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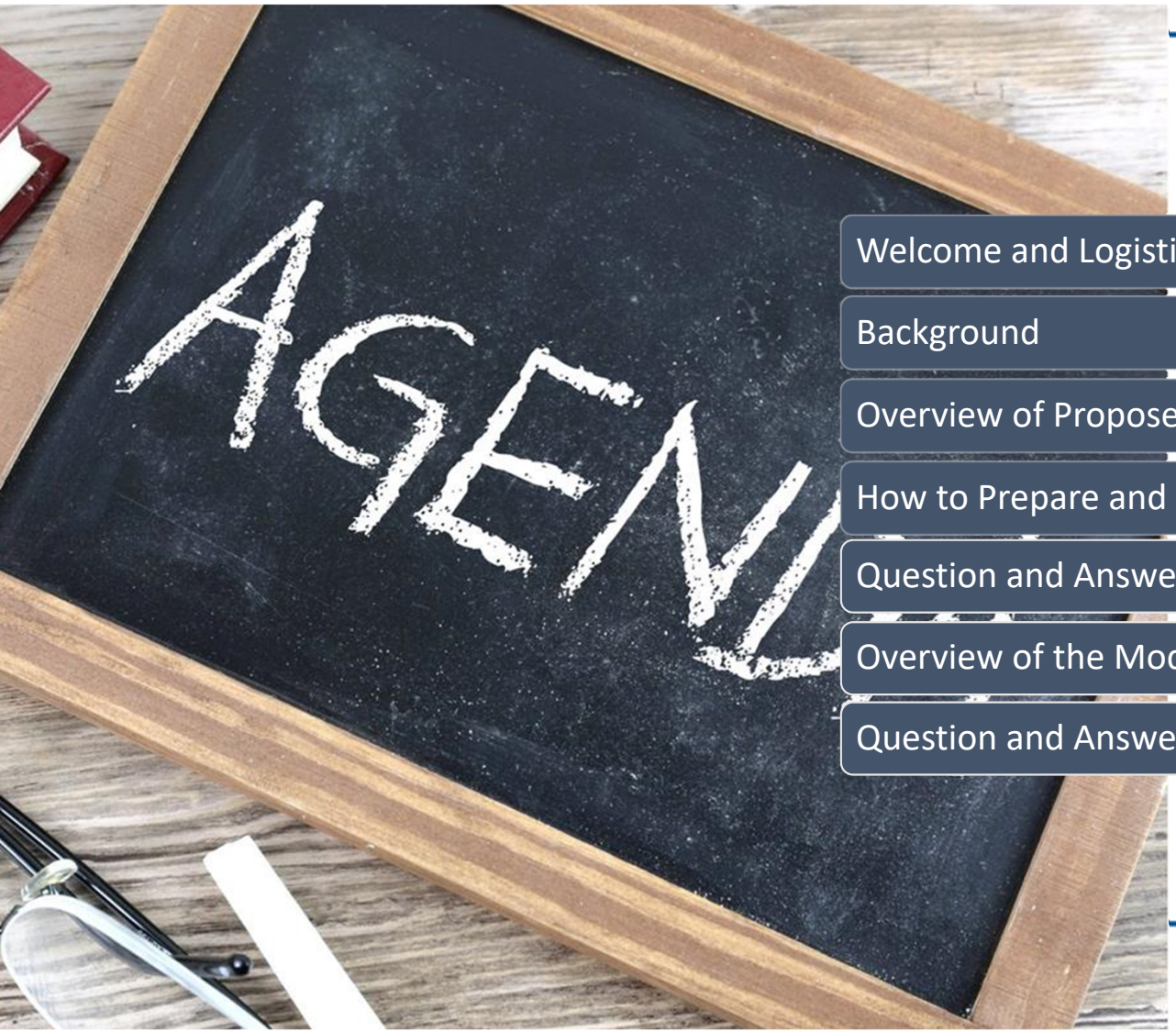
Public Meeting on Information Request

Draft Regulatory Guide 8061, "Release of Patients Administered Radioactive Material."

July 20, 2023



Agenda

- Welcome and Logistics
- Background
- Overview of Proposed Changes (Patient Perspective)
- How to Prepare and Submit Comments
- Question and Answer Session
- Overview of the Modifying Factors and Examples of Calculations
- Question and Answer Session

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Logistics

- Meeting is being transcribed
- Keep the line muted until you intend to speak
- Raise hand button in Teams (*5 on phone)
- Unmute button in Teams (*6 on phone)
- Chat feature available
- Presentation slides shown on the Microsoft Teams screen and in ADAMS at ML23198A203
- Phone attendees should email Brian.Allen3@nrc.gov for attendance

Purpose

- Provide an overview of the proposed changes to the NRC Regulatory Draft Guide (DG)-8061, “Release of Patients Administered Radioactive Material, ” to help the public prepare comments on the guide
- Share the different methods by which you may submit comments on the DG
  - The NRC is not seeking comments at this meeting.
  - *Comments should be submitted according to the instructions in the FRN (88 FR 38407) by August 20, 2023.*

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Opening Remarks

Kevin Williams
Division Director
Division of Materials Safety, Security, State, and Tribal Programs

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Background

Katie Tapp, PhD
Medical Physicist
Medical Radiation Safety Team

NRC Policy on Medical Use of Radioactive Materials

- The Nuclear Regulatory Commission (NRC) will regulate the uses of radioactive material in medicine as necessary to provide the radiation safety of workers and the general public.
- The NRC will not intrude into medical judgements affecting patients, except as necessary to provide for the radiation safety of workers and the general public.

Patient Release Regulations (10 CFR 35.75)

- 10 CFR 35.75 allows the licensee to **release from its control** any patient who has been administered radioactive material if the total radiation dose to any other individual from exposure to the released patient is **not likely to exceed 5 mSv** (500 mrem).
- Licensees **must provide written instructions** to the patient to maintain doses ALARA if the exposure to any other individual is **likely to exceed 1 mSv** (100 mrem).
- Licensee **must also provide specific instructions** if the total effective dose equivalent to a nursing infant or child could exceed **1 mSv (100 mrem), assuming there was no interruption of breastfeeding**.

Patient Release Regulations (10 CFR 35.75)

- The limits are for **each patient treatment**.
- The NRC regulations apply to the licensee, and not the patients.
- Regulatory Guide 8.39 provides **guidance** on how licensees can demonstrate they meet this requirement.

Evaluation of Regulatory Requirements for Patient Release

- In January 2018, the NRC completed an evaluation of its patient release program.
- Results were published in SECY-18-0015, Staff Evaluation of the U.S. Nuclear Regulatory Commission's Program Regulating Patient Release After Radioisotope Therapy
- Findings –
  - The regulations are adequate to protect the public
  - Guidance update is needed as methodology in the guidance can **UNDERESTIMATE** potential dose to a member of the public in some situations.

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RG 8.39, Release of patients administered radioactive material, Revision 1

- Current version of patient release guidance
- Issued in April 2020 to include recommendations for:
  - Pretreatment discussions
  - Patient instructions to maintain doses ALARA
  - Additional instructions provided to the NRC during public comments by the industry
  - Patient acknowledgement of instructions
- The current draft did not include significant updates to these sections

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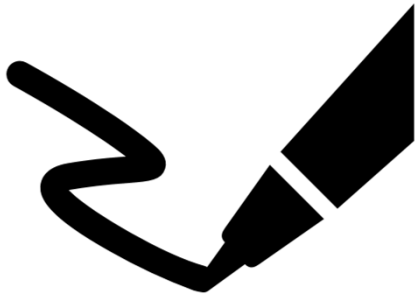
General Overview of Proposed Changes

Katie Tapp, PhD
Medical Physicist
Medical Radiation Safety Team

DG 8061, Release of patients administered radioactive material



- Proposed Draft Regulatory Guidance (DG) to update Regulatory Guide (RG) 8.39
- Proposed changes include
  - Updated dosimetry methodology
  - Updated breastfeeding cessation guidelines
- The NRC is requesting public comments until August 20, 2023 (88 FR 38407)

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Baseline and patient specific release

Two-tiered approach to release - baseline thresholds and patient specific release values

Administered activity and measured dose rate baseline thresholds that licensees can use to release patients without gathering patient specific information.

The proposed revision provides updated guidance on how patient specific information can be used to demonstrate release would comply with regulations.

Exposure Pathways

- The equations provided in the DG consider external exposure and do not include internal exposure due to uptake by the individual other than the patient.
- Previous studies and NRC evaluation found potential intake by household members and other members of the public is negligible (less than a few percent) relative to external doses, when instructions are followed.
- Instructions and precaution recommendation were not updated in this DG as they were recently updated in the last revision.

Baseline Thresholds

- Added new radionuclides to the table, such as Lu-177.
- Used **CONSERVATIVE** assumptions to ensure all released patients are not likely to cause exposure to other individuals in excess of 5 mSv (500 mrem).
- Due to these **CONSERVATIVE** assumptions, licensees do not need patient specific information to release patients who have administered activity (or have measured dose rates) below values found in the tables.

Table 1. Basic Activity Thresholds for Radionuclides

RADIONUCLIDE	COLUMN 1 Patient Release Threshold[d] Q_{rel} (GBq)	(mCi)	COLUMN 2 Instruction Threshold[d] Q_{ins} (GBq)	(mCi)
F-18	13	350	2.5	68
Ga-67	2.1	57	0.42	11
Ga-68	22	590	4.4	120
Ho-166[a]	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[c]	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[c]	0.016	0.43	0.0033	0.089
Kr-81m[b]	-	-	-	-
Lu-177	4.1	110	0.82	22
N-13[b]	-	-	-	-
O-15[b]	-	-	-	-
P-32[a]	9.2	250	1.8	49

Patient Specific Release

- If a patient has administered activity (or measured dose rate) **above** baseline thresholds, patient specific information is needed to determine if release can be **authorized**.
- Patient specific information is used to add **realism** to the **conservative** assumptions used to develop the baseline threshold values.

Patient Specific Release

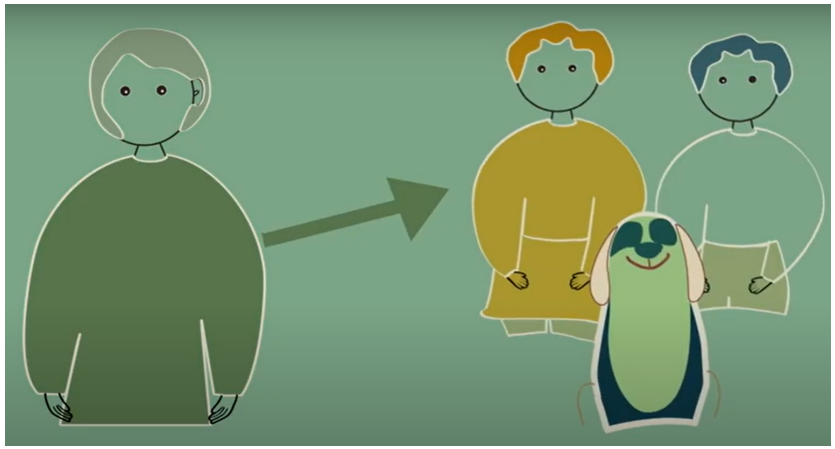
- The proposed draft guidance recommends use of 4 modifying factors to change the baseline thresholds based on patient release information.
  - Occupancy (F_O)
  - Geometry (F_G)
  - Attenuation (F_A)
  - Biokinetics (F_B)
- Licensees can choose to use patient specific information for some factors while keeping conservative values for others

Occupancy Factor

- Occupancy factor is the amount of time an individual is near the patient while the radioactive material decays.
- The less time the individual is near the patient while the material decays, the less exposure they will receive.
- The baseline threshold assumes an individual is 1 meter away from a patient all the time.
- To determine a patient specific occupancy factor, patient specific information is necessary.

Geometry Factor

- The baseline threshold assumes:
  - A **conservative** geometry where the source and individual exposed are points
  - That the patient and individual are **always** 1 meter away
- The geometry factor allows licensees to modify the likely exposure scenarios based on:
  - Conversations with the patient to determine likely distance and geometry of exposure scenarios, and
  - Medical knowledge of where the radionuclide will travel inside the patient



Patient Questionnaire to Determine Patient-Specific Occupancy and Geometry Modifying Factors to Ensure Compliance with 10 CFR 35.75 Release Criteria

Patient Name: **Referring Physician:**

Patient Identification Number: _____ **Age:**_____

Prescribed Dose:_____**Radiopharmaceutical:** _____

1. For female patients between 12-55 years old:
   - Confirmation that the patient is not pregnant
     - Date of negative pregnancy test: _____ (Should be within 24 hours of dosing)
     - Other (Tubal Ligation, Hysterectomy, etc.): _____
   - Is the patient breastfeeding? Yes _____ No _____ NA _____
2. What will be the mode of transportation for the patient to travel to place of residence (e.g., car, train, bus), how long will it take to travel, and who will be traveling with the patient?
   _____
3. List individuals who will have significant contact with the patient after administration. For each individual, list the type(s) of close contact to determine distance and geometry and length of time they expect to have contact with the patient? Consider all places where patient will spend significant time such as work and residence (Additional fields maybe necessary if the patient has significant contact with more individuals).

   The following questions should be used to support filling out the table.
   - Who will the patient reside with after administration?
   - Will the patient share a bed with anyone after administration?
   - Will the patient care for any young children or individuals requiring assistance?
   - Will the patient require living or medical assistance?
   - Will the patient have close contact at their occupation or other places outside their residence?

Person	Type of Close Contact	Length of Time (hrs/day)

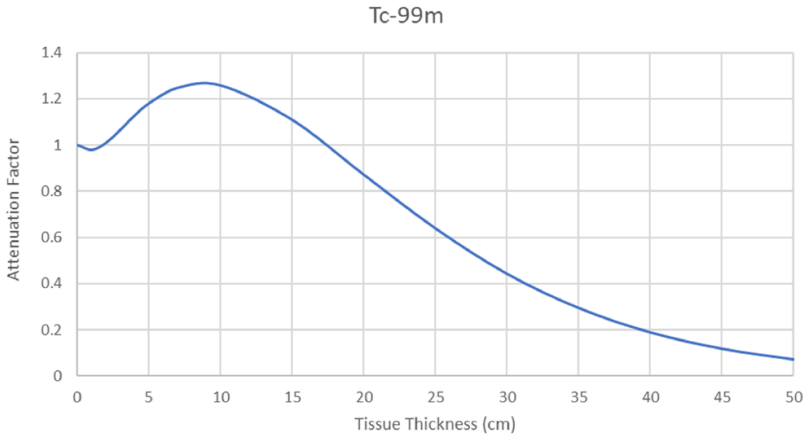
4. Is the patient scheduled for travel, vacation, or medical procedure for 2 weeks after administration? Yes _____ No _____
5. Is the patient incontinent or have any urinary bladder control problems? Yes ____ No____
6. Is the patient able and willing to follow any necessary discharge instructions, including behavior restrictions, based on discussions before administration? Yes _____ No _____
7. 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: _____

Individual who verified questionnaire answers and patient understanding of instructions (as necessary) on date of administration: _____ Date:_____

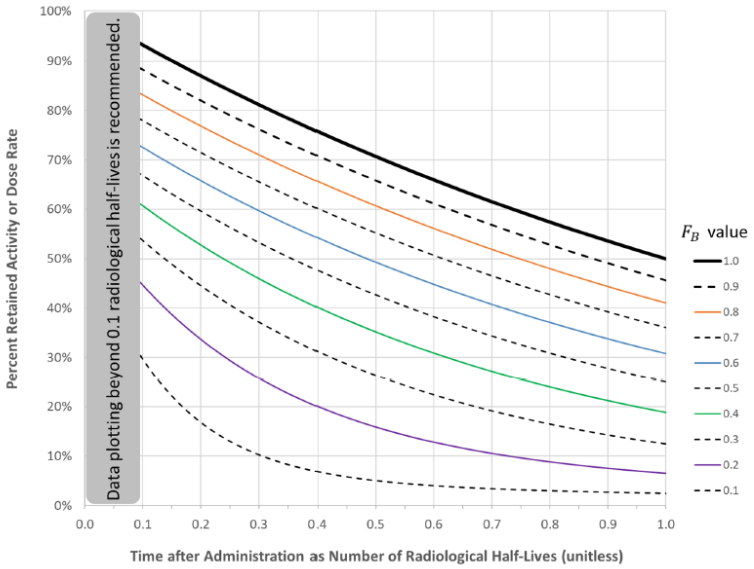
Attenuation Factors

- Baseline threshold assumes no attenuation (shielding) or buildup between source and individual.
- Patient specific attenuation factor is dependent on the expected depth of the source in the body.
- Attenuation factors can be greater than 1.
- Licensees should use the most conservative attenuation factor for the radionuclide if they do not plan to determine patient specific attenuation factors as conservatism is being removed from other factors.
- The DG provides the most conservative values and graphs for licensees to select attenuation values if thickness is known.



Biokinetic Factors

- The baseline threshold **conservatively** assumes no biological removal of the radionuclide.
- Licensees can continue to use this conservative assumption when patient's retention data is unknown.
- The DG provides guidance on how licensees can adjust for patient specific excretion (i.e., removal) for additional realism.



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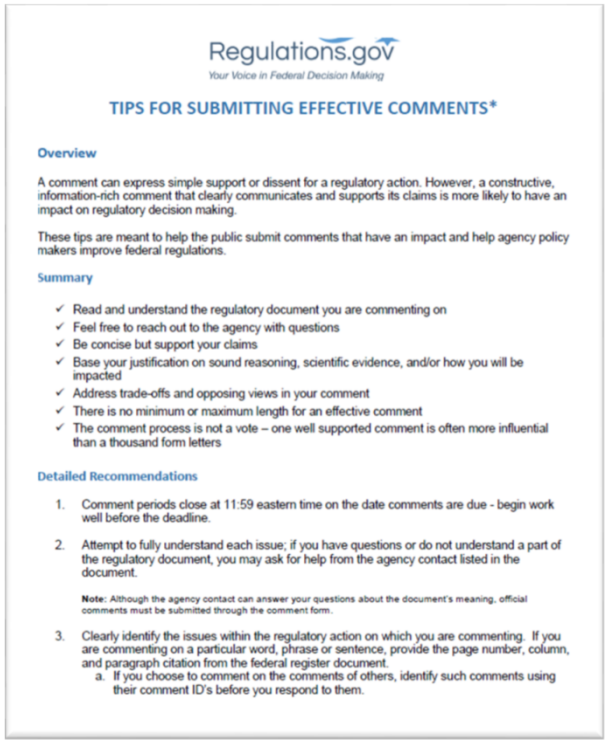
How to Prepare and Submit Comments

Tips for Preparing Comments

- Review the Commenter's Checklist on Regulations.gov



Regulations.gov
Your Voice in Federal Decision Making

TIPS FOR SUBMITTING EFFECTIVE COMMENTS*

Overview

A comment can express simple support or dissent for a regulatory action. However, a constructive, information-rich comment that clearly communicates and supports its claims is more likely to have an impact on regulatory decision making.

These tips are meant to help the public submit comments that have an impact and help agency policy makers improve federal regulations.

Summary

- ✓ Read and understand the regulatory document you are commenting on
- ✓ Feel free to reach out to the agency with questions
- ✓ Be concise but support your claims
- ✓ Base your justification on sound reasoning, scientific evidence, and/or how you will be impacted
- ✓ Address trade-offs and opposing views in your comment
- ✓ There is no minimum or maximum length for an effective comment
- ✓ The comment process is not a vote – one well supported comment is often more influential than a thousand form letters

Detailed Recommendations

1. Comment periods close at 11:59 eastern time on the date comments are due - begin work well before the deadline.
2. Attempt to fully understand each issue; if you have questions or do not understand a part of the regulatory document, you may ask for help from the agency contact listed in the document.

   Note: Although the agency contact can answer your questions about the document's meaning, official comments must be submitted through the comment form.
3. Clearly identify the issues within the regulatory action on which you are commenting. If you are commenting on a particular word, phrase or sentence, provide the page number, column, and paragraph citation from the federal register document.
   a. If you choose to comment on the comments of others, identify such comments using their comment ID's before you respond to them.

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Methods for Submitting Comments

- **Regulations.gov**: comment form
  Docket ID NRC-2023-0086

  or

- **Email**: Rulemaking.Comments@nrc.gov

  or

- **Mail**: Secretary, U.S. Nuclear Regulatory Commission, Washington, DC 20555–0001
  ATTN: Rulemakings and Adjudications Staff

33407

Proposed Rules

Federal Register
Vol. 88, No. 113
Tuesday, June 13, 2023

This section of the FEDERAL REGISTER contains notices to the public of the proposed issuance of rules and regulations. The purpose of these notices is to give interested persons an opportunity to participate in the rule making prior to the adoption of the final rules.

NUCLEAR REGULATORY COMMISSION

10 CFR Part 35

[NRC–2023–0086]

Draft Regulatory Guide: Release of Patients Administered Radioactive Material

AGENCY: Nuclear Regulatory Commission.

ACTION: Draft guide; extension of comment period.

SUMMARY: On April 21, 2023, the U.S. Nuclear Regulatory Commission (NRC) solicited comments on draft regulatory guide (DG), DG–0067, ''Release of Patients Administered Radioactive Material.'' The public comment period was originally scheduled to close on June 20, 2023. The NRC has decided to extend the public comment period to allow more time for members of the public to develop and submit their comments.

DATES: The due date for comments requested in the document published on April 21, 2023 (88 FR 24468) is extended. Comments should be submitted no later than August 20, 2023. Comments received after this date will be considered, if it is practical to do so, but the Commission is able to ensure consideration only for comments received on or before this date.

ADDRESSES: You may submit comments by any of the following methods; however, the NRC encourages electronic comment submission through the Federal rulemaking website:

• *Federal rulemaking website:* Go to https://www.regulations.gov and search for Docket ID NRC–2023–0086. Address questions about Docket IDs in Regulations.gov to Stacy Schumann; telephone: 301–415–0624; email: Stacy.Schumann@nrc.gov. For technical questions, contact the individuals listed in the **FOR FURTHER INFORMATION CONTACT** section of this document.

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

For additional direction on obtaining information and submitting comments, see ''Obtaining Information and Submitting Comments'' in the **SUPPLEMENTARY INFORMATION** section of this document.

FOR FURTHER INFORMATION CONTACT: Katherine Tapp, Office of Nuclear Material Safety and Safeguards, telephone: 301–415–0236, email: Katherine.Tapp@nrc.gov, or Brian Allen, Office of Nuclear Regulatory Research, telephone: 301–415–6462, email: Brian.Allen@nrc.gov, or Rigel Flora, Office of Nuclear Regulatory Research, telephone: 301–415–3090, email: Rigel.Flora@nrc.gov, or Harriet Karagiannis, Office of Nuclear Regulatory Research, telephone: 301–415–2493, email: Harriet.Karagiannis@nrc.gov. All are staff of the U.S. Nuclear Regulatory Commission, Washington, DC 20555–0001.

SUPPLEMENTARY INFORMATION:

I. Obtaining Information and Submitting Comments

I. Obtaining Information

Please refer to Docket ID NRC–2023–0086 when contacting the NRC about the availability of information for this action. You may obtain publicly available information related to this action by any of the following methods:

• *Federal Rulemaking website:* Go to https://www.regulations.gov and search for Docket ID NRC–2023–0086.

• *NRC's Agencywide Documents Access and Management System (ADAMS):* You may obtain publicly available documents online in the ADAMS Public Documents collection at https://www.nrc.gov/reading-rm/adams.html. To begin the search, select ''Begin Web-based ADAMS Search.'' For problems with ADAMS, please contact the NRC's Public Document Room (PDR) reference staff at 1–800–397–4209, 301–415–4737, or by email to PDR.Resource@nrc.gov.

• *NRC's PDR:* You may examine and purchase copies of public documents, by appointment, at the NRC's PDR, Room P1 B35, One White Flint North, 11555 Rockville Pike, Rockville, Maryland 20852. To make an appointment to visit the PDR, please send an email to PDR.Resource@nrc.gov or call 1–800–397–4209 or 301–415–4737, between 8 a.m. and 4 p.m. eastern time (ET), Monday through Friday, except Federal holidays.

II. Submitting Comments

The NRC encourages electronic comment submission through the Federal rulemaking website (https://www.regulations.gov). Please include Docket ID NRC–2023–0086 in your comment submission.

The NRC cautions you not to include identifying or contact information that you do not want to be publicly disclosed in your comment submission. The NRC will post all comment submissions at https://www.regulations.gov as well as enter the comment submissions into ADAMS. The NRC does not routinely edit comment submissions to remove identifying or contact information.

If you are requesting or aggregating comments from other persons for submission to the NRC, then you should inform those persons not to include identifying or contact information that they do not want to be publicly disclosed in their comment submission. Your request should state that the NRC does not routinely edit comment submissions to remove such information before making the comment submissions available to the public or entering the comment into ADAMS.

II. Discussion

On April 21, 2023, the NRC published a document in the **Federal Register** (88 FR 24468) requesting comments on DG–0067, ''Release of Patients Administered Radioactive Material.'' This DG is proposed Revision 2 to Regulatory Guide (RG) 8.39 of the same title. This proposed revision provides licensees with methods that are acceptable to the NRC for the release of patients after a medical procedure involving the administration of unsealed byproduct material, such as radiopharmaceuticals, or implants that contain radioactive material. The comment period was originally scheduled to close on June 20, 2023. Upon the request of the medical community, the NRC has decided to extend the public comment period on this document until August 20, 2023, to allow more time for members of the public to submit their comments.

Next Steps

- Public comment period ends: August 20, 2023
- NRC staff updates draft regulatory guide based on public comments and feedback prior to publishing final regulatory guide 8.39, “Release of Patients Administered Radioactive Material.”

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Public Feedback and Questions

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WE ARE ON BREAK.

We will return at 1:30pm ET for the second part of the meeting.

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PROPOSED PHASE 2 UPDATES TO REGULATORY GUIDE 8.39 ON PATIENT RELEASE: DOSIMETRY METHODOLOGY

JULY 20, 2023

RCD RADIATION PROTECTION ASSOCIATES

David M. Hamby, PhD

OVERVIEW

- Phase 2 revisions to Regulatory Guide 8.39 are intended to update the dosimetry methodology
- Proposed direction provides versatile, realistically-conservative dosimetry
- Basic activity thresholds with the ability, if necessary, to generate patient-specific values
- Thresholds are based on maximum dose equivalent limits found in 10 CFR 35.75
- Through patient instruction & interruption, breastfeeding infants are protected to 1 mSv
- Emerging technologies are easily supported with the new methodology

WHAT'S DIFFERENT GIVEN PHASE 2 REVISIONS?

- If the administered activity (A_0) is less than the basic activity threshold appearing in Table 1:
  - there is no change for the licensee
- If, however, A_0 is greater than the activity threshold listed in Table 1, the license should select one of the following options for patient release:
  - release the patient based on measured dose rates (Table 2);
  - release the patient based on retained activity instead of administered activity;
  - calculate patient-specific activity thresholds to determine patient release; or
  - calculate a hold time prior to patient release.
- For a breastfeeding patient …
  - if A_0 is less than the revised breastfeeding threshold (Table 3), there is no change for the licensee
  - if, however, A_0 is greater than the breastfeeding threshold, the licensee should calculate a breastfeeding interruption time and advise the patient accordingly

TABLE 1

RADIONUCLIDE	COLUMN 1 ACTIVITY AT OR BELOW WHICH PATIENTS MAY BE RELEASED (GBq)	(mCi)	DOSE RATE AT 1 METER, AT OR BELOW WHICH PATIENTS MAY BE RELEASED (mSv/h)	(mrem/h)
Ag-111	20	540	0.08	8
Au-198	3.7	93	0.21	21
Cr-51	4.8	130	0.02	2
Cu-64	8.4	230	0.27	27
Cu-67	14	390	0.22	22
Ga-67	8.7	240	0.18	18
I-123	6.0	160	0.26	26
I-125	0.25	7	0.01	1
I-125 implant	0.33	9	0.01	1
I-131	1.2	33	0.07	7
In-111	2.4	64	0.2	20
Ir-192 implant	0.074	2	0.008	0.8
P-32[c]	c	c	c	c
Pd-103 implant	1.5	40	0.03	3
Re-186	28	770	0.15	15
Re-188	29	790	0.20	20
Sc-47	11	310	0.17	17
Se-75	0.089	2	0.005	0.5
Sm-153	26	700	0.3	30
Sn-117m	1.1	29	0.04	4
Sr-89[c]	c	c	c	c
Tc-99m	28	760	0.58	58
Tl-201	16	430	0.19	19
Yb-169	0.37	10	0.02	2

Current

RADIONUCLIDE	COLUMN 1 ACTIVITY AT OR BELOW WHICH PATIENTS MAY BE RELEASED (GBq)	(mCi)	DOSE RATE AT 1 METER, AT OR BELOW WHICH PATIENTS MAY BE RELEASED (mSv/h)	(mrem/h)
I-124	5.4	140	0.20	20
I-125	2.0	54	0.074	7.4
I-125 implant[a]	2.3	62	0.084	8.4
I-131	8.6	230	0.32	32
In-111	17	460	0.64	64
Ir-192	0.41	11	0.015	1.5
Ir-192 implant[a]	0.43	11	0.016	1.6
Lu-177	110	3000	4.1	410
N-13	3800	100000	140	14000
O-15	18,000	490000	680	68000
P-32[b]	250	6700	9.2	920
P-33[b]	1,700	46000	64	6400
Pd-103	7.3	200	0.27	27
Pd-103 implant[a]	11	290	0.39	39
Ra-223	7.3	200	0.27	27
Rb-82	26,000	700000	960	96000
Re-186	170	4500	6.2	620
Re-188	180	4900	6.6	660
Ru-106[b]	430	11000	16	1600
Ru-106[b] implant[a]	4,900	130000	180	18000
Sc-47	5,400	150000	200	20000
Se-75	84	2300	3.1	310
Sm-153	0.22	6	0.0080	0.8
Sn-117m	180	4900	6.8	680
Sr-89[b]	810	22000	30	3000
Sr-90[b]	32	860	1.2	120
Tc-99m	2.0	54	0.073	7.3
Tl-201	57	1500	2.1	210
Xe-127	920	25000	34	3400
Xe-133	2.5	68	0.094	9.4
Y-90[b]			0.21	21
Yb-169				
Zr-89				

Proposed

RADIONUCLIDE	COLUMN 1 Patient Release Threshold Q_{rel} (GBq)	(mCi)	COLUMN 2 Instruction Threshold Q_{ins} (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[a]	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	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	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	0.065	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	0.085
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	33
Re-188	16	430	3.1	84
Ru-106[b]	180	4,900	36	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	0.24	6.4
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

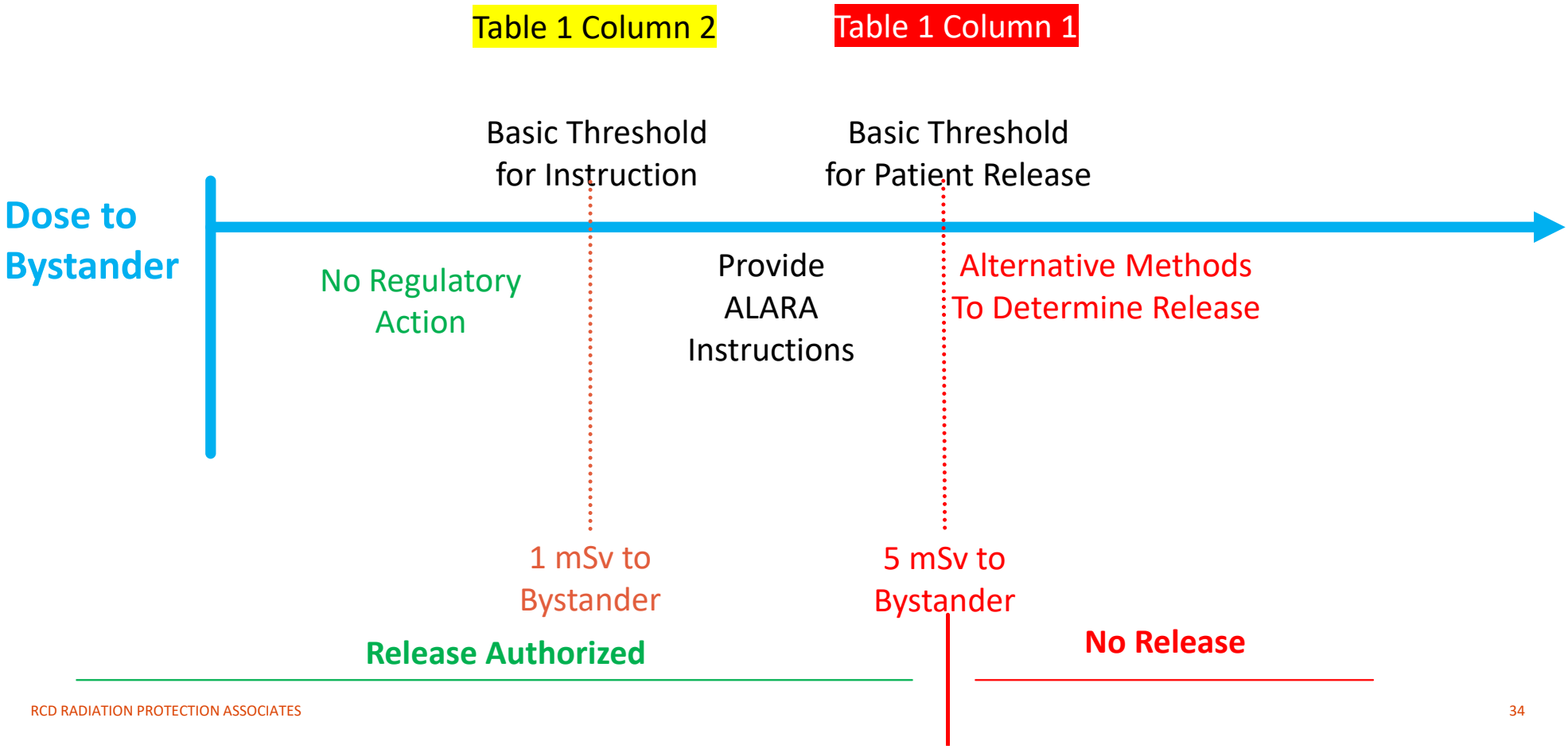
Several radionuclides have been added (from 22 to 52)

Threshold decreases from 1.2 GBq to 0.32 GBq (a factor of 4) because the assumption of 25% occupancy for nuclides with $T_r > 1$ day has been removed

At this stage of the methodology, 100% occupancy is assumed for all radionuclides

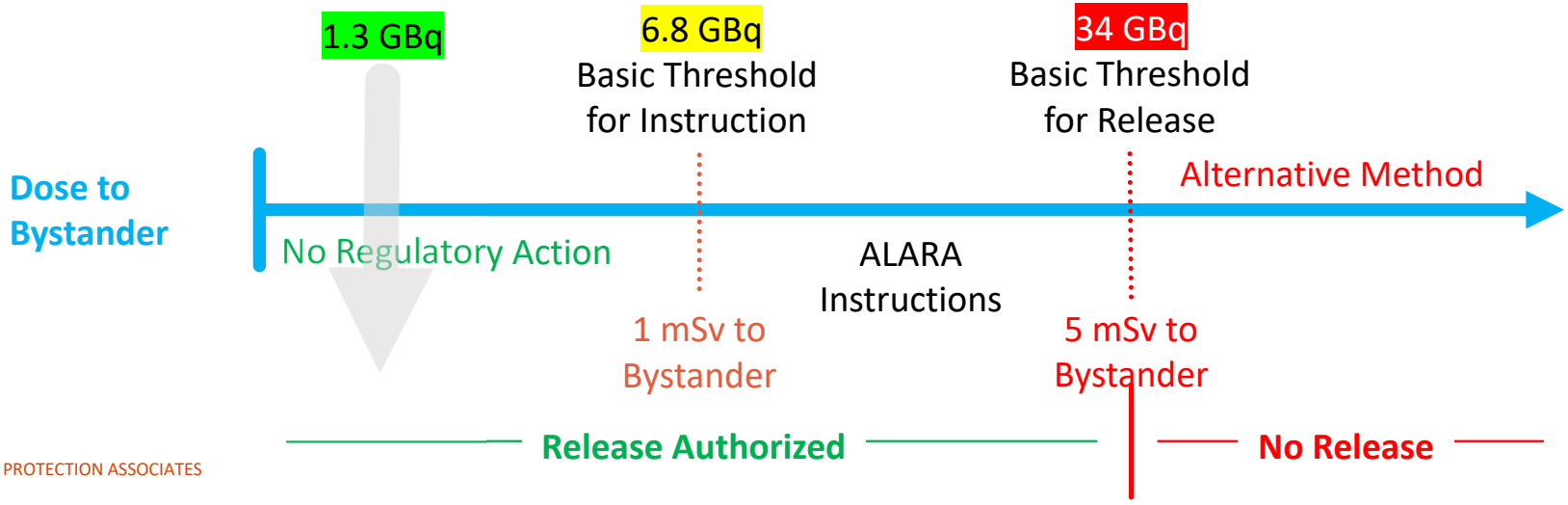
Pure beta emitters have been added (bremsstrahlung)

THRESHOLD FRAMEWORK



EXAMPLE 1: BASELINE RELEASE

- 56-year-old male administered 1.3 GBq of ^{90}Y microspheres for the treatment of hepatocellular carcinoma
- Because this is a pure beta emitter, the current release/instruction thresholds are non-existent
- From proposed Table 1, the basic activity thresholds are 34 GBq (for release) and 6.8 GBq (for instructions)
- Because 1.3 GBq is below both thresholds, the licensee is authorized to release the patient without dose-minimizing instructions



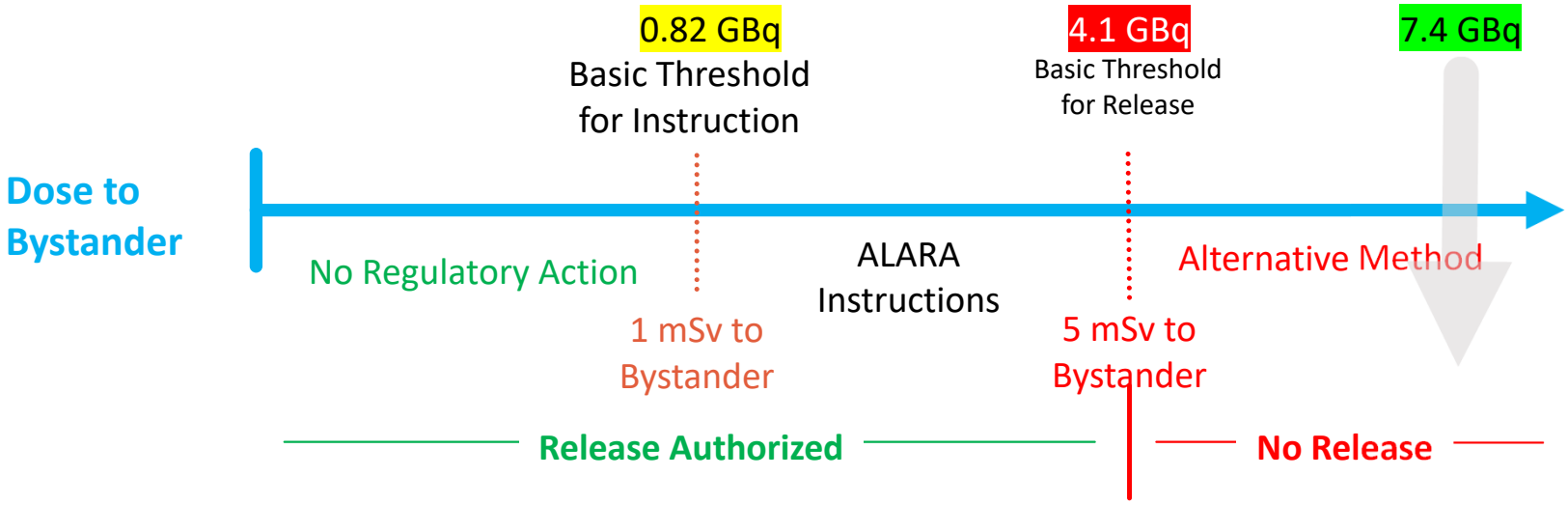
CALCULATING THE PATIENT-SPECIFIC THRESHOLDS

- In the proposed method, if a patient cannot be released based on the basic activity thresholds (Q) found in Table 1, the licensee may want to determine patient-specific activity thresholds (Q')
- To carry out this calculation, modifying factors for biokinetics (F_B), occupancy (F_O), geometry (F_G), and attenuation (F_A) are determined
- The patient-specific threshold is calculated using:

$$Q' = \frac{Q}{F_B \cdot F_O \cdot F_G \cdot F_A}$$

EXAMPLE 2: PATIENT-SPECIFIC RELEASE

- 75-year-old male administered 7.4 GBq of ^{177}Lu vipipotide tetraxetan for the treatment of metastatic castration-resistant prostate cancer
- From proposed Table 1, the basic activity thresholds are 4.1 GBq (for release) and 0.82 GBq (for instructions)
- 7.4 GBq is above both thresholds, therefore the licensee decides to calculate patient-specific thresholds



EXAMPLE 2: OCCUPANCY FACTOR

- During the initial patient interview, the patient states:
  - his spouse will drive him home after administration; he is sitting in the back seat of a private vehicle
  - as normal, he plans to sleep next to his spouse (king-size bed)
  - he eats meals with his spouse, but the two are in close proximity for no more than 4 waking hours in a day
  - no other individuals live in the house, but his daughter plans to stop by for dinner a few days after treatment
  - he is retired and can stay home for the first few days after treatment
  - he plans to get groceries and go to church on the weekends
- Thus, over the first few weeks (6.7-day half-life), the maximally exposed individual is likely the patient's spouse
- Assuming 8 hours of sleep and 4 hours of contact, the CONSERVATIVE patient-specific occupancy factor is:

$$F_O = \frac{(8+4)\ h}{24\ h} = 0.5$$

EXAMPLE 2: GEOMETRY FACTOR

- The patient's spouse is likely the maximally exposed individual and it is assumed that exposures (on average) will occur at approximately 1 meter
- The licensee chooses to assume that the radiation source is a point, but that radiation dose absorbed by the spouse (bystander) is better represented assuming a line receptor
- From Table B-1 of the draft Regulatory Guide 8.39, this orientation results in a geometry modifying factor of:

Patient-to-Bystander Separation Distance, r (m)	Point-Line[a] F_G (unitless)	Line-Line F_G (unitless)	Point-Point F_G (unitless)
0.3 (typical for mobility assistance, holding child[b], holding while co-sleeping[b])	5.6	4.6	11
0.5	2.7	2.3	4.0
0.7 (typical for travel seating)	1.6	1.4	2.0
1.0 (typical for close contact[b] activities)	0.87	0.79	1
1.5	0.42	0.39	0.44
2.0	0.25	0.25	0.25
Distances greater than 2 m	$\frac{1}{r^2}$	$\frac{1}{r^2}$	$\frac{1}{r^2}$

$$F_G = 0.87$$

EXAMPLE 2: BIOKINETIC AND ATTENUATION FACTORS

- In this initial determination, the licensee chooses to use the most conservative biokinetic and attenuation factors in place of patient specific values
- Most conservative biokinetic factor is always: $F_B = 1$
- Attenuation factors are radionuclide specific, and their maximum value can be found in Table A-1 of the draft regulatory guide
- This factor includes both attenuation and build up and, at times, can be greater than 1; the maximum value listed in Table A-1 for ^{177}Lu is:

$$F_A = 1.25$$

EXAMPLE 2: PATIENT-SPECIFIC ACTIVITY THRESHOLDS

- For this patient, and depending on their stated plans, habits, etc., the release and instruction thresholds for an administration of Lu-177 are:

$$Q'_{rel} = \frac{Q_{rel}}{F_B \cdot F_O \cdot F_G \cdot F_A} = \frac{4.1\ GBq}{1 \cdot 0.5 \cdot 0.87 \cdot 1.25} = 7.5\ GBq$$

7.4 GBq

$$Q'_{ins} = \frac{Q_{ins}}{F_B \cdot F_O \cdot F_G \cdot F_A} = \frac{0.82\ GBq}{1 \cdot 0.5 \cdot 0.87 \cdot 1.25} = 1.5\ GBq$$

- Recall, this patient received an administration of 7.4 GBq
- The patient can be released, but must be provided dose-minimizing instructions
  - … and those instructions must be consistent with stated plans, sleeping arrangement, etc. and ALARA considerations

EXAMPLE 3: IODINE ADMINISTRATION

- 46-year-old female administered 1.8 GBq of ^{131}I as sodium iodide
- Proposed basic activity thresholds (Table 1) for ^{131}I are Q_{rel} = 0.32 GBq (release) and Q_{ins} = 0.063 GBq (instructions)
  - recall, current release threshold is 1.2 GBq for ^{131}I
- Because 1.8 GBq is greater than both thresholds, the licensee decides to calculate patient-specific thresholds
- The licensee chooses to determine a value for each modifying factor

- With patient-specific thresholds, is immediate release allowable?
- Are instructions required?

EXAMPLE 3: BIOKINETICS, F_B

- Consistent with current guidance (Table B-1) and several citations in the literature, the licensee assumes a double-exponential retention model for elemental iodine
- Uptake fractions of 0.2 and 0.8 for the extrathyroidal and thyroid components are assumed, with effective half-lives of 7.7 hours and 125 hours, respectively
- I-131 has a radiological half-life of 192 hours
- The biokinetic modifying factor can be calculated as a weighted sum of effective half-lives in the two components divided by the radiological half-life:

$$F_B \equiv \frac{T_e}{T_r} = \frac{(0.2)(7.7\ h) + (0.8)(125\ h)}{192\ h} = 0.53$$

EXAMPLE 3: OCCUPANCY, F_O

- During the initial patient interview regarding the treatment plan, the patient states …
  - she will drive herself to/from her appointment;
  - she will sleep with her husband, but will keep her distance otherwise;
  - she is retired, but her husband is still working;
  - and no other individuals live in their home.
- Thus, the maximally exposed individual is very likely to be her husband
- Assuming 8 hours of sleep, the patient-specific occupancy factor is:

$$F_O = \frac{8\ h}{24\ h} = 0.33$$

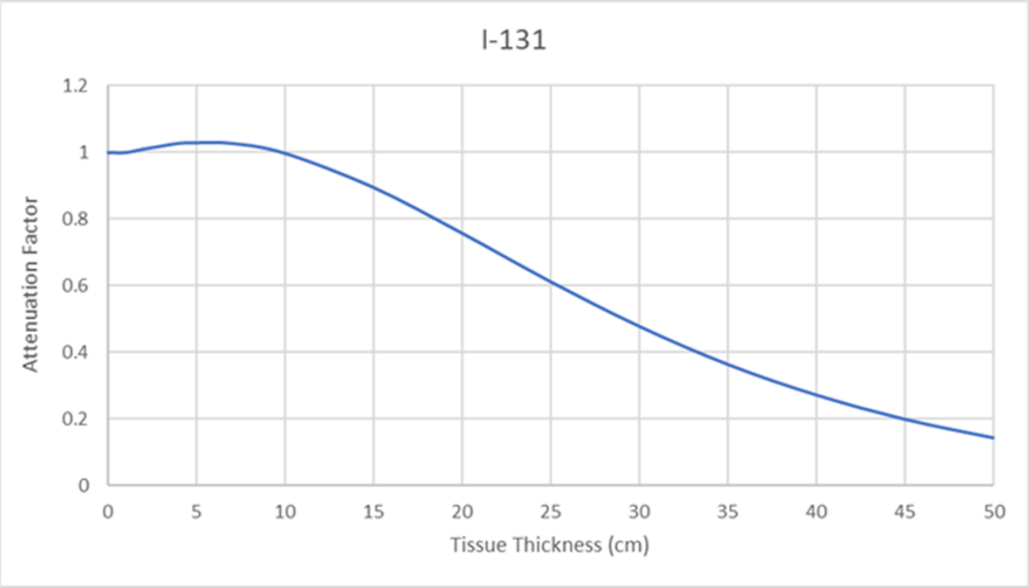
EXAMPLE 3: GEOMETRY, F_G

- The patient has been administered I-131 as sodium iodide
- Thus, the bulk of the radionuclide is expected to concentrate in the thyroid (a "point" source)
- Basic thresholds assume point-to-point geometry at 1 meter, but for this patient-specific case, the licensee assumes a point source (thyroid) and a line receptor (torso of the maximum bystander)
- Again, from Table B-1 of the draft Regulatory Guide, this orientation results in a geometry factor of:

Patient-to-Bystander Separation Distance, r (m)	Point-Line[a] F_G (unitless)	Line-Line F_G (unitless)	Point-Point F_G (unitless)
0.3 (typical for mobility assistance, holding child[b], holding while co-sleeping[b])	5.6	4.6	11
0.5	2.7	2.3	4.0
0.7 (typical for travel seating)	1.6	1.4	2.0
1.0 (typical for close contact[b] activities)	0.87	0.79	1
1.5	0.42	0.39	0.44
2.0	0.25	0.25	0.25
Distances greater than 2 m	$\frac{1}{r^2}$	$\frac{1}{r^2}$	$\frac{1}{r^2}$

$$F_G = 0.87$$

EXAMPLE 3: ATTENUATION, F_A



$F_A = 1.0$

- Because the radioactivity is likely concentrated in the thyroid, the licensee estimates 2 cm of overlying tissue in that area of the body
- The figure to the left is a plot of the attenuation modifying factor (F_A) as a function of thickness of overlying tissue for I-131
- F_A accounts for both attenuation AND photon buildup (we've seen that F_A can exceed 1.0)
- At a thickness of 2 cm, this patient-specific attenuation factor is 1.0

EXAMPLE 3: PATIENT-SPECIFIC ACTIVITY THRESHOLDS

- For this patient, and depending on their stated plans, habits, etc., the release and instruction thresholds for an administration of I-131 (as NaI) are:

$$Q'_{rel} = \frac{Q_{rel}}{F_B \cdot F_O \cdot F_G \cdot F_A} = \frac{0.32\ GBq}{0.53 \cdot 0.33 \cdot 0.87 \cdot 1.0} = 2.1\ GBq$$

1.8 GBq

$$Q'_{ins} = \frac{Q_{ins}}{F_B \cdot F_O \cdot F_G \cdot F_A} = \frac{0.063\ GBq}{0.53 \cdot 0.33 \cdot 0.87 \cdot 1.0} = 0.41\ GBq$$

- This patient can be released, but must be provided dose-minimizing instructions
  - … consistent with stated plans, sleeping arrangement, etc.

EXAMPLE 4: CALCULATION OF A HOLD TIME

- Let's use the previous example, but change the administered activity to 2.3 GBq
- With a Q'_{rel} of 2.1 GBq, the patient must be held, but for how long?
- Retention data for this patient indicates that about 70% of a pretreatment I-131 administration remained in the patient's body after 48 hours
- Then, using equation 11 (Section 2.3, Page 17), the hold time for this patient is:

$$t_{hold} = \frac{48\ h}{\ln(0.70)} \ln\left(\frac{2.1}{2.3}\right) = 12\ h$$

EXAMPLE 5: WHAT IF THE PATIENT IS BREASTFEEDING?

- 26-year-old female is administered 0.04 GBq ^{89}Zr panitumumab for imaging
- Proposed Table 1 indicates basic release and instruction thresholds of 0.26 GBq and 0.052 GBq for ^{89}Zr
- The patient can be released without instruction

HOWEVER, the patient tells you they are breastfeeding …

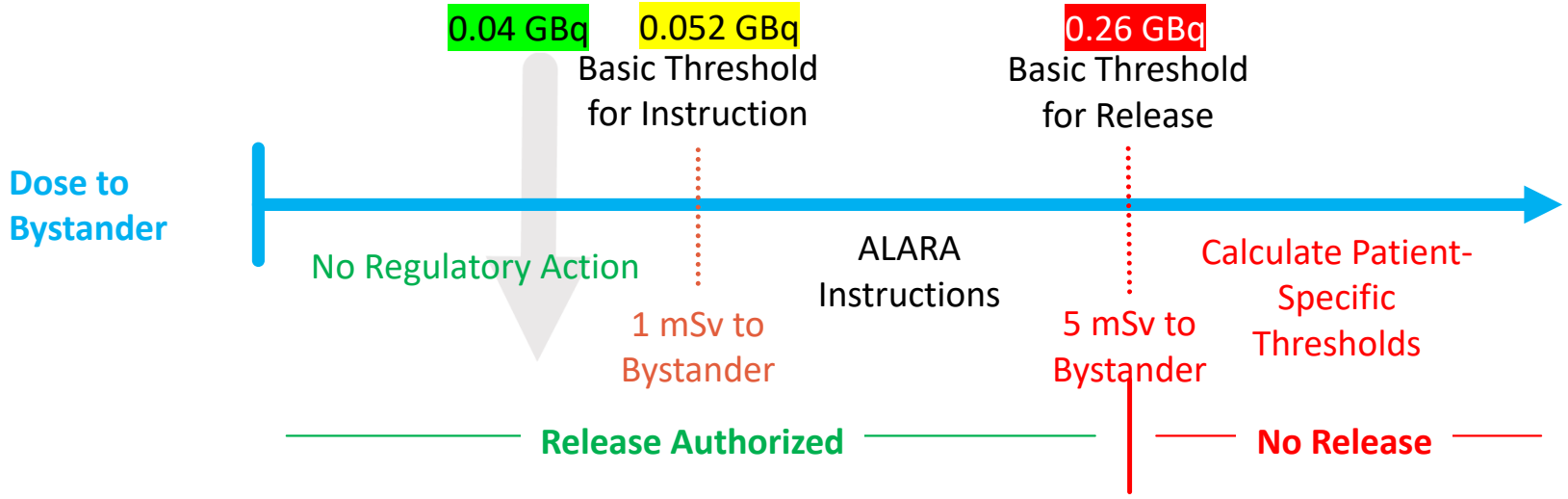


TABLE 3

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

Breastfeeding Activity Thresholds

0.04 GBq is to be administered.

The activity thresholds for requiring a record and requiring instructions are exceeded.

WHAT IS THE RECOMMENDED INTERRUPTION TIME?

- Table 3 provides the breastfeeding thresholds for maintaining records and providing instructions:

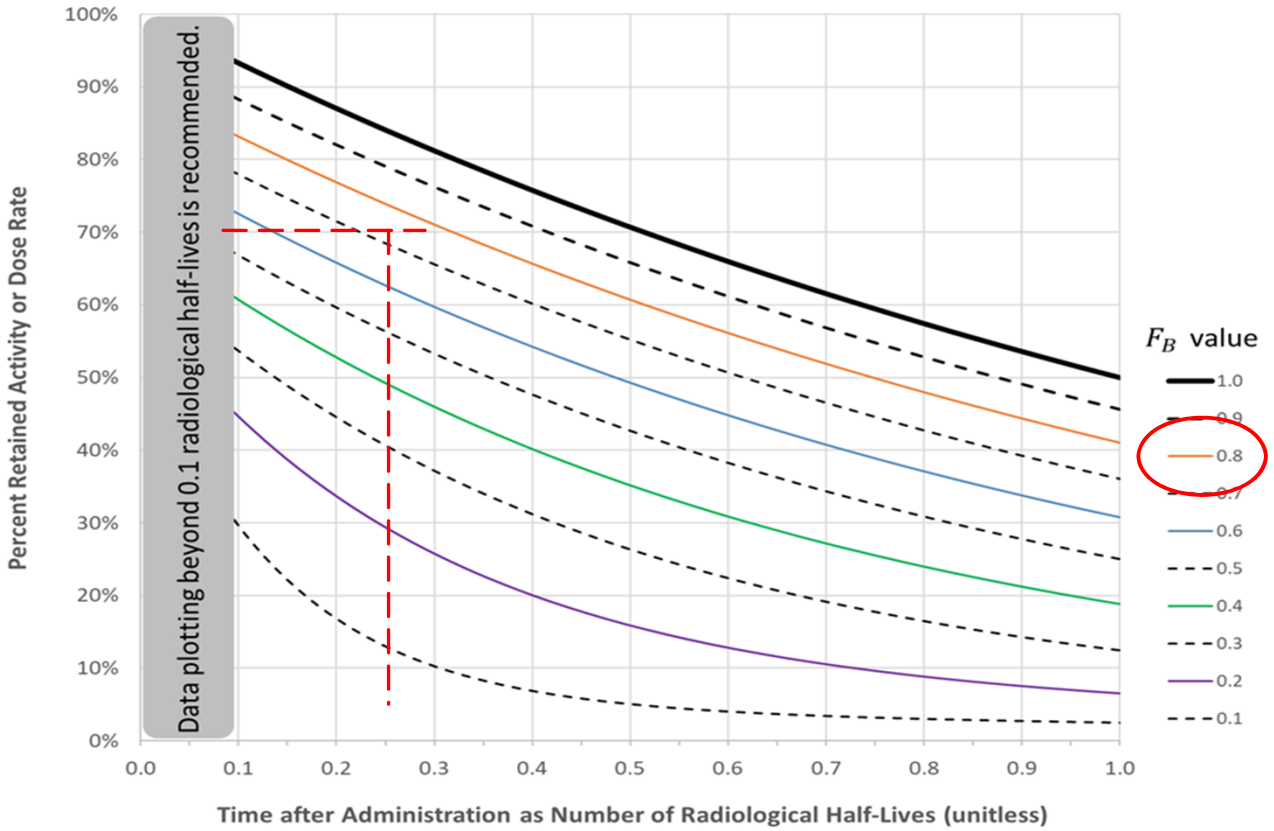
$$Q_{B/rec} = 0.01 \text{ GBq}$$
$$Q_{B/ins} = 0.002 \text{ GBq}$$

- With an administration of 0.04 GBq and a patient-specific effective half-life determination of 55 h, this patient is instructed to interrupt breastfeeding for …

$$\tau = 1.44 \cdot T_e \cdot \ln\left({A_0}/{Q_{B|ins}}\right) = 1.44 \cdot 55\ [h] \cdot \ln\left({0.04}/{0.002}\right) = 240\ [h]$$

ALTERNATIVE METHOD FOR DETERMINING F_B

- Generalized and conservative approach for estimating the modifying factor for biokinetics
- For example, if pretreatment measurements indicate 70% retention 48 hours after administration of I-131 (192-hr physical half-life)
  - y-axis = 70%
  - x-axis = 48/192 = 0.25
- F_B = 0.8



DETAILED MODIFYING FACTOR FOR OCCUPANCY, F_O

- F_O is the fraction of time the maximum bystander is exposed to the patient
- Occupancy and geometry can be taken together to help determine the maximally exposed individual
- The occupancy factor can be as simple as that shown earlier, i.e., $F_O = 8/24 = 0.33$
- Or it can be more detailed depending on the importance of early and late exposure potential (e.g., a radionuclide with short and long loss components)
- Occupancy can be segment into (F_1) short-term exposure (e.g., the initial period) and (F_2) long-term exposure (e.g., the instruction period and thereafter); F_1 and F_2 are summed if for the same bystander
- F_1 and F_2 are essentially the fractions of time spent in close contact with the patient, modified by the expected loss of radioactive material prior to and during that exposure period (Appendix B)

SUMMARY

- Patient release is authorized if radiation dose to any other individual is not likely to exceed 5 mSv
- Written instructions must be provided to maintain ALARA if radiation dose to any other individual is likely to exceed 1 mSv
- Updated release methodology was presented
- Updated breastfeeding interruption/cessation guidelines (providing 1 mSv protection to the infant/child)
- Allows for patient-specific exposure situations with modifying factors for biokinetics, occupancy, geometry, and attenuation
- Easily updated for emerging technologies

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Public Feedback and Questions

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NRC Patient Release Website