-) indicates that no interruption of breastfeeding is required.

3. Patient Specific Dose Calculations

The threshold activity and dose rate values provided in Section 1 were calculated using highly conservative assumptions to demonstrate dose limits in 10 CFR 35.75 following release of a generic patient without knowledge of patient-specific information. Licensees may release patients with larger activities or dose rates than that shown in Tables 1 and 2 by applying patient-specific information to demonstrate that the maximally exposed bystander is not likely to exceed 5 mSv (0.5 rem). Licensees must maintain a record of the basis authorizing patient release in accordance with the criteria in 10 CFR 35.2075(a). 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 (e.g., patient interview, patient image, etc.). Patient instructions must match or be more limiting than patient-specific factors used to release patients to assure that dose limits will not likely be exceeded after release in accordance with 10 CFR 35.75.

Based on the same fundamentals in Equation 1, second-tier assessments include four additional terms with patient specific information. These terms are referred to as modifying factors. When patient-specific details are considered, the basic dose assessment shown in Equation 1 includes four unitless modifying factors

$$D = 1.44 \cdot T_r \cdot \Delta_{pr} \cdot A_0 \cdot F_B \cdot F_O \cdot F_G \cdot F_A \qquad \text{(Equation 7)}$$

where

D	=	External dose equivalent, mSv
1.44	=	Constant for reciprocal of the natural logarithm of 2
T_r	=	Radiological (physical) half-life, h
Δ_{pr}	=	Dose-rate constant for a point source at 1 m, $\frac{\text{mSv}}{\text{GBq h}}$
A_0	=	Activity of the radionuclide administered to the patient, GBq
F_B	=	Biokinetic modifying factor, unitless
F_O	=	Occupancy modifying factor, unitless
F_G	=	Geometry modifying factor, unitless
F_A	=	Attenuation modifying factor, unitless

The external dose pathway is considered to be dominant, and internal dose pathways are not included. Therefore, the external dose equivalent, D, in Equation 7 is also the TEDE.

When basic thresholds are calculated according to Equation 2, the four modifying factors were not shown because they were each assigned a value of unity (1) according to conservative assumptions. Refer to Appendix B (and Ref. 9) for modifying factor definitions and methods to determine patient-specific values. The patient-specific activity threshold is determined by modifying the basic activity threshold as follows

$$Q' = \frac{Q}{F_B \cdot F_O \cdot F_G \cdot F_A} \qquad \text{(Equation 8)}$$

where

Q	=	Basic activity threshold, GBq
Q'	=	Patient-specific activity threshold at administration, GBq

Patient-specific activity thresholds for dose limits of 5 mSv (0.5 rem) for patient release and 1 mSv (0.1 rem) for issuing dose-minimizing instructions are denoted as Q'_{rel} and Q'_{ins}, respectively.

Patient-specific information is needed when a licensee utilizes modifying factors to demonstrate that release will not result in a dose in excess of limits contained in 10 CFR 35.75. Patient-specific information should be obtained by the licensee through discussions with the patient.

3.1 Release of Patients Based on the Administered Activity

To demonstrate compliance, licensees may calculate patient-specific thresholds on a case-by-case basis. Licensees can justify the release of patients with activities greater than the basic threshold listed in Column 1 of Table 1 by accounting for patient biokinetics, bystander occupancy, exposure geometry, and patient attenuation factors. When licensees calculate a patient-specific activity threshold, Q'_{rel} (GBq), according to Equation 8, the patient can be released when the administered activity, A_0 (GBq), does not exceed Q'_{rel}.

When the administered activity exceeds the patient-specific activity threshold ($A_0 > Q'_{rel}$), licensees can consider releasing patients based on the measured dose rate according to Section 3.2 or based on a calculated hold time in Section 3.3.

3.2 Release of Patients Based on the Measured Dose Rate

Licensees may decide to release patients based on measuring the external dose rate at 1 m from the patient. As biokinetics, attenuation, and geometry already influence survey measurements, these factors must not be used to modify the measurement threshold because doing so would underestimate dose. Measured dose rates are independent of occupancy; therefore, modification of the measurement threshold is only permitted by considering the occupancy factor for the maximally exposed bystander.

When the measured dose rate at 1 m from a patient exceeds the basic measurement threshold for patient release shown in Column 1 of Table 2, the licensee can either:

a. Calculate a patient-specific measurement threshold as $\frac{M_{rel}}{F_O}$ by considering occupancy. Refer to Appendix B for calculating occupancy factor values.

b. Wait for the measured dose rate to decrease below the basic measurement threshold without considering occupancy.

c. Calculate a hold time described in Section 3.3.

3.3 Release of a Patient After a Hold Time

When the administered activity exceeds the patient-specific activity threshold for release, an administrative hold time, t_{hold}, shall be calculated based on administered activity as well as radioactive decay and biological removal via patient retention as follows

$$t_{hold} = \frac{t_n}{\ln(R_n)} \ln\left(\frac{Q'_{rel}}{A_0}\right) \quad \text{(Equation 9)}$$

where

t_n = Time after administration corresponding to the patient's radionuclide retention, h
R_n = Retention fraction of radionuclide in the patient at time t_n, unitless

Hold times are only needed when $A_0 > Q'_{rel}$. When radiopharmaceutical retention data are

available for the patient (e.g., retention curve over time), the hold time can be assigned to the time when the patient's retention fraction equals $\frac{Q'_{rel}}{A_0}$. Refer to Appendix B, Section B.3 to determine R_n and t_n, including how F_B is calculated from these parameters. To confirm retention data, a dose rate from the patient should be measured prior to release from hold. The ratio of measured dose rate to the basic measurement threshold should be generally consistent with $\frac{A_0}{Q'_{rel}}$ (Section 3.2).

4. Instructions

4.1 Activities and Dose Rates That Require Instructions

In accordance with 10 CFR 35.75(b), licensees must give instructions to released patients, including written instructions, on how to maintain doses to other individuals ALARA if the TEDE to any other individual is likely to exceed 1 mSv (0.1 rem). Licensees may always choose to provide instructions to keep radiation dose ALARA even if the dose limit is not likely to be exceeded. Licensees may use Column 2 of Table 1 to determine the administered activity or Column 2 of Table 2 for the corresponding dose rates at 1 m above which instructions must be given.

To determine if dose-minimizing instructions are required based on activity thresholds:

a. Compare the administered radionuclide activity, A_0 (GBq), to the basic activity threshold for issuing instructions shown in Column 2 of Table 1, Q_{ins} (GBq).

b. If the administered radionuclide activity does not exceed the basic activity threshold for instructions ($A_0 \leq Q_{ins}$), the patient can be released without dose-minimizing instructions.

c. When patient-specific calculations are performed as described in Section 3, the administered radionuclide activity can be compared to the patient-specific activity threshold for issuing instructions, Q'_{ins} (GBq). Appendix B provides details on determining the modifying factors.

d. If the administered radionuclide activity does not exceed the patient-specific activity threshold for issuing instructions ($A_0 \leq Q'_{ins}$), the patient can be released without dose-minimizing instructions.

e. Dose-minimizing instructions are required for cases when neither criterion b nor d are met. In addition, instructions must be issued if the basis for the occupancy modifying factor relies on restrictions to patient behavior regarding time spent near bystanders.

The decision process for providing instructions based on activity thresholds is summarized in Figure 1.

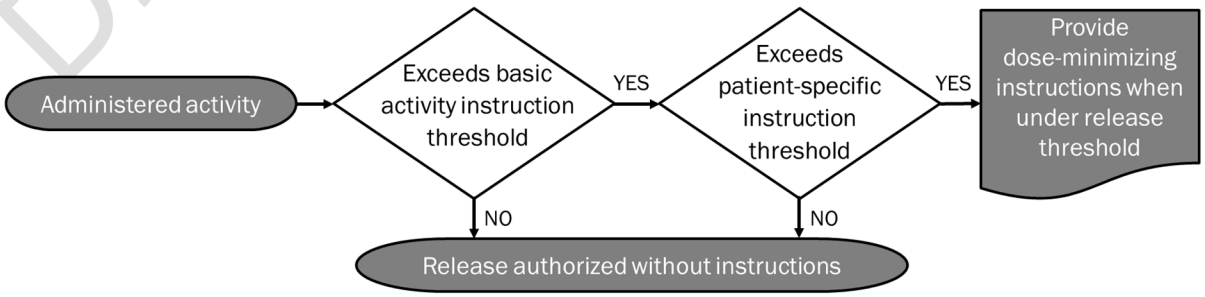

Figure 1. Patient instruction decision based on activity thresholds.

Alternatively, the dose rate measured at 1 m can be compared to the instruction threshold. Note, measured dose rates are influenced by patient biokinetics, radioactive decay, geometric distribution, and attenuation so those factors should not be used if patient specific dose rates are used for this determination. For these reasons, the measured dose rate after administration can be compared to the basic measurement threshold divided by the occupancy modifying factor, F_0 (unitless). Refer to Appendix B for details on determining the occupancy modifying factor.

To determine if dose-minimizing instructions are required based on measurement thresholds:

a. Compare the measured dose rate at 1 m at administration, d_0 (mSv/h), to the basic measurement threshold for issuing instructions shown in Column 2 of Table 2, M_{ins} (mSv/h).

b. If the dose rate at administration does not exceed the basic measurement threshold for instructions ($d_0 \leq M_{ins}$), the patient can be released without dose-minimizing instructions.

c. If the dose rate at 1 m at the time of release, d_{rel} (mSv/h), does not exceed the basic measurement threshold divided by the occupancy modifying factor $\left(d_{rel} \leq \frac{M_{ins}}{F_O}\right)$, the patient can be released without dose-minimizing instructions.

d. Dose-minimizing instructions are required for cases when neither criterion b nor d are met. In addition, instructions must be issued if the basis for the occupancy modifying factor relies on restrictions to patient behavior regarding time spent near bystanders to ensure dose is unlikely to exceed dose limits in accordance with 10 CFR 35.75.

Figure 2 summarizes the decision process for providing instructions based on measurement thresholds.

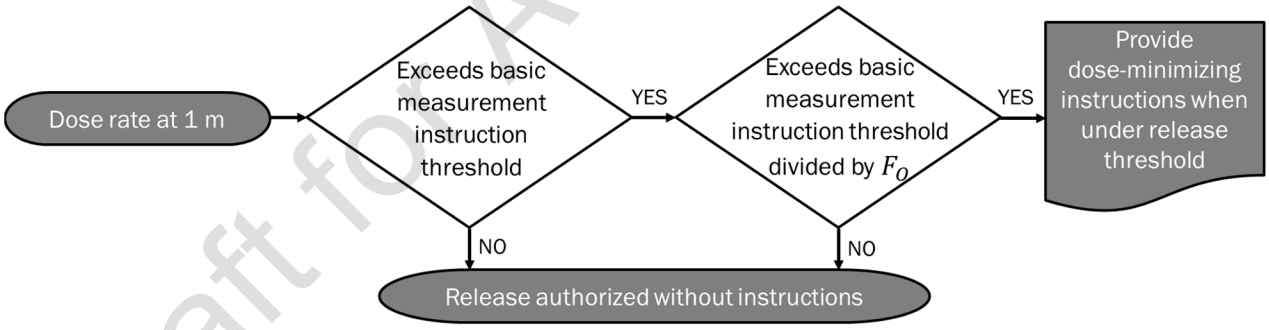

Figure 2. Patient instruction decision based on measured dose rates at 1 meter.

If the patient is breastfeeding an infant or child, additional instructions may be required (refer to Sections 2 and 5.2).

4.2 Content of Instructions

This section describes different aspects that the licensee should consider when developing patient release instructions before and after a patient's treatment based on discussions with the patient or caregiver. Generally, when a licensee releases a patient, it is to the patient's home where family or other caregivers may be present. To provide adequate release instructions under 10 CFR 35.75(b), the licensee should confirm the patient or caregiver ability to understand and follow the release instructions. The

licensee must thoroughly ascertain the patient's posttreatment destination(s) including means of travel to provide instructions and recommended restrictions to maintain doses ALARA and ensure that the dose limit will not likely be exceeded. Note that the proposed pretreatment plans made days before treatment may change and the instructions that were developed based on those plans may need to be changed to reflect the actual arrangements made the day of administration.

I-131 is currently the medical radioisotope of highest concern, as it is the most commonly used radionuclide in radiopharmaceutical therapy and has the potential for a higher external exposure to members of the public because of its high-energy gamma emission and potential volatility (Ref. 10). However, the regulations in 10 CFR 35.75 apply to other medical radioisotope therapies such as yttrium (Y)-90, I-125, lutetium (Lu)-177, and radium (Ra)-223. Instructions should be specific to the type of treatment given and should include additional information for the patient's posttreatment situations. Note that instructions that are needed to meet the requirements for release should also not interfere with or contradict the best medical judgment of the treating physician. Instructions should include a telephone number for the patient to contact with any questions.

4.2.1 Pretreatment Discussions on the Administration of Radiopharmaceuticals

Engaging the patient, and caregiver or family member, early in the treatment process (i.e., during treatment planning) may help the licensee better familiarize the patient and caregiver or family member with the treatment procedures, posttreatment radiation safety precautions, and protective measures to minimize radiation exposure to bystanders. In addition, prerelease discussions are necessary if licensees intend to use patient-specific modifying factors such as occupancy as part of their release basis. The prerelease discussion also lets the licensee make appropriate arrangements if the patient cannot be immediately released (i.e., arrange a temporary hold or hospitalization if necessary). Early engagement helps to identify any patient-specific aspects that may prohibit release after treatment due to the potential of exceeding the 10 CFR 35.75 dose limit, determine whether the patient will be able to follow necessary release instructions, and allow time for the patient or caregivers to ask questions on following instructions to keep doses ALARA. If the licensee determines that the patient's posttreatment plans—including planned mode of transportation, posttreatment destination(s), or any instructions that it believes the patient cannot follow—are likely to cause a dose to bystanders that will exceed 5 mSv (0.5 rem), the licensee cannot release the patient until the dose to bystanders is not likely to exceed 5 mSv (0.5 rem). This discussion should include medical issues such as complications, side effects, and dietary and medication changes, as appropriate.

As soon as radiopharmaceutical or implant therapy is considered as a treatment option, the licensee should interview the patient or caregiver, or both, to fully assess the patient's specific circumstances, especially if the licensee intends to use patient-specific occupancy factors. The licensee and patient or caregiver should discuss and consider the following topics during the pretreatment discussion:

a. What type of posttreatment lodging (e.g., single family home, group home, apartment, nursing home, hotel, detention facility) will the patient use?

b. What are the patient's plans for travel to his or her posttreatment recovery location?

    (1) Will the patient use a private vehicle, taxi service, ride-booking service, or public transportation (i.e., bus, train, or airplane)? The use of public transportation should be discouraged.

    (2) If the patient is traveling with other individuals, what is the duration of the trip? Based on the duration of the trip, can the patient keep an adequate distance from others? Emphasis

should be made to minimize the number of traveling companions.

(3) Will the patient be traveling internationally post treatment? Patients who travel via motor vehicles through international border checkpoints or on airplanes are subject to screening for radiation. Patients should be advised of this fact and provided appropriate documentation (procedure, isotope, date/time of release, treating facility and physician, contact information, etc.) to present to officials when alarms are triggered.

c. Which household members, if any, will be present at the patient's posttreatment recovery location? For example, consider their age and gender and whether there is a nursing infant or pregnant woman in the household.

d. Can the patient be appropriately isolated from others in the household after treatment?

e. Can the patient take care of himself or herself, and is he or she capable of complying with the release instructions?

f. Can the patient sleep alone in a separate bedroom or area?

g. Is the patient incontinent?

h. Are there any necessary household or dietary changes, or fluid intake restrictions (e.g., preexisting medical conditions)?

i. Are there any factors that might prevent treatment (e.g., breastfeeding, pregnancy)?

j. Can the patient delay their return to work? What kind of work does the person do (e.g., daycare provider)?

k. What are the potential restrictions on burial or cremation should the patient pass away within a certain period of time following treatment?

By gathering this information before the treatment (i.e., during the treatment planning stage) when the activity to be administered is expected to exceed the basic activity threshold for release, the licensee can begin to estimate patient-specific modifying factors for use in the release calculations. This information can be used to (1) provide a patient-specific estimate of the likely cumulative dose to other members of the public, (2) direct appropriate protective measures, (3) allow the licensee to make arrangements if the patient cannot be immediately released (i.e. arrangements to temporarily hold the patient or hospitalize the patient), (4) allow the patient time to plan for his or her potential isolation after release, and (5) allow the licensee to assess the patient's capacity to understand the procedure and precautions to ensure dose limits in 10 CFR 35.75 will not likely be exceeded. Note that immediately prior to treatment, licensees should verify that the patient's plans did not change in a way that would alter the patient-specific factors used in release calculations which might require a different plan (i.e., need for instructions or inability to release at planned time) or content of the final release instructions.

4.2.2 Patient Instructions

To comply with 10 CFR 35.75, the licensee must ensure that the radiation dose to bystanders is not likely to exceed 5 mSv (0.5 rem) from a released patient who has been administered radiopharmaceuticals or permanent implants that contain radioactive material before releasing the patient. It is understood that once a patient is released, the licensee has no control of the patient. However, licensees can rely on

discussions with the patients where the patient or caregivers demonstrate they are able and willing take the necessary precautions described in instructions to ensure dose to the maximum bystander is not likely to exceed 5 mSv (0.5 rem) from the released patient. In addition, patient instructions must be given to keep exposures ALARA in accordance with 10 CFR 35.75(b).

The instructions should be appropriate and easy to follow to enable the patient to understand how to minimize radiation exposure to bystanders (Ref. 7). Consideration should be given to providing instructions in the patient's native or primary language. For most therapies, experience shows that radiation exposure from patients can be safely controlled through appropriate treatment specific release instructions provided by licensees and followed by patients. However, if the patient or caregiver is mentally, physically unable, or will not agree to comply with the release instructions, the licensee may have to consider holding the patient as an in-patient following treatment until the patient can be released without having to follow any specific instructions. The licensee must hold the patient as an in-patient following treatment in these cases until the dose to bystanders is not likely to exceed 5 mSv (0.5 rem) without the instructions the patient cannot or will not follow.

The list below provides some basic posttreatment instructions that the patient may need to follow for managing radiation exposure to bystanders. The instructions should always be tailored to the specific patient situation and type and amount of radioactive material administered or implanted. 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. Instruction should also be realistic and provide how long the precautions should be followed. As a guideline, the licensee may consider using several (three to five) effective half-lives of the administered radionuclide for the instruction duration.

a. Wash hands frequently and bathe daily.

b. Wash laundry separately from others.

c. Use dedicated or disposable kitchen utensils, and do not share them with others.

d. Use a dedicated sole-use bathroom, if possible. Always sit on the toilet. Flush the toilet twice after each use.

e. Use disposable gloves and wipes when cleaning.

f. Discard trash separately and hold it to allow for radioactive decay.

g. Sleep alone in a separate bedroom.

h. Abstain from any intimate contact.

i. Avoid preparing or sharing food with others.

j. Avoid using public transportation.

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

l. Minimize the amount of time in close proximity to other people, especially children and pregnant women.

The licensee should instruct family members and caregivers to notify the treating medical facility of a medical emergency or if a patient dies. Further information on death of a patient following radiopharmaceutical administration or implants can be found in Section 4.3. 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.

4.2.3 Patient Acknowledgment of Instructions

The patient should acknowledge receipt of instructions before he or she is released, and the licensee may acknowledge that the patient received the instructions as communicated using a form signed by both parties. Through the form, the patient acknowledges the receipt of the following:

a. He or she has received a clear explanation of the treatment process prior to treatment.

b. He or she has been informed of the need to limit exposure to others, especially to young children and pregnant women, and has been informed on how long he or she must exercise special care.

c. He or she has discussed with the healthcare provider final plans for the following:

(1) transportation from the clinic to home or to the posttreatment destination;

(2) arrangements for protecting others once he or she has arrived at the posttreatment destination;

(3) minimization of the exposure of people both inside and outside the home;

(4) management of biological wastes and trash;

(5) emergency care; and

(6) contact information (i.e., the name and telephone number of a knowledgeable person) if questions arise about the radiation safety instructions during the recovery period.

4.2.4 Patient Precautions

The licensee should consider the following precautions or measures for most patients to minimize exposures to others and to keep radiation exposures to others at or below the 5-mSv (0.5-rem) limit. The patient precautions can be considered by the licensee but are not requirements of the NRC. The licensee should use judgement with the instructions needed for the patient on a case-by-case basis based on the treatment. The licensee should discuss the following precautions and measures with the patient as appropriate. Note that this list is not inclusive and should be modified for each treatment or radioactive material administered.

a. The greatest radiation dose potential to bystanders from the released patient is from external exposure. Therefore, the most important precautions to take are measures to reduce or avoid the radiation exposure emanating from the patient, especially in the early time period after the administration.

(1) Emphasize the importance of keeping an adequate distance from others, especially

children and pregnant women. 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?

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

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

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

(1) Encourage the patient not to prepare or share food with others.

(2) Encourage the use of a bathroom reserved exclusively for the patient, if possible.

(3) Encourage the use of kitchen utensils that are dedicated solely to the patient (i.e., not shared with other household members) and that are washed separately from other dishes. Alternately, encourage patients to use disposable eating utensils.

(4) Encourage the use of disposable gloves and wipes and frequent hand washing.

(5) Encourage the laundering of a patient's clothing separately from another household members' clothing.

(6) Advise the patient on the recommended length of time he or she should wait before becoming pregnant to minimize radiation exposures to a developing fetus.

(7) Discuss how to clean up an area contaminated with body fluids (e.g., urine, vomit) and how to dispose of cleaning materials.

(8) Evaluate the need to dispose of patient-related trash in a separate strong plastic bag that is not mixed with other household members' trash, holding the patient's trash to allow for radioactive decay and implementing ways to reduce radiation exposure from this trash. Holding trash to allow for radioactive decay will be important as most landfills can detect the radiation and send the trash back to the patient.

(9) Discuss how the patient may contact the licensee if needed. Provide information to a family member or caregiver to contact the treatment medical facility if the patient has a medical emergency or passes away.

(10) In the case of a medical emergency, the patient, or a caregiver or family member, should inform the ambulance or the emergency care location of the recentness of the radioactive therapy treatment.

(11) Provide posttreatment release instructions to the patient verbally and in writing, including how long he or she should follow the release instructions.

The licensee may encourage patients to have available plastic bags, disposable gloves and wipes before treatment. The licensee should provide specific information on how to limit direct contact with others and on measures necessary to limit the contamination of objects, surfaces, and the spread of radioactive contamination. Patient education and awareness of how to minimize, isolate, and clean radioactive contamination is important in minimizing exposure to others.

With regard to female patients of child-bearing age, the NRC recognizes that pregnancy tests have limited ability to detect early pregnancies. The NRC encourages licensees to advise their patients to contact the licensee immediately if a female patient discovers that she was pregnant at the time the medical treatment was administered. Licensees must report any dose to an embryo or fetus that is greater than the 50-mSv (5-rem) dose equivalent resulting from the treatment to a pregnant individual unless the authorized user specifically approved the dose to the embryo or fetus in advance in accordance with 10 CFR 35.3047, "Report and Notification of a Dose to an Embryo/Fetus or a Nursing Child."

Patients receiving radiopharmaceutical treatment need to be aware that they might trigger the alarms of radiation detectors at national borders, at airports, at cruise ports, within cities, or at their place of employment for several weeks or months following treatment. Consequently, the licensee should consider issuing the patient a letter or card that contains appropriate information about the treatment in case any officials need to verify that information.

4.3 Death of a Patient Following Radiopharmaceutical Administration or Implants

The licensee should instruct the patient's family to notify the treating authorized user and the radiation safety office (RSO) immediately if a patient has died after recent administration of a therapeutic quantity of radioactive material. If the death occurs in an NRC licensed hospital, the hospital should have internal procedures to handle the death of a radioactive patient. If the hospital does not have a radioactive material license, the licensee that administered the radioactive material or a nearby licensee should provide radiation safety support information to the non-licensed hospital to control access to the room occupied by the deceased.

For the vast majority of administered radiopharmaceuticals, activity levels in released patients will not result in radioactive cadaver exposure exceeding the dose limits of 10 CFR Part 20. However, the analysis of administration of ^{131}I (in five different pharmaceuticals), ^{166}Ho, ^{177}Lu, and ^{188}Re indicates that dose rates exceeding 0.02 mSv/h (2 mrem/hr) or total doses in excess of 1 mSv (0.1 rem) are possible if unexpected death were to occur within days of release and knowledge of the radioactive administration is not communicated (Ref. 9). Dependent on administered activity of a given pharmaceutical and timing of unexpected patient death, the potential exists for exceeding a regulatory limit for several identified procedures. Radionuclides with a hypothetical total dose to a bystander above 1 mSv (0.1 rem) exceeded the limit by no more than a factor of two with conservative exposure assumptions. Dose rates, however, are more restrictive because potential dose rates were found to exceed 0.02 mSv/h (2 mrem/hr) by more than an order of magnitude at short times after patient release. From a patient death perspective, limiting dose rate to an acceptable level for all radionuclides will be protective in terms of total dose. No radioactive implant was identified as potentially important from the perspective of external exposure following patient death. For patient death outside the medical facility, there is a low likelihood that regulatory limits on external dose would be exceeded if the radioactive implant were to remain in place.

The RSO should be consulted to determine the amount of activity remaining in the deceased patient and a determination should be made if there are any state or municipal restrictions on burial or cremation.

a. If the activity remaining in the body results in an external dose that is greater than regulatory public dose limits of 10 CFR Part 20, the RSO should determine the radiation precautions that should be followed.

b. Precautions should be based on dose limits, a generic safety assessment of the need for monitoring personnel who carry out these procedures, the need for monitoring the premises, the need for minimizing external radiation exposure, and the potential for contamination (Ref. 3).

The administering licensee should provide precautions to the family members and the public to follow during visitation prior to burial or internment.

5. Records

5.1 Records of Release

The NRC has no requirement for recordkeeping on the release of patients who were released in accordance with the information in Column 1 of Table 1. However, if the release of the patient is based on a dose calculation that considered retained activity, an occupancy factor of less than 0.25 at 1 meter, the effective half-life, or shielding by tissue, 10 CFR 35.2075(a) requires the licensee to maintain a record of the basis for authorizing the patient's release. Therefore, calculating and releasing patients based on patient-specific thresholds will often require a record unless the occupancy factor is greater than 0.25 and geometry, biokinetic, and attenuation factors are equal to or greater than 1.

This record should include the patient's identifier in a way that ensures that confidential patient information is not traceable or attributable to a specific patient, the radioactive material administered, the administered dosage, and the date of the administration. In addition, depending on the basis for authorizing the release of patients, records should include the following information:

a. **For Immediate Release of a Patient Based on a Patient-Specific Calculation**. The record shall include the basis for authorizing release in accordance with 10 CFR 35.75, including the equation used and bases for the patient-specific modifying factors (see Appendix B to this guide). As exposure is highly dependent on patient-specific behavior following release, use of generic instructions without patient acknowledgment that they can follow them is not an appropriate basis to modify occupancy factors to demonstrate compliance with 10 CFR 35.75. Examples of appropriate bases for occupancy factors include patient questionnaires or notes from discussions with patients to discuss their intended behavior following treatment and acknowledge they can follow instructions as given. In some situations, a calculation may be case specific for a class of patients who all have the same patient-specific factors. In this case, the record for a particular patient's release may reference the calculation for the class of patients, but a basis may be necessary to demonstrate how this patient meets the class of patients. See Appendix C for additional examples of appropriate bases for other modifying factors.

b. **For Immediate Release of a Patient Based on a Measured Dose Rate**. The record should include the results of the measurement, the specific survey instrument used, and the name of the individual performing the survey.

c. **For Delayed Release of a Patient Based on a Radioactive Decay Calculation**. The record should include the time of the administration, the date and time of release, and the results of the decay calculation. If release is based on patient-specific calculations in addition to radioactive decay, then the record should include items listed in a.

d. **For Delayed Release of a Patient Based on a Measured Dose Rate**. The record should include the results of the survey meter measurement, the specific survey instrument used, and the name of the individual who performed the survey. If release is based on patient-specific calculations in addition to measured dose rate, then the record should include items listed in a.

Records should be kept in a manner that ensures the patient's privacy and confidentiality (i.e., the records should not contain the patient's name but instead a patient identification number, date, and treatment type). These recordkeeping requirements may be used to verify that licensees have proper procedures in place for assessing bystander exposure associated with and arising from exposure to patients administered radioactive material.

5.2 Records of Instructions for Breastfeeding Patients

If a patient's failure to interrupt or discontinue breastfeeding could result in a dose to the infant or child in excess of 5 mSv (0.5 rem), 10 CFR 35.2075(b) requires a record that the licensee gave the patient instructions. For the radiopharmaceuticals commonly used in medical diagnosis and treatment, Column 1 of Table 3 lists the activities that require such records when administered to patients who are breastfeeding. The record should include the patient's identifier, the radiopharmaceutical administered, the administered dosage, the date of the administration, and whether instructions were provided to the patient who could be breastfeeding an infant or child. The patient's identifier should be prepared in a way that ensures the confidentiality of the information.

6. Material Separated from the Patient

While public dose limits in 10 CFR Part 20 do not apply to exposure from individuals administered radioactive material and released under 10 CFR 35.75 as described in 10 CFR 20.1003, dose limits in 10 CFR Part 20 do apply to exposure from radioactive material separated from a released patient, such as contaminated bodily fluids, dislodged implants or sources. Public dose limits in 10 CFR Part 20 apply to all members of the public, other than the patient, when exposure is from the radioactive material separated, excreted, removed, or dislodged from a patient's body. If a licensee discovers a member of the public exceeds the public dose limits in 10 CFR 20.1301 from radioactive material no longer affixed to a released patient, licensees must report the event in accordance with 10 CFR 20.2203.

Licensees should ensure all temporary and permanent implants are affixed to the patient so that they are highly unlikely to become dislodged. Patients must not be released from the licensed facility if it is possible under normal conditions for a source to become dislodged and separated from the patient. If there is a potential for a source to become dislodged under unique situations, licensees must have preventative measures in place to ensure public dose limits are not exceeded. Licensees must report lost sources in accordance with 10 CFR 20.2201 if an implant becomes dislodged and is not recovered or if temporary implants issued to a patient are not returned to the licensee. In addition, licensees must have written procedures to determine if a medical event as defined in 10 CFR 35.3045 has occurred in accordance with 10 CFR 35.41. If a patient is released in accordance with 10 CFR 35.75 while treatment is ongoing, these procedures need to include how a licensee will determine if the source moved or became dislodged to determine if a medical event occurred.

Licensees must evaluate unique patient-specific situations following radiopharmaceutical therapy

which could result in increased exposure from radioactive material in body fluids, excreted in urine or feces to ensure dose limits are not exceeded. For example, if a patient proposed to receive radiopharmaceutical therapy is incontinent or requires dialysis an evaluation is necessary to determine if a bystander could be exposed in excess of public limits listed in 10 CFR 20.1301 by material separated from the patient. If it appears the bystander could be exposed in excess of the public limits, the licensee must consider actions to ensure the public dose limits are not exceeded, such as ensuring the patient can manage their own waste, provide shielded containers for waste, or hold the patient at the licensee's facility until it is possible to release the patient. Dialysis is another patient-specific situation for which additional patient-specific evaluation may be necessary. For additional awareness, licensees may need to have supplementary controls to minimize dose to the patient's organs or tissues other than the treatment site, such as the skin, due to unique patient-specific conditions such as incontinence. Licensees must report a medical event as defined in 10 CFR 35.3045 even if the exposure occurs after the patient is released under 10 CFR 35.75.

D. IMPLEMENTATION

The NRC staff may use this regulatory guide as a reference in its regulatory processes, such as licensing, inspection, or enforcement. Backfitting, forward fitting, and issue finality considerations do not apply to 10 CFR Part 35, "Medical Use of Byproduct Material" licensees and applicants because 10 CFR Part 35 does not include backfitting or issue finality provisions and the forward fitting policy in Management Directive 8.4, "Management of Backfitting, Forward Fitting, Issue Finality, and Information Requests," (Ref. 13) does not apply to these licensees.

REFERENCES

1. *U.S. Code of Federal Regulations*, "Medical Use of Byproduct Material," Part 35, Chapter 1, Title 10, "Energy."

2. U.S. Nuclear Regulatory Commission (NRC), NUREG-1556, "Consolidated Guidance about Materials Licenses: Program-Specific Guidance about Medical Use Licenses," Volume 9, Washington, DC.[2]

3. National Council on Radiation Protection and Measurements (NCRP) Report No. 155, "Management of Radionuclide Therapy Patients," Bethesda, MD: December 2006.[3]

4. NCRP Report No. 37, "Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides," Bethesda, MD, October 1, 1970.

5. NRC, "Nuclear Regulatory Commission International Policy Statement," Federal Register, Vol. 79, No. 132, July 10, 2014, pp. 39415–39418.

6. NRC, "Regulatory Guides," Management Directive 6.6, ADAMS Accession No. ML18073A170.

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9. 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)

10. NRC, SECY-18-0015, "Staff Evaluation of the U.S. Nuclear Regulatory Commission's Program Regulating Patient Release after Radioisotope Therapy," Washington, DC, January 29, 2018. [ADAMS Accession No. ML17279B139 (package)].

11. Peplow, D.E. Specific gamma-ray dose constants with current emission data. *Health Physics*. 118(4): 402-416; 2020.

12. Smith, D.S.; Stabin M.G. Exposure rate constants and lead shielding values for over 1,100 radionuclides. *Health Physics*. 102(3): 271-291; 2012.

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[2] Publicly available NRC published documents are available electronically through the NRC Library on the NRC's public Web site at http://www.nrc.gov/reading-rm/doc-collections/ and through the NRC's Agencywide Documents Access and Management System (ADAMS) at http://www.nrc.gov/reading-rm/adams.html. The documents can also be viewed online or printed for a fee in the NRC's Public Document Room (PDR) at 11555 Rockville Pike, Rockville, MD. For problems with ADAMS, contact the PDR staff at (301) 415-4737 or (800) 397-4209; fax (301) 415-3548; or e-mail pdr.resource@nrc.gov.

[3] Copies of reports from The National Council on Radiation Protection and Measurements (NCRP) may be obtained through its Web site: http://www.ncrponline.org/Publications/Publications.html] or by writing to the NCRP at 7910 Woodmont Avenue, Suite 400, Bethesda, Maryland 20814-3095, Phone: 301-657-2652, fax: 301-907-8768.

13. NRC Management Directive 8.4, "Management of Facility-Specific Backfitting and Information Collection," Washington, DC.

APPENDIX A — RADIONUCLIDE DATA TABLES

Table A-1. Radiological Half-Lives and Dose-Rate Constants for Radionuclides

RADIONUCLIDE	RADIOLOGICAL[c] HALF-LIFE, T_r (days)	DOSE-RATE CONSTANT[d] AT 1 METER, Δ_{pr} $\left(\frac{\text{mSv}}{\text{GBq h}}\right)$
Ag-111	7.45	0.00442
At-211	0.3006	0.0288
Au-198	2.696	0.0615
Bi-213	0.0317	0.0218
C-11	0.0142	0.154
C-14[b]	2,080,000	0.00000502
Cr-51	27.703	0.00465
Cs-131	9.689	0.0144
Cs-131 implant[a]	9.689	0.0130
Cu-64	0.5292	0.0277
Cu-67	2.576	0.0150
Dy-165	0.09725	0.00464
Er-169[b]	9.4	0.000121
F-18	0.0762	0.148
Ga-67	3.261	0.0207
Ga-68	0.04702	0.143
Ho-166[b]	1.117	0.00507
I-123	0.553	0.0390
I-124	4.176	0.167
I-125	59.4	0.0332
I-125 implant[a]	59.4	0.0291
I-131	8.0207	0.0576
In-111	2.8047	0.0798
Ir-192	73.827	0.125
Ir-192 implant[a]	73.827	0.121
Kr-81m	0.000152	0.0385
Lu-177	6.647	0.00527
N-13	0.00692	0.154
O-15	0.00141	0.154
P-32[b]	14.263	0.00105
P-33[b]	25.4	0.0000887
Pd-103	16.991	0.0306
Pd-103 implant[a]	16.991	0.0220
Ra-223	11.43	0.0475
Rb-82	0.000884	0.172
Re-186	3.7183	0.00631
Re-188[b]	0.7085	0.0127
Ru-106[b]	373.59	0.00000212
Ru-106[b] implant[a]	373.59	0.00000188
Sc-47	3.3492	0.0140
Se-75	119.78	0.153
Sm-153	1.938	0.0115

Sn-117m	13.76	0.0364
Sr-89[b]	50.53	0.000875
Sr-90[b]	10,508	0.000255
Tc-99m	0.2506	0.0194
Tl-201	3.038	0.0405
Xe-127	36.41	0.0535
Xe-133	5.243	0.0128
Y-90[b]	2.67	0.00157
Yb-169	32.026	0.0477
Zr-89	3.267	0.207

a. Implants and eye plaques assumed to be encapsulated in 50 μm of titanium
b. Greater than 5% of Δ_{pr} due to bremsstrahlung production
c. Nuclear decay data based on International Commission on Radiological Protection (ICRP) Publication 107 (Ref. A-1)
d. External dose equivalent rate to tissue from photon and electron emissions with bremsstrahlung for a point source surrounded by an infinitely thin sphere of tissue (Ref. A-2)

REFERENCES FOR APPENDIX A

A-1. International Commission on Radiological Protection. Nuclear Decay Data for Dosimetric Calculations. Annals of the ICRP. Publication 107. Vol. 38(3); 2008.

A-2. 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) [1]

[1] Publicly available NRC published documents are available electronically through the NRC Library on the NRC's public Web site at http://www.nrc.gov/reading-rm/doc-collections/ and through the NRC's Agencywide Documents Access and Management System (ADAMS) at http://www.nrc.gov/reading-rm/adams.html. The documents can also be viewed online or printed for a fee in the NRC's Public Document Room (PDR) at 11555 Rockville Pike, Rockville, MD. For problems with ADAMS, contact the PDR staff at (301) 415-4737 or (800) 397-4209; fax (301) 415-3548; or e-mail pdr.resource@nrc.gov.

APPENDIX B

PATIENT-SPECIFIC MODIFYING FACTORS AND METHODS

Licensees may authorize the release of any individual who has been administered unsealed byproduct material or implants containing byproduct material 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) in accordance with 10 CFR 35.75(a). Basic activity thresholds provided in Table 1 were calculated using conservative assumptions so that they can be used without patient-specific information to demonstrate that the release of an individual is unlikely to exceed 5 mSv (0.5 rem) (see Section 1 of the Regulatory Guidance). However, licensees can release patients above these thresholds if patient-specific information is known and demonstrates that the maximally exposed bystander is not likely to exceed 5 mSv (0.5 rem) from exposure to the released individual in accordance with 10 CFR 35.75(a). Consistent with Section 3, patient-specific modification includes four factors:

$$D = 1.44 \cdot T_r \cdot \Delta_{pr} \cdot A_0 \cdot F_B \cdot F_O \cdot F_G \cdot F_A \qquad \text{(Equation B-1)}$$

where

D	=	External dose equivalent, mSv
1.44	=	Constant for reciprocal of the natural logarithm of 2
T_r	=	Radiological (physical) half-life, h
Δ_{pr}	=	Dose-rate constant for a point source at 1 m, $\frac{\text{mSv}}{\text{GBq h}}$
A_0	=	Activity of the radionuclide administered to the patient, GBq
F_B	=	Biokinetic modifying factor, unitless
F_O	=	Occupancy modifying factor, unitless
F_G	=	Geometry modifying factor, unitless
F_A	=	Attenuation modifying factor, unitless

Several acceptable approaches for determining the modifying factors are presented in this appendix. The likely dose to the maximally exposed bystander (i.e., person for whom the product of modifying factors is greatest) must be determined for demonstrating compliance with 10 CFR 35.75. To demonstrate TEDE is below 5 mSv (0.5 rem), modifying factors for biokinetics, occupancy, geometry, and attenuation are incorporated into a patient-specific activity threshold as follows

$$Q' = \frac{Q}{F_B \cdot F_O \cdot F_G \cdot F_A} \qquad \text{(Equation B-2)}$$

where

Q	=	Basic activity threshold, GBq
Q'	=	Patient-specific activity release threshold at administration, GBq

Patient-specific activity thresholds should be calculated prior to administration. This assures the licensee and the patient are prepared in case it is determined the patient needs to be held following treatment. In addition, this allows the licensee to determine appropriate and realistic modifying factor values and determine if the patient will have to follow any instructions to assure dose limits are not exceeded. Licensees should confirm any instructions needed to ensure dose limits are ones that the patient can and is willing to follow prior to administration as a patient might not be able to be released in accordance with 10 CFR 35.75 if a licensee learns a patient is not able to follow them after administration. If a licensee decides to perform a patient-specific calculation for a breastfeeding infant or child, further information is available (Ref. B-1).

Modifying factors for geometry and attenuation can take values greater than 1 as described below. The assumption of unity for occupancy and biokinetics provides significant conservatism such that this possibility is unlikely to lead to exposures greater than 5 mSv (0.5 rem). However, if a licensee chooses to use more realistic, patient-specific information to modify occupancy or biokinetic factors such that a record is required per 10 CFR 35.2075, a basis for geometry and attenuation factors must also be provided as values could realistically be greater than 1. Attenuation plots are available for 40 radionuclides (Ref. B-1). When added realism is incorporated by applying patient-specific information to other modifying factors, licensees should also estimate an attenuation factor for the patient. Note that in some cases attenuation factors may be greater than 1 due to buildup of scattered radiation. The combination of geometry and attenuation factors should be defensible or conservative for the patient.

A patient questionnaire, such as that shown in Figure B-1, while not required, is one acceptable method to gather patient-specific information. Modification of the survey is encouraged for the types of procedures performed at the medical facility. Licensees may need additional discussions based on the patient's responses to the questions to determine patient specific modifying factors.

Figure B-1. Example Patient Questionnaire for Determining Patient-Specific Modifying Factors.

To Be Completed by the Licensee								
Patient Identification Number								
Patient is able and willing to follow discharge instructions including behavior restrictions based on discussions prior to administration?							yes	no
Estimate the patient's overlying tissue for attenuation and buildup: _____ cm								
Is a patient-to-bystander distance less than 1 m expected with a geometric modifying factor greater than 1?							yes	no
To Be Completed with Patient Input								
How long is the return trip home?								
Will someone accompany you on the return trip home?	yes / no	How will you be returning home?	my vehicle	bus	taxi			
			train	plane	other			
When will you return to work?		Do you spend more than 10 hours per week closer than 10 feet from the same person at work?					yes	no
Who do you see in person on a routine basis?								
Do you anticipate spending more than an hour a day closer than arm's length (1 meter) from another individual?	yes / no	If yes, at what distance and for how long?						
Do you/have you ever needed help with the following tasks?	getting on and off chairs	walking	using the restroom	bathing				
	getting in and out of vehicles	cooking/ eating	reading/understanding instructions	none of the above				
Do you live in an apartment or facility with other people in adjacent rooms/on adjacent floors?							yes	no
Are you currently nursing (breastfeeding) a child?	yes / no	Could you be pregnant?	yes / no	Do you share a bed with anyone?			yes	no
Are you able to sleep in your own bed without another person for some length of time after the procedure?							yes	no
Are you able and willing to change your behavior as directed by the specific preliminary posttreatment instructions discussed with and explained to you to minimize exposure to bystanders?							yes	no
Are you able and willing to change your behavior as directed by the specific final posttreatment instructions discussed with and explained to you to minimize exposure to bystanders?							yes	no
To Be Completed the Day of Administration by Licensee								
Confirm appropriate changes were made to the form and calculations if patient plans changed.							yes	no

B.1 Modifying Factor for Occupancy, F_O

The occupancy factor represents the total number of radionuclide disintegrations during the bystander's close contacts with the patient relative to total disintegrations in the patient. Behaviors during early times after release have a greater relative importance when the effective half-life of the administered radiopharmaceutical is short. To accommodate a large range of potential patient-specific factors, bystander behaviors, and occupancy values, F_O is calculated by applying the effective half-life of the radiopharmaceutical in two parts: (1) bystander exposure during the patient's travel from the medical facility; and (2) bystander exposure to the patient after travel. Note if biological half-life is not known, physical half-life can be used in place of effective half-life.

Occupancy is calculated for short-term exposure during travel as F_1 and long-term exposure after travel as F_2. If the same bystander is exposed during travel and after travel, add them such that F_O equals $F_1 + F_2$. Compliance must be demonstrated for the maximally exposed bystander. Licensees should note that the maximally exposed bystander is not always the bystander with the highest occupancy but is likely the bystander who has the highest product of both the geometry and occupancy factors. When the licensee instructs a patient to follow specific behavior restrictions, the occupancy factor can be based on anticipated bystander exposure, including appropriate and realistic restricted behavior when the patient states they are able and willing to follow the instructions. The instructions issued to the patient must communicate those same restrictions if they are used as basis to demonstrate dose limits will not be exceeded. If a patient or caregiver states they are unable or unwilling to follow the appropriate instructions, occupancy factor will need to be modified accordingly. Note F_1 and F_2 can be 0 if a bystander does not have contact with the patient during the travel or post-travel time periods, respectively.

Occupancy during travel is calculated as

$$F_1 = s_1\left[e^{-0.693(t_0)} - e^{-0.693(t_0+t_1)}\right] \qquad \text{(Equation B-3)}$$

where

F_1 = Occupancy factor for the maximally exposed bystander during travel, unitless
s_1 = Fraction of time bystander spends in close contact with the patient during travel, unitless
t_0 = Time between medical administration and patient release in effective half-lives, unitless
t_1 = Travel duration in effective half-lives, unitless

In many travel situations (e.g., plane, bus, car) when the patient travels with a companion, the bystander exposure fraction for close contact with the patient can be conservatively assumed to be 100% ($s_1 \approx 1$). When it is advantageous, Equation B-3 can also accommodate single exposure events for which the start and end times may be different from travel.

Occupancy during potential long-term exposure after travel is calculated as

$$F_2 = s_2\left[e^{-0.693(t_0+t_1)} - e^{-0.693(t_0+t_1+t_2)}\right] + s_3\left[e^{-0.693(t_0+t_1+t_2)}\right] \qquad \text{(Equation B-4)}$$

where

F_2 = Occupancy factor for the maximally exposed bystander after travel, unitless
s_2 = Fraction of time bystander spends in close contact during the instruction period, unitless
s_3 = Fraction of time bystander spends in close contact after the instruction period, unitless
t_2 = Instruction period duration in effective half-lives, unitless

Figure B-2 depicts the time periods used in the calculation. Times (typically in hours) are intentionally converted into the number of effective half-lives (unitless) so that a single set of tabulated values will apply to a broad range of radiopharmaceuticals. Licensees with details on the timing of anticipated exposure may calculate F_O for specific bystanders.

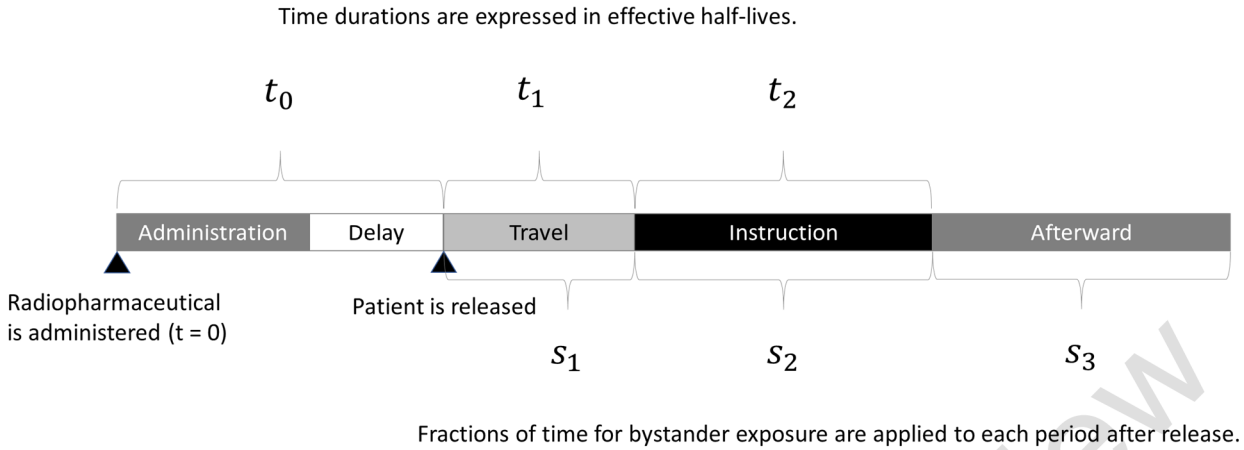

Figure B-2. Time Periods and Parameters Utilized to Calculate Occupancy.

If the licensee determines that a patient is willing and able to follow instructions to minimize bystander exposure, then s_2 can be modified based on the instruction. In addition to direct discussions with the patient, questionnaire responses can be useful to determine if a patient can follow instructions and if anticipated behavior after release is realistic for the patient. It is inappropriate and unrealistic to assume a patient will isolate or physically separate from bystanders if the patient has difficulty in understanding or following dose-minimizing instructions, such as someone needing assistance to perform daily tasks. Instead, a more appropriate, realistically conservative value for occupancy should be selected.

For example, based on discussions with a patient, a daily fraction for close contact greater than 0.1 should be used when a patient does not believe they can follow the instructions to restrict close contact to less than 2 hours per day. No adjustment is needed when the licensee confirms the appropriateness of the issued instructions for the patient and is confident that those instructions will be followed. If instructions direct the patient to avoid close contact with others for a specified instruction duration and a licensee determines the patient is willing and able to follow the instructions, then s_2 can be assigned a small value, including 0 while the patient is in isolation. If the patient is expected to have close contact with a bystander for more than a negligible time (i.e., more than a couple minutes per day of close contact) during the instruction period, assign s_2 to a value greater than 0.

Per 10 CFR 35.2075(a)(2), a record of the basis for authorizing release is required when an occupancy factor less than 0.25 at 1 m is used. A patient questionnaire, similar in format to Figure B-1, and its arising conclusions may be used as a basis of patient-specific information. Licensees should exercise caution on low occupancy factors based solely on a patient's typical behavior. For example, if an occupancy factor is determined to be less than 0.1 due to minimal close contact with bystanders on a typical basis, licensees may need to enquire about the patient's specific plans following treatment and ensure the instructions match this expected behavior prior to using an occupancy factor less than 0.1 to justify bystander exposure will likely not exceed 5 mSv (0.5 rem).

Occupancy considers exposure components during travel and after travel. Patient-specific instructions on dose minimization tend to be more effective when they address the larger of the two components. The patient's ability to adhere to instructions is most important in situations when patient release relies on behavior to meet the stated restrictions in the instructions. This condition can be confirmed when an alternate "unrestricted" occupancy factor, assuming no restrictions on patient behavior, yields a bystander dose exceeding 5 mSv (0.5 rem). There is no requirement for determining unrestricted occupancy factors; however, if the patient-specific unrestricted occupancy factor results in bystander dose exceeding 5 mSv (0.5 rem) then the licensee must have confidence the patient and their caregivers understands, are willing, and are able to comply with the instructions before using them as a basis for release. Record of the method for verifying patient ability and intent to follow these instructions must be in accordance with 10 CFR 35.2075 for these types of release.

B.2 Modifying Factor for Geometry, F_G

For the basic threshold calculation, the conservative geometry between a patient and the bystander is assumed to be point to point at a 1 m distance. One meter is used because it is assumed to be the average typical close contact distance over time. Licensees can modify the geometry to provide realism using the geometry modifying factor. The geometry modifying factor, F_G, is a unitless factor to represent dose rate to a bystander at a distance r from the patient's body relative to the tissue dose rate at a point 1 m away from a point-source of the radionuclide. Equation 1 already utilizes a dose-rate constant for a point at 1 m away from a point source. The geometry factor modifies this equation for patient-specific exposure geometries. As shown in Table B-1, this factor is highly dependent on the patient-to-bystander separation distance (Ref. B-1). Values of F_G can exceed unity (1) for instances with separation distances of less than 1 m. Time spent closer than 1 m, such as time spent holding another person, traveling immediately after release, and sleeping in the same bed with another person, should be included in the patient-specific assessment, especially if they occur within two effective half-lives following administration. In addition, the geometry factor can be modified to remove the conservatism from an assumption that both the source and bystander are points (Ref. B-1).

F_G should be selected for the bystander's total exposure without overestimating separation distance. Point-Line refers to a point-like source across from the end of a 0.7-m receptor line for distributed bystander organs; these geometry values are supplied in Table B-1 for point-like sources, implants, or radionuclides concentrating in a particular organ (e.g., hyperthyroid retention of radioiodine in the thyroid or prostate implants). Line-Line refers to a 1.7-m source length with a 0.7-m receptor length. Line-Line values are provided for more widely distributed radionuclides within the patient's body (e.g., radioiodine treatment for thyroid cancer). Alternatively, licensees may make patient-specific geometric adjustments or perform more detailed three-dimensional modeling to calculate F_G (Ref. B-1).

Table B-1. Geometric modifying factors, F_G, at various bystander separation distances, r (m).

Patient-to-Bystander Separation Distance, r (m)	Point-Line F_G (unitless)	Line-Line F_G (unitless)
0.2 (typical for holding a child)	7.6	9.2
0.3 (typical for mobility assistance)	5.6	4.6
0.5	2.7	2.3
0.7 (typical for travel seating)	1.6	1.4
1.0 (typical for close contact)	0.87	0.79
1.5	0.42	0.39
2.0	0.25	0.25
Distances greater than 2 m	$\frac{1}{r^2}$	$\frac{1}{r^2}$

Exposure to bystanders during travel must be considered when the patient does not travel alone if it is possible that dose limits could be exceeded; this includes public transportation and ride sharing. Travel includes the return trip home (or to work) and would include time spent in lodging during the trip. When the patient travels alone using private transportation, exposure to members of the public during travel would be small and can be neglected when the maximally exposed bystander is associated with exposure after travel. Judgment should be applied on when and to whom external doses are expected to be the largest. For the combination of very short-lived radionuclides with patient travel times that represent several half-lives, retained activity in the patient after travel can be a small fraction of that at the beginning of travel. In this situation, the travel period would be important to consider. Exposure considerations must include both occupancy (time spent) and geometry (separation distance) when exposure is expected to be significant at distances closer than 1 m. Patients who require mobility

assistance or aid another person can be assumed to hold that person for two hours per day unless patient-specific details indicate differently. Although exposures to bystanders more than 3 m away and not within the direct line of sight of the patient are seldom limiting, patients who live alone in an apartment or other facility with nearby occupants may expose those bystanders for prolonged periods of time.

B.3 Modifying Factor for Time-Integrated Biokinetics, F_B

F_B is the ratio of the total disintegrations occurring in the patient to the total disintegrations of the administered activity. Licensees with radiopharmaceutical retention data for the patient can quickly obtain a conservative estimation of the biokinetic modifying factor using a single data point as shown

$$F_{\mathrm{B}} = -\frac{0.693\ t_n}{T_r \cdot \ln(R_n)} \qquad \text{(Equation B-5)}$$

where

T_r = Radiological half-life for the radionuclide, h
t_n = Time after administration when latest retention fraction is determined, h
R_n = Retention fraction in the patient at time t_n after administration, unitless

Values for t_n and R_n represent a data point in the patient's retention curve. Note: $t_n > 48$ h is recommended for radionuclides with $T_r > 24$ h. For example, given a patient who exhibits 19% retention 96 hours after administration of a radionuclide with a radiological half-life of 160 h, Equation B-5 yields

$$F_{\mathrm{B}} = -\frac{0.693 \cdot 96\ h}{160\ h \cdot \ln(0.19)} = 0.24. \qquad \text{(Equation B-6)}$$

Alternatively, licensees with patient retention data for the radiopharmaceutical can utilize the generalized template shown in Figure B-3. After plotting patient retention data on the template, the retention curve can be drawn from the initial point at 100% through each data point. The value of F_B equals the smallest template value intercepted by the data. To accommodate all radionuclides, time after administration was converted into the number of radiological half-lives. For the same example above, 96 h represents 0.6 radiological half-lives. Plotting 19% at 0.6 radiological half-lives generates a data point below the dashed line for 0.3. Thus, $F_B = 0.3$ from the template in Figure B-3, which is slightly more conservative than Equation B-1. Radionuclide retention over time can be inferred from several dose rate measurements at the same distance from the patient. For therapeutic procedures with a pretreatment planning administration, the patient's pretreatment data could estimate retention after the therapeutic dosage of the radiopharmaceutical is administered especially when the same radiopharmaceutical is used. When patient retention data are not available, licensees can assume the patient exhibits slow biological clearance according to the manufacturer excretion information unless the patient's medical condition or voiding habits affects biological clearance and excretion rates. Medical conditions such as reduced kidney or liver function may affect clearance rates. For permanent capsulated implants or seeds, or when biological clearance rates are unknown, use $F_B = 1$.

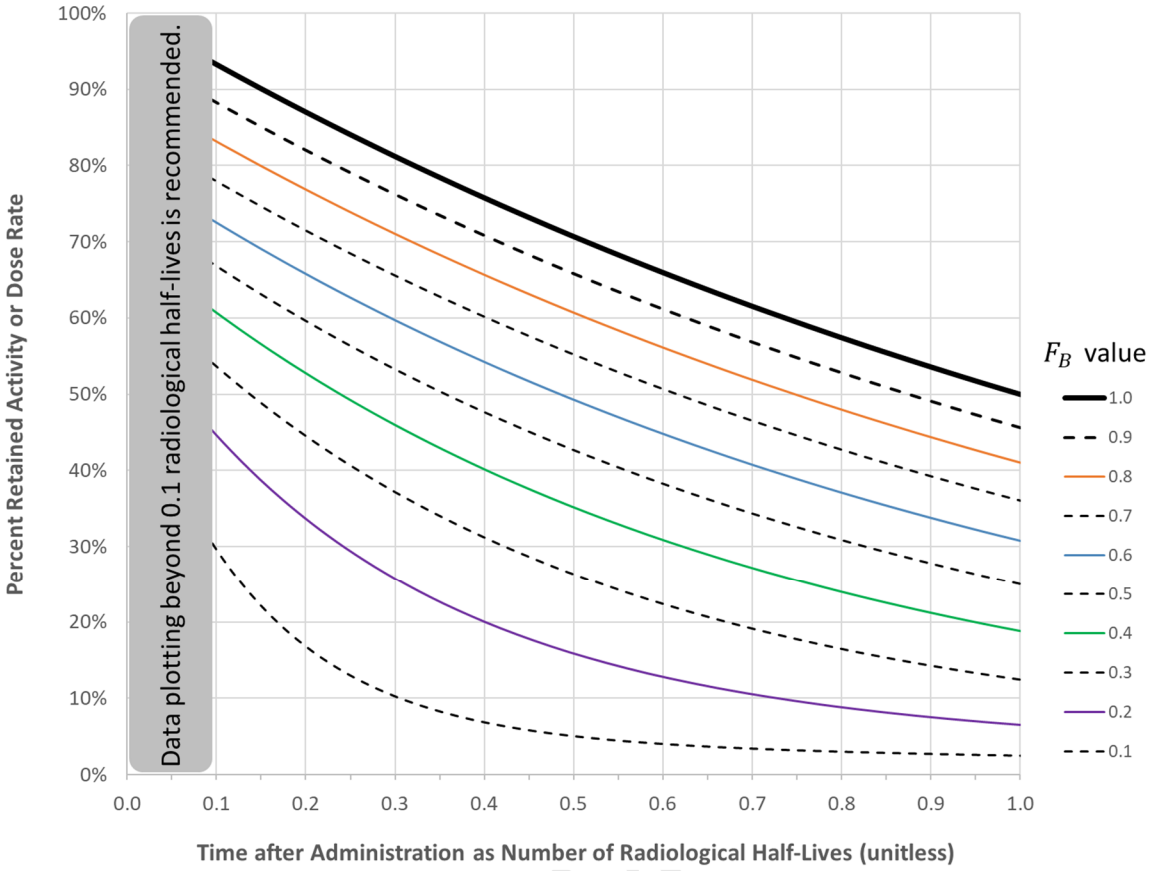

Figure B-3. Generalized graphical template to determine F_B from patient retention data.

Mathematical integration of more detailed retention functions (e.g., double exponential relationships for fast and slow clearance) provides the greatest flexibility when specific exposure times are either known or approximated from patient-specific data. Equations in this subsection were derived from mathematical integration with radiopharmaceutical retention modeled by a single exponential. Modifications for double exponential retention can be pursued on a case-by-case basis. Supporting details are available (Ref. B-1). Example calculations are presented in Appendix C.

B.4 Modifying Factor for Attenuation, F_A

The modifying factor for attenuation, F_A, accounts for photon scatter, buildup, and absorption at patient tissue thicknesses different than standard zero thickness of tissue. F_A is unitless. Provided in Appendix A, dose-rate constants from a point source at 1 m assume no shielding from tissue and were used in calculating the activity and measurement thresholds in Tables 1 and 2. These thresholds can be modified using F_A to account for photon scatter, buildup, and absorption in tissue. As an example, the influence of tissue thickness on the standard dose-rate constant is provided in Figure B-4 for ^{99m}Tc. As shown, values of F_A can exceed unity (1) when photons only travel through a short distance of tissue before leaving the body. Patient attenuation and buildup can be significant. F_A should be justified in the calculation of patient-specific thresholds when other patient specific modifying factors are used to remove conservatism. To consider patient attenuation with buildup, licensees may select the tissue thickness appropriate for the patient by estimating torso radius for widely distributed radionuclides or the thickness of tissue overlying the thyroid for radioiodine treatments. Attenuation factors have been precalculated for 40 radionuclides (Ref. B-1).

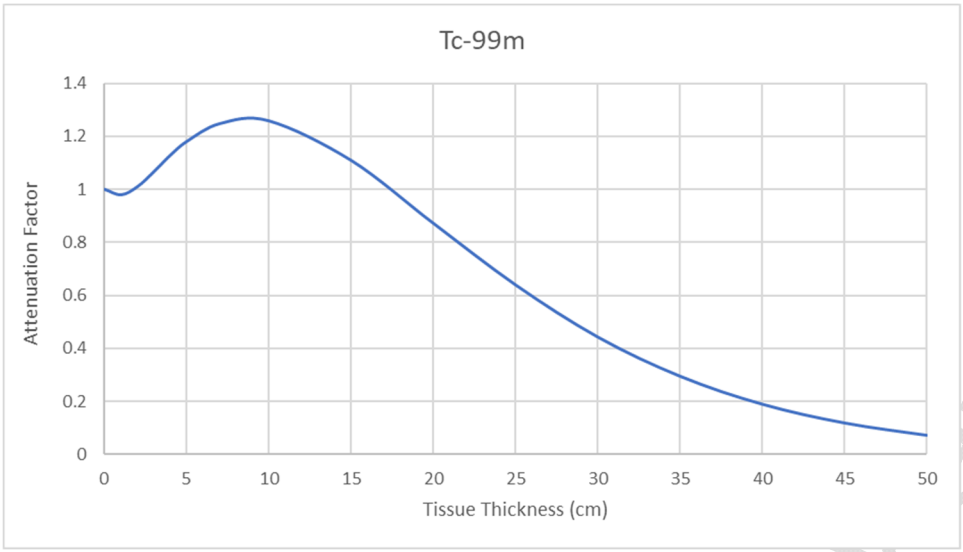

Figure B-4. Attenuation modifying factor for Tc-99m as a function of attenuating tissue thickness.

REFERENCE FOR APPENDIX B

B-1. 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) [1]

[1] Publicly available NRC published documents are available electronically through the NRC Library on the NRC's public Web site at http://www.nrc.gov/reading-rm/doc-collections/ and through the NRC's Agencywide Documents Access and Management System (ADAMS) at http://www.nrc.gov/reading-rm/adams.html. The documents can also be viewed online or printed for a fee in the NRC's Public Document Room (PDR) at 11555 Rockville Pike, Rockville, MD. For problems with ADAMS, contact the PDR staff at (301) 415-4737 or (800) 397-4209; fax (301) 415-3548; or e-mail pdr.resource@nrc.gov.

APPENDIX C

EXAMPLE CALCULATIONS

Several examples illustrate the methodologies discussed in this guide.

EXAMPLE A – USE OF QUESTIONNAIRE TO DETERMINE MODIFYING FACTORS

Information collected by the questionnaire can support modifying factor selection. The two brief examples of completed questionnaires for different patients below, however, emphasize the occupancy factor. Refer to other examples in this appendix for determinations of the remaining modifying factors.

Example 1: On Friday afternoon, a patient travels home by private automobile without a companion after a medical administration of a radiopharmaceutical with an effective half-life of 60 hours. The patient lives alone and returns to work on Monday morning. Figure C-1 shows a completed questionnaire.

The maximally exposed bystanders will likely be coworkers as this patient lives and travels home alone in a private vehicle. Because the patient does not expect to return to work until Monday morning, the total time elapsed between administration and the start of coworkers' prolonged exposure is about 66 hours or $\frac{66}{60} = 1.1$ effective half-lives. Through discussion with the patient, the licensee understands the patient's typical workday is eight hours. For an eight-hour workday, the fraction of time for bystander close contact, s_3, is $\frac{8}{24}$ or approximately 0.33. For this patient. Equation B-3 is not necessary for calculating the occupancy factor because there is no bystander exposure during travel. Additionally, there is no close bystander contact during the instruction period while the patient is home alone before returning to work. For these conditions, Equation B-4 simplifies to

$$F_2 = s_3\left[e^{-0.693(t_0+t_1+t_2)}\right] \qquad \text{(Equation C-1)}$$

where

F_2	=	Occupancy factor for the maximally exposed bystander after travel, unitless
s_3	=	Fraction of time for bystander close contact after the instruction period, unitless
$t_0 + t_1 + t_2$	=	Total elapsed time between medical administration and bystander exposure in effective half-lives, unitless.

For the parameter values described above, the following calculation is performed

$$F_2 = 0.33\left[e^{-0.693(1.1)}\right] = 0.15 \qquad \text{(Equation C-2)}$$

The occupancy factor, F_O, is 0.15 for this patient.

Figure C-1. Completed Questionnaire for Example Patient Who Lives and Travels Home Alone.

To Be Completed by the Licensee						
Patient Identification Number	1342966322					
Patient is able and willing to follow discharge instructions including behavior restrictions based on discussions prior to administration?					(yes)	no
Estimate the patient's overlying tissue for attenuation and buildup: 5 cm						
Is a patient-to-bystander distance less than 1 m expected with a geometric modifying factor greater than 1?					yes	(no)
To Be Completed with Patient Input						
How long is the return trip home?	1 hour					
Will someone accompany you on the return trip home?	yes / (no)	How will you be returning home?	(my vehicle)	bus	taxi	
			train	plane	other	
When will you return to work?	Next week	Do you spend more than 10 hours per week closer than 10 feet from the same person at work?				(yes) / no
Who do you see in person on a routine basis?	Coworkers on workdays					
Do you anticipate spending more than an hour a day closer than arm's length (1 meter) from another individual?	yes / (no)	If yes, at what distance and for how long?	n/a			
Do you/have you ever needed help with the following tasks?	getting on and off chairs	walking	using the restroom	bathing		
	getting in and out of vehicles	cooking /eating	reading/understanding instructions	(none of the above)		
Do you live in an apartment or facility with other people in adjacent rooms/on adjacent floors?					yes	(no)
Are you currently nursing (breastfeeding) a child?	yes / (no)	Could you be pregnant?	yes / (no)	Do you share a bed with anyone?		yes / (no)
Are you able to sleep in your own bed without another person for some length of time after the procedure?						yes / no
Are you able and willing to change your behavior as directed by the specific preliminary posttreatment instructions discussed with and explained to you to minimize exposure to bystanders?						(yes) / no
Are you able and willing to change your behavior as directed by the specific final posttreatment instructions discussed with and explained to you to minimize exposure to bystanders?						(yes) / no
To Be Completed the Day of Administration by Licensee						
Confirm appropriate changes were made to the form and calculations if patient plans changed.						(yes) / no

Example 2: A different patient travels a long distance with a companion to arrive at the medical facility for the same radiopharmaceutical administration and effective half-life of 60 h. The companion is the patient's spouse, and they share a bed. The patient is released 6 hours after the administration. This delay time equates to $\frac{6}{60} = 0.1$ effective half-lives. The spouse and patient travel together on Friday and during the weekend and return home on Sunday. The full duration of travel is estimated to be 42 hours after release or $\frac{42}{60} = 0.7$ effective half-lives. Through a discussion with the patient, the patient indicated that during the day at home, close contact with the spouse is not expected. At night however, the patient will typically spend 8 hours (equal to 0.33 fraction of a day) in the same bed, and the patient is unable to change this pattern. Based on discussions with the patient, the licensee determines that the maximally exposed bystander is the patient's spouse. A completed patient questionnaire is displayed in Figure C-2.

Exposure to the patient's spouse should be considered during travel and at home after travel. The licensee conservatively assumes the patient is in close contact with the spouse during the entire trip. The occupancy factor is calculated from Equations B-3 and B-4. Occupancy during travel is calculated as

$$F_1 = s_1\left[e^{-0.693(t_0)} - e^{-0.693(t_0+t_1)}\right] \quad \text{(Equation C-3)}$$

where

F_1 = Occupancy factor for the maximally exposed bystander during travel, unitless
s_1 = Fraction of time bystander spends in close contact with the patient during travel, unitless
t_0 = Time between medical administration and patient release in effective half-lives, unitless
t_1 = Travel duration in effective half-lives, unitless

For the parameter values described above, the following occupancy calculation is performed during travel

$$F_1 = 1\left[e^{-0.693(0.1)} - e^{-0.693(0.1+0.7)}\right] = 0.36 \quad \text{(Equation C-4)}$$

After travel, there is no difference in behavior expected for this patient. As shown in Figure C-2, the patient is not willing to follow behavior changes in posttreatment instructions to minimize exposure to bystanders. For this reason, an instruction period, during which behavior restrictions would be followed, is unnecessary for determining bystander occupancy after travel. According to Equation B-4, both parameters associated with the instruction period take values of zero. For this patient, Equation B-4 reduces to

$$F_2 = s_3\left[e^{-0.693(t_0+t_1)}\right] \quad \text{(Equation C-5)}$$

For the parameter values described above, bystander occupancy during potential long-term exposure after travel is calculated as

$$F_2 = 0.33\left[e^{-0.693(0.1+0.7)}\right] = 0.19 \quad \text{(Equation C-6)}$$

Because bystander occupancy during and after travel relate to the same person (patient's spouse), these results are summed to yield an occupancy factor of 0.55 for the maximally exposed bystander.

Figure C-2 also shows that the licensee elected to not estimate overlying tissue thickness when acquiring patient-specific information to reduce conservatism and modify thresholds. When patient-specific modification is pursued and no information is available to justify a modifying factor, a conservative value must be applied to that modifying factor. In this case, the largest value of the attenuation factor should be selected for the administered radionuclide. As shown in precalculated plots (Ref. C-1), the largest value could exceed unity (1).

Figure C-2. Completed Questionnaire for Example Patient With a Travel and Living Companion.

To Be Completed by the Licensee						
Patient Identification Number	70784431					
Patient is able and willing to follow discharge instructions including behavior restrictions based on discussions prior to administration?					yes	(no)
Estimate the patient's overlying tissue for attenuation and buildup: _____ cm	Not estimated					
Is a patient-to-bystander distance less than 1 m expected with a geometric modifying factor greater than 1?					(yes)	no
To Be Completed with Patient Input						
How long is the return trip home?	3 days with overnight stays					
Will someone accompany you on the return trip home?	(yes) / no	How will you be returning home?	(my vehicle)	bus	taxi	
			train	plane	other	
When will you return to work?	Retired	Do you spend more than 10 hours per week closer than 10 feet from the same person at work?			yes / (no)	
Who do you see in person on a routine basis?	Spouse and friends					
Do you anticipate spending more than an hour a day closer than arm's length (1 meter) from another individual?	(yes) / no	If yes, at what distance and for how long?	Sleeping with spouse			
Do you/have you ever needed help with the following tasks?	getting on and off chairs	walking	using the restroom	bathing		
	getting in and out of vehicles	cooking /eating	reading/understanding instructions	(none of the above)		
Do you live in an apartment or facility with other people in adjacent rooms/on adjacent floors?					yes	(no)
Are you currently nursing (breastfeeding) a child?	yes / (no)	Could you be pregnant?	yes / (no)	Do you share a bed with anyone?		(yes) / no
Are you able to sleep in your own bed without another person for some length of time after the procedure?						yes / (no)
Are you able and willing to change your behavior as directed by the specific preliminary posttreatment instructions discussed with and explained to you to minimize exposure to bystanders?						yes / (no)
Are you able and willing to change your behavior as directed by the specific final posttreatment instructions discussed with and explained to you to minimize exposure to bystanders?						yes / (no)
To Be Completed the Day of Administration by Licensee						
Confirm appropriate changes were made to the form and calculations if patient plans changed.						(yes) / no

EXAMPLE B – RELEASE OF PATIENT BASED ON ADMINISTERED ACTIVITY

A 56-year-old male receives an administration of 1.29 GBq ^{90}Y microspheres for the treatment of hepatocellular carcinoma. As shown in Columns 1 and 2 of Table 1, the basic activity thresholds are 34 GBq for authorizing patient release and 6.8 GBq for requiring dose-minimizing instructions, respectively. Because the administered activity of 1.29 GBq is below these basic thresholds, the licensee is authorized to release the patient without dose-minimizing instructions. Although some licensees may independently decide to issue dose-minimizing instructions to the patient, there is no regulatory requirement to do so. In this case, a patient-specific determination of modifying factors for biokinetics, occupancy, geometry, and attenuation is unnecessary. No records are required for regulatory purposes.

EXAMPLE C – RELEASE OF PATIENT WHO IS BREASTFEEDING

A 35-year-old female, who is breastfeeding a child, receives 0.74 GBq ^{18}F fluorodeoxyglucose for positron emission tomographic imaging. From Columns 1 and 2 of Table 1, the basic activity release threshold for ^{18}F is 13 GBq, and the threshold for instruction is 2.5 GBq, respectively. The assessment progresses through multiple stages as numerated in Figures C-3 and C-4 and described in the text.

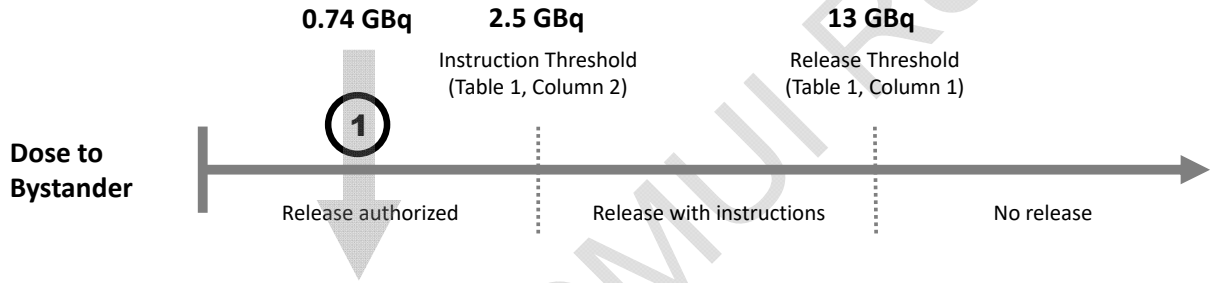

Figure C-3. Administered activity comparison to instruction and patient release thresholds.

The administered activity is less than both basic thresholds (release and instruction). Dose-minimizing instructions are not required to satisfy regulatory requirements for 10 CFR 35.75(a). Although some licensees may independently decide to issue dose-minimizing instructions in the patient's discharge instructions, there is no regulatory requirement to issue instructions. In this case, a patient-specific determination of modifying factors for biokinetics, occupancy, geometry, and attenuation is unnecessary.

Because the patient is breastfeeding, dose to the child from nursing is initially assessed assuming no breastfeeding interruption. From Column 2 of Table 3, the administered activity of 0.74 GBq is shown to exceed the 1-mSv activity threshold $Q_{B|ins}$ of 0.20 GBq. Therefore, a breastfeeding interruption time must be established and incorporated into the required breastfeeding instructions for discharge.

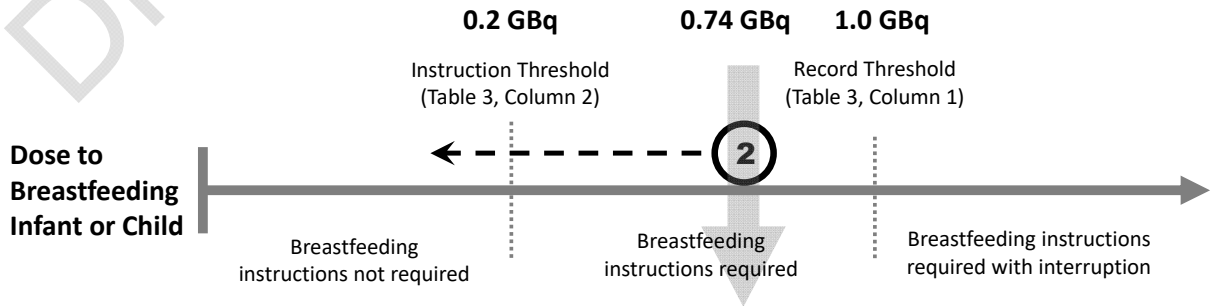

Figure C-4. Administered activity comparison to breastfeeding thresholds.

The licensee suggests a breastfeeding interruption time corresponding to a child dose of less than 1 mSv (0.1 rem). From Column 2 of Table 3, the retained activity in the patient of 0.20 GBq for $Q_{B|ins}$ equates to a child dose of 1 mSv (0.1 rem) for breastfeeding. For ^{18}F ($T_r = 1.83$ h) fluorodeoxyglucose, the licensee estimates the biological half-life specific to this patient as $T_b = 100$ h. The effective half-life is calculated as 1.80 h from Equation 5. According to Equation 6 for a retained activity equaling the tabulated $Q_{B|ins}$ value of 0.20 GBq, the breastfeeding interruption time is calculated to be 3.4 h from $1.44 \cdot 1.80 \cdot \ln\left(\frac{0.74}{0.20}\right)$. This interruption time is consistent with the recommendation in Table 4.

Because the administered activity exceeds $Q_{B|ins}$, the licensee is required to issue breastfeeding instructions if the patient could be breastfeeding after release. The patient can be released with instruction to interrupt breastfeeding and discard breastmilk for the specified time. As an alternative to discarding pumped breastmilk, breastmilk storage for radioactive decay can be permitted under direction by the licensee if desired. Because the administered activity did not exceed the record threshold $Q_{B|rec}$ of 1 GBq shown in Column 1 of Table 3, a record of instructions provided to the patient is not required.

EXAMPLE D – RELEASE OF PATIENT WITH INSTRUCTIONS BUT WITHOUT BEHAVIOR MODIFICATION

A 46-year-old female receives 2.0 GBq ^{131}I as sodium iodide for hyperthyroidism (i.e., thyroid ablation). From Columns 1 and 2 of Table 1, the basic activity threshold of ^{131}I for patient release is 0.32 GBq and the threshold over which instructions must be provided is 0.063 GBq. The administered activity is greater than both basic thresholds. The licensee decides to calculate patient-specific thresholds to determine if immediate release is allowable and if instructions are required.

The licensee applies a double exponential model for ^{131}I retention with uptake fractions of 0.2 and 0.8 for the extrathyroidal and thyroid components with respective effective half-lives of 7.7 h and 125 h. The biokinetic modifying factor for double exponential retention is calculated as a weighted sum of effective half-lives relative to the radiological half-life (Ref. C-1):

$$F_B = \frac{(0.20)(7.7\text{ h}) + (0.80)(125\text{ h})}{192\text{ h}} = 0.53. \qquad \text{(Equation C-7)}$$

During initial treatment plan discussions with the patient, the patient stated that she will be sleeping with her spouse 8 hours a day. The licensee determined that the spouse was the maximally exposed individual and the patient-specific occupancy factor was estimated to be 0.33. The geometry factor was estimated at 0.87 for a separation distance of 1 m for close contact with a point-like source for ^{131}I concentrated in the thyroid. To account for attenuation and buildup for this patient, the licensee assigns 2 cm as the tissue thickness overlying the thyroid and obtains F_A = 1.0 from Figure C-5, as reproduced from precalculated plots (Ref. C-1).

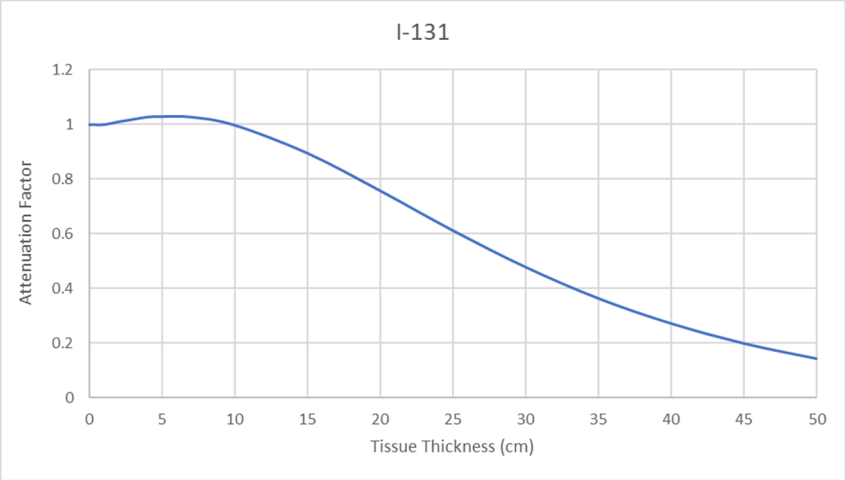

Figure C-5. Attenuation modifying factor for I-131 as a function of attenuating tissue thickness.

Using this initial information and Equation 8, the licensee calculates the following patient-specific thresholds for release and instruction

$$Q'_{rel} = \frac{0.32\ GBq}{0.53 \cdot 0.33 \cdot 0.87 \cdot 1.0} = 2.1\ GBq \qquad \text{(Equation C-8)}$$

and

$$Q'_{ins} = \frac{0.063\ GBq}{0.53 \cdot 0.33 \cdot 0.87 \cdot 1.0} = 0.41\ GBq. \qquad \text{(Equation C-9)}$$

However, on the day of procedure, the patient stated to the licensee that her plans had changed and she was going on a family vacation the very next day and the patient was not willing to modify any of her behaviors post treatment. The licensee amends the patient questionnaire, as shown in Figure C-6, in order to re-calculate the occupancy factor. The family trip is expected to take approximately 4 days (96 hours). During this trip, the licensee assumes 12 h per day of close contact (50 percent) for the maximally exposed bystander at a distance of 1 m. After this trip, 6 h per day of close contact (25 percent) is expected during routine family behavior. To account for these plans, the licensee calculates occupancy according to Equations B-3 and B-4 with a single effective half-life of 102 h (i.e., product of radiological half-life and the result from Equation C-7). In other words, and the effective half-life can be approximated as

$$T_e = F_B \times T_r = 0.53 \times 192\ \text{h} = 102\ \text{h}. \qquad \text{(Equation C-10)}$$

By neglecting a delay in bystander exposure on the day of administration and not including a time period for behavior modification, the licensee assigns the following delay, travel, and instruction times equate to

$$t_0 = \frac{0\ \text{h}}{102\ \text{h}} = 0;\quad t_1 = \frac{96\ \text{h}}{102\ \text{h}} = 0.94;\ \text{and}\ t_2 = \frac{0\ \text{h}}{102\ \text{h}} = 0 \qquad \text{(Equation C-11)}$$

effective half-lives, respectively. For parameter values described above, occupancy during the family trip (travel) is calculated as

$$F_1 = 0.5\left[e^{-0.693(0)} - e^{-0.693(0.94)}\right] = 0.24 \qquad \text{(Equation C-12)}$$

Occupancy for the long-time period after the family trip is calculated without an instruction period of behavior modification as

$$F_2 = 0.25\left[e^{-0.693(0.94)}\right] = 0.12 \qquad \text{(Equation C-13)}$$

Because bystander occupancy during and after travel relate to the same person in the patient's family, these results are summed to yield an occupancy factor of 0.36 for the maximally exposed bystander.

Based on this updated information according to the patient's plans, the licensee recalculates patient-specific thresholds for release and instruction

$$Q'_{rel} = \frac{0.32\ GBq}{0.53 \cdot 0.36 \cdot 0.87 \cdot 1.0} = 1.93\ GBq \qquad \text{(Equation C-14)}$$

and

$$Q'_{ins} = \frac{0.063\ GBq}{0.53 \cdot 0.36 \cdot 0.87 \cdot 1.0} = 0.38\ GBq. \qquad \text{(Equation C-15)}$$

The administered activity of 2.0 GBq exceeds the patient-specific activity threshold for release. By substituting terms in Equations 9 and B-5, a hold time can be calculated from the following relationship

$$t_{hold} = -\frac{T_e}{0.693} \ln\left(\frac{Q'_{rel}}{A_0}\right) \qquad \text{(Equation C-16)}$$

For the parameter values in this example,

$$t_{hold} = -\frac{102\ \text{h}}{0.693} \ln\left(\frac{1.93}{2.0}\right) = 5.2\ \text{h}. \qquad \text{(Equation C-17)}$$

After this hold time, the patient is authorized for release with dose-minimizing instructions. In this case, behavioral restrictions are not required over a specified time period, because the patient does not intend to adhere to those restrictions and the licensee has established a sufficient basis for release without behavior restrictions. A record of the basis for release is required because the calculation involved one or more of the following considerations: retained activity, occupancy factor less 0.25 at 1 meter, biological or effective half-life, or tissue shielding. The record must be retained for 3 years after the date of release. Calculating and releasing patients based on patient-specific thresholds will often require a record. Exceptions include an occupancy factor of at least 0.25 with a geometry factor consistent with 1 meter or closer and biokinetic and attenuation factors both equaling unity (1).

Figure C-6. Completed Questionnaire for Patient in Example D.

To Be Completed by the Licensee					
Patient Identification Number	802764113				
Patient is able and willing to follow discharge instructions including behavior restrictions based on discussions prior to administration?				yes	**no**
Estimate the patient's overlying tissue for attenuation and buildup: 2 cm					
Is a patient-to-bystander distance less than 1 m expected with a geometric modifying factor greater than 1?				**yes**	no
To Be Completed with Patient Input					
How long is the return trip home?	0.5 hours				
Will someone accompany you on the return trip home?	**yes** / no	How will you be returning home?	**my vehicle** / train	bus / plane	taxi / other
When will you return to work?	In 3 weeks	Do you spend more than 10 hours per week closer than 10 feet from the same person at work?			yes / **no**
Who do you see in person on a routine basis?	Husband and children				
Do you anticipate spending more than an hour a day closer than arm's length (1 meter) from another individual?	**yes** / no	If yes, at what distance and for how long?	Family vacation starting tomorrow		
Do you/have you ever needed help with the following tasks?	getting on and off chairs; walking; using the restroom; bathing; getting in and out of vehicles; cooking /eating; reading/understanding instructions; **none of the above**				
Do you live in an apartment or facility with other people in adjacent rooms/on adjacent floors?				yes	**no**
Are you currently nursing (breastfeeding) a child?	yes / **no**	Could you be pregnant?	yes / **no**	Do you share a bed with anyone?	**yes** / no
Are you able to sleep in your own bed without another person for some length of time after the procedure?					yes / **no**
Are you able and willing to change your behavior as directed by the specific preliminary posttreatment instructions discussed with and explained to you to minimize exposure to bystanders?					yes / **no**
Are you able and willing to change your behavior as directed by the specific final posttreatment instructions discussed with and explained to you to minimize exposure to bystanders?					yes / **no**
To Be Completed the Day of Administration by Licensee					
Confirm appropriate changes were made to the form and calculations if patient plans changed.					**yes** / no

EXAMPLE E – RELEASE OF PATIENT AFTER AN ADMINISTRATIVE HOLD

A 63-year-old male receives the first administration of 18.5 GBq ^{131}I iobenguane (AZEDRA) for cancer treatment. From Columns 1 and 2 of Table 1, the basic activity threshold of ^{131}I for patient release is 0.32 GBq and the threshold over which instructions must be provided is 0.063 GBq. The administered activity is greater than both basic thresholds. The licensee decides to calculate patient-specific thresholds to determine if immediate release is allowable and if instructions are required. Evaluation of patient release initially considers release at 56 hours after administration and the patient's spouse accompanying the patient on the 1-h trip home by private automobile. Per licensee direction and instruction, the patient agrees to sleep in a separate bed and minimize close contact with others for 7 days after returning home but requires physical assistance while at home. Dose-minimizing instructions are prepared consistent with these restrictions, and the daily close contact for physical assistance is assumed to be 2.4 h (10 percent) during the instruction period. After the instruction period of 7 days, the licensee anticipates that the patient and spouse will resume sharing a bed during the night and increases the fraction of daily close contact to 12 h (50 percent) after the instruction period.

The licensee obtains biokinetic information from pretreatment dosimetric data and finds the patient retained 38% of radioactivity at 96 h after administration. Therefore, according to Equation B-5,

$$F_B = -\frac{(0.693)\,(96\text{ h})}{(192\text{ h})\cdot\ln(0.38)} = 0.36, \qquad \text{(Equation C-18)}$$

and the effective half-life can be approximated as

$$T_e = F_B \times T_r = 0.36 \times 192\text{ h} = 69\text{ h}. \qquad \text{(Equation C-19)}$$

As described in Figure B-2, the delay, travel, and instruction times equate to

$$t_0 = \frac{56\text{ h}}{69\text{ h}} = 0.812;\quad t_1 = \frac{1\text{ h}}{69\text{ h}} = 0.014;\ \text{and}\ t_2 = \frac{168\text{ h}}{69\text{ h}} = 2.43 \qquad \text{(Equation C-20)}$$

effective half-lives, respectively.

Exposure to the patient's spouse is considered during travel and at home after travel. The licensee assumes the patient is in close contact with the spouse during the 1-h trip home. The occupancy factor is calculated from Equations B-3 and B-4.

For the parameter values described above, occupancy during travel is calculated from Equation B-3 as

$$F_1 = 1\left[e^{-0.693(0.812)} - e^{-0.693(0.826)}\right] = 0.006 \qquad \text{(Equation C-21)}$$

For this patient, the bystander occupancy during travel is small because the 1-h trip duration is a small fraction of the 69-h effective half-life, and the trip commences after a delay time of nearly one effective half-life.

According to Equation B-4, occupancy after travel includes exposure during and after the instruction period as follows

$$F_2 = 0.1\left[e^{-0.693(0.826)} - e^{-0.693(3.256)}\right] + 0.5\left[e^{-0.693(3.256)}\right] = 0.098 \qquad \text{(Equation C-22)}$$

Because bystander occupancy during and after travel relate to the same person (patient's spouse), these results are summed to yield an occupancy factor of 0.104 for the maximally exposed bystander. A record of the basis for authorizing patient release is required when the licensee uses an occupancy factor less than 0.25.

According to Table B-1, a geometry factor of 1.4 is assigned to a separation distance of 0.7 m for travel and daily physical assistance when instructions are followed to limit prolonged close contact. Because exposure during travel is negligible, the geometry factor of 1.4 is applied to close contact while the patient is receiving physical assistance.

To account for attenuation and buildup in the patient, the licensee obtains a girth measurement to estimate the torso radius (a measure of average tissue thickness) of 14 cm for this patient. From Figure C-7 as reproduced from supporting documentation (Ref. C-1), the licensee determines that $F_A = 0.92$.

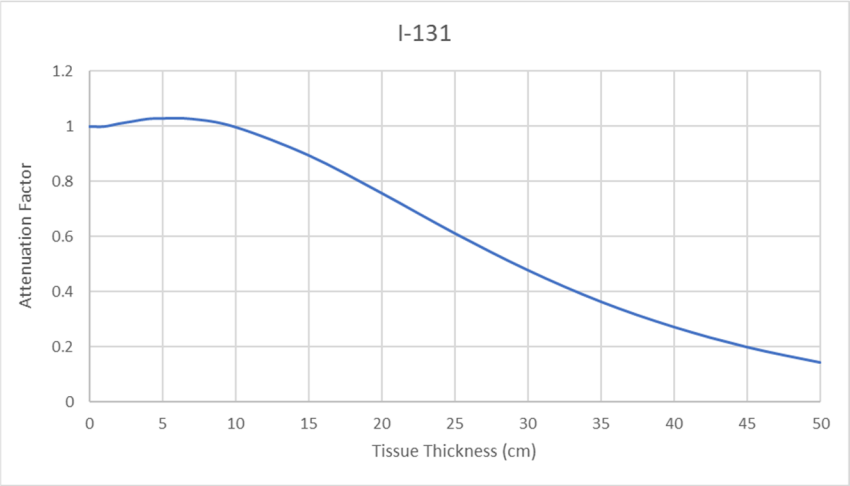

Figure C-7. Attenuation modifying factor for I-131 as a function of attenuating tissue thickness.

From Equation 8, patient-specific thresholds for release and instruction become

$$Q'_{rel} = \frac{0.32\ GBq}{0.36 \cdot 0.104 \cdot 1.4 \cdot 0.92} = 6.6\ GBq \qquad \text{(Equation C-23)}$$

and

$$Q'_{ins} = \frac{0.063\ GBq}{0.36 \cdot 0.104 \cdot 1.4 \cdot 0.92} = 1.3\ GBq \qquad \text{(Equation C-24)}$$

The administered activity of 18.5 GBq is greater than both patient-specific thresholds, so a hold time is calculated according to Equation 9 as

$$t_{hold} = \frac{96\ \text{h}}{\ln(0.38)} \ln\left(\frac{6.6}{18.5}\right) = 102\ \text{h} \qquad \text{(Equation C-25)}$$

For this high external dose-rate therapeutic procedure, this patient will be held in the medical facility for a total of 102 h after administration prior to being released to assure the 5-mSv dose limit will not likely be exceeded. After this hold time, the patient's retained activity is calculated to be less than the patient-specific release threshold (Q'_{rel}) but greater than the patient-specific instruction threshold (Q'_{ins}). A record of the basis for release is required because the calculation involved one or more of the following considerations: retained activity, occupancy factor less 0.25 at 1 meter, biological or effective half-life, or tissue shielding. The record must be retained for 3 years after the date of release. The record could include specifics of the administration, instructions provided to the patient, and justification for the selection of each modifying factor used in the calculation including the patient questionnaire or notes from a pretreatment discussion regarding patient behavior. Refer to Section 5 for guidance on records.

REFERENCE FOR APPENDIX C

C-1. 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) [1]

[1] Publicly available NRC published documents are available electronically through the NRC Library on the NRC's public Web site at http://www.nrc.gov/reading-rm/doc-collections/ and through the NRC's Agencywide Documents Access and Management System (ADAMS) at http://www.nrc.gov/reading-rm/adams.html. The documents can also be viewed online or printed for a fee in the NRC's Public Document Room (PDR) at 11555 Rockville Pike, Rockville, MD. For problems with ADAMS, contact the PDR staff at (301) 415-4737 or (800) 397-4209; fax (301) 415-3548; or e-mail pdr.resource@nrc.gov.