From: Beth C. St. Mary (BCS)
To: SAM2
Date: Wednesday, June 7, 1995 4:03 pm
Subject: RULE CONCURRENCE

Steve,

IRM concurs in the final rulemaking, "Criteria for the Release of Individuals Administered Radioactive Material," subject to the following changes.

Change the PRAS to the enclosure. The burden reflected in the PRAS also appears to need revision as it currently reflects the burden for the proposed rule and has changed. done

Change section 35.8 to the enclosure. Since the time the proposed rule was published, a final rule has become effective that changes the sections containing information collections. done

I have not yet reviewed the OMB clearance package, but I will send you comments as soon the review is complete. If you have any questions, please e-mail me at BCS or phone me at 415-5878.

CC: BJS1

Files: P:\PRAS, P:\OMBPT35

9708150209

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

March 12, 1996

MEMORANDUM TO: Hugh L. Thompson, Jr., Deputy Executive Director
for Nuclear Materials Safety, Safeguards
and Operations Support
Office of the Executive Director for Operations

FROM: David L. Morrison, Director
Office of Nuclear Regulatory Research David L. Morrison

SUBJECT: REVISED FINAL RULEMAKING PACKAGE - CRITERIA FOR THE RELEASE OF INDIVIDUALS ADMINISTERED RADIOACTIVE MATERIALS (PARTS 20 AND 35)

Attached is the Commission paper and its attachments on the subject final rulemaking. The Regulatory Analysis (RA) has been revised in accordance with the recent changes to the RA guidelines. Conforming changes have also been made to the Federal Register Notice (FRN) and the Environmental Assessment (EA). There are no changes in the staff paper, except for adding a footnote on the first page, and other attachments.

In the revised RA, the staff used $2,000 per person-rem instead of $1,000. In addition, the staff used effective half-life instead of physical half-life. Since effective half-life includes biological elimination, its use results in more realistic estimates of exposures to the patient's family members. In fact, these exposures are now estimated to result in a collective dose which is about one third of that previously estimated.

Specifically, as compared to the status quo, the savings in hospital costs was estimated at $14 million, whereas the collective dose would be increased by about 2,700 person-rem which corresponds to a cost of about $5 million based on $2,000 per person-rem.

The revised cost-benefit analysis indicates that almost all patients who receive radiopharmaceutical therapy may be released from the hospital immediately if the physician elected to perform a case-specific calculation to show compliance with the dose-based release criteria. Any individual associated with the patient's family would be unlikely to receive a dose of 500 mrem within a year.

Marked up sheets of the FRN, RA, and EA showing significant changes are attached under "BACKGROUND."

Attachments:
1. Commission paper w/atts & disk
2. Marked up sheets

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NUREG-1492

Regulatory Analysis on Criteria for the Release of Patients Administered Radioactive Material

Final Report

Prepared by:

Stewart Schneider and Stephen A. McGuire

Office of Nuclear Regulatory Research
U.S. Nuclear Regulatory Commission
Washington, D.C. 20555

April 23, 1996

4. Impact on breast-feeding woman and infant (section 4.2.4.3)

Original RA: Some discussion.

Revised RA: Expanded discussion.

5. Changes in Cost and benefit estimates

	Increase in Collective Dose			Decrease in Hospital Cost
	person-rem	$1,000	$2,000	
Original RA: Using physical $T_{1/2}$ and $1000 per person-rem	9,000	$9M	$18M	$8M
Revised RA*: Using physical and BIOLOGICAL $T_{1/2}$ and $2000 per person-rem	2,700	$2.7M	$5M	$14M

* The revised cost-benefit analysis indicates that almost all patients who receive radiopharmaceutical therapy may be released from the hospital immediately if the physician elects to perform a case-specific calculation to show compliance with the dose-based release criteria. Any individual associated with the patient's family would be unlikely to receive a dose of 500 mrem within a year.

SUMMARY OF MAJOR CHANGES TO REGULATORY ANALYSIS

(CRITERIA FOR THE RELEASE OF PATIENTS ADMINISTERED RADIOACTIVE MATERIAL)

1. Costs per person-rem

Original RA: Used $1,000 per person-rem.

Revised RA: Used $2,000 per person-rem.

2. Half-lives of radiopharmaceuticals in body

Original RA: Used physical half-life.
For I-131, T_p=8.04 days.

Revised RA: Used effective half-life (biological and physical).
For I-131 in thyroid, T_e=20 days (approximate, it varies slightly with uptake fraction); T_e=5.73 days.

For I-131 in whole body (other than thyroid), T_e=0.33 days; T_e=0.32 days.

3. Uptake fraction for thyroid and the whole body (other than thyroid)

Original RA: Since physical half-life was used, the use of uptake fraction was not necessary.

Revised RA: For thyroid ablation, four uptake fractions for thyroid and for whole body are used. An average dose is estimated by averaging four doses calculated by each uptake fraction.

For thyroid cancer, uptake fractions for thyroid of 0.95 and for whole body of 0.05 are used.

ATTACHMENT 3

REGULATORY ANALYSIS/NUREG-1492

REGULATORY ANALYSIS

"Regulatory Analysis on Criteria for the Release of Patients Administered Radioactive Material" (NUREG-1492, S. Schneider et al., 1996), provides the regulatory basis for this guide and examines the costs and benefits. A copy of NUREG-1492 is available for inspection and copying for a fee at the NRC Public Document Room, 2120 L Street NW., Washington, DC.

APPENDIX C

SAMPLE INSTRUCTIONS FOR PATIENTS RECEIVING PERMANENT IMPLANTS

A small radioactive source has been placed (implanted) inside your body. The source is actually many small metallic pellets or seeds, which are about 1/3 to 1/4 of an inch long, similar in size and shape to a grain of rice. To minimize exposure to radiation to others from the source inside your body and to yourself if the source falls out or comes out, you should do the following for _____ days:

- Stay at a distance of _____ feet from _____.
  Maintain separate sleeping arrangements.
- Minimize time with children and pregnant women.
- Do not hold or cuddle children.
- Avoid public transportation.
- Examine any bandages or linens that come into contact with the implant site for any pellets or seeds that may have come out of the implant site.
  - Take the following action if you find a seed or pellet:
    - Do not handle it with your fingers. Use something like a spoon or tweezers to place it in a jar or other container that you can close with a lid.
    - Place the container with the seed/pellet in a location away from people.
    - Notify one of the individuals listed below.

If you have any questions, contact the following individual(s):

Name _____ Phone number _____ Beeper number _____
Name _____ Phone number _____ Beeper number _____

REFERENCES FOR APPENDIX B

B-1. Stewart Schneider and Stephen A. McGuire, "Regulatory Analysis on Criteria for the Release of Patients Administered Radioactive Material," NUREG-1492 (Final Report), NRC, 1996.*

B-2. A. Brodsky, "Resuspension Factors and Probabilities of Intake of Material in Process (Or 'Is 10^{-6} a Magic Number in Health Physics?')," Health Physics, Volume 39, Number 6, 1980.

B-3. R.C.T. Buchanan and J.M. Brindle, "Radioiodine Therapy to Out-patients - The Contamination Hazard," British Journal of Radiology, Volume 43, 1970.

B-4. A.P. Jacobson, P.A. Plato, and D. Toeroek, "Contamination of the Home Environment by Patients Treated with Iodine-131," American Journal of Public Health, Volume 68, Number 3, 1978.

B-5. National Council on Radiation Protection and Measurements, "Dose Limits for Individuals Who Receive Exposure from Radionuclide Therapy Patients," Commentary No. 11, February 28, 1995.

B-6 Keith F. Eckerman, Anthony B. Wolbarst, and Allan C. B. Richardson, Limiting Values of Radionuclide Intake and Air Concentration and Dose Conversion Factors for Inhalation, Submersion, and Ingestion, Federal Guidance Report No. 11, U. S. Environmental Protection Agency, Washington, 1988.

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*Requests for single copies of drafts should be made in writing to the U.S. Nuclear Regulatory Commission, Washington, DC 20555, Attention: Distribution and Mail Services Section. Requests for drafts will be filled as long as supplies last. Copies of drafts are also available for inspection and copying for a fee from the NRC Public Document Room at 2120 L Street NW. (Lower Level), Washington, DC. The PDR's mailing address is Mail Stop LL-6, Washington, DC 20555; telephone (202)634-3273; fax (202)634-3343.

the risk of intake of radionuclides from patients' secretions and excreta in NCRP Commentary No. 11, "Dose Limits for Individuals Who Receive Exposure from Radionuclide Therapy Patients." The NCRP concluded that, "Thus, a contamination incident that could lead to a significant intake of radioactive material is very unlikely."(B-5). For additional discussion on the subject, see Reference B-1.

Q = the activity administered to the patient in microcuries.

10^{-5} = the assumed fractional intake.

DCF = the dose conversion factor to convert an intake in millicuries to an internal committed effective dose equivalent (such as tabulated in Reference B-6).

Equation B-11 uses a value of 10^{-5} as the fraction of the activity administered to the patient that would be taken in by the individual exposed to the patient. A common rule of thumb is to assume that no more than one 1-millionth of the activity being handled will become an intake to an individual working with the material. This rule of thumb was developed in Reference B-2 for cases of worker intakes during normal workplace operations, worker intakes from accidental exposures, and public intakes from accidental airborne releases from a facility, but it does not specifically apply for cases of intake by an individual exposed to a patient. However, two studies (Refs. B-3 and B-4) regarding the intakes of individuals exposed to patients administered iodine-131 indicated that intakes were generally of the magnitude of one 1-millionth of the activity administered to the patient and that internal doses were far below external doses. To account for the most highly exposed individual and to add a degree of conservatism to the calculations, a fractional transfer of 10^{-5} has been assumed.

As an example of the use of Equation B-11, assume that 30 millicuries of iodine-131 was administered to a patient. The dose conversion factor DCF for the ingestion pathway is 53 rems/millicurie from Table 2.2 of Reference B-6. The ingestion pathway was selected since it is likely that most of the intake would be through the mouth or through the skin, which is most closely approximated by the ingestion pathway. Thus, the maximum internal dose to the individual D_i would be calculated to be 0.016 rem. In this case, the internal dose would be about 3 percent of the assumed 5 millisieverts (0.5 rem) external gamma dose. Internal doses may be ignored in the calculations if they are likely to be less than 10 percent of the external dose since the internal dose would be significantly less than the uncertainty in the external dose.

The conclusion that internal contamination is relatively unimportant in the case of patient release was also reached by the NCRP. The NCRP addressed

Based on empirical assessment involving patients with implants, soft tissue shielding for iodine-125 is likely to exceed 5 or more half value layers (Ref. B-1).

Solution: The dose is calculated using Equation B-10:

$$D = \frac{34.6(1.11\,R \cdot cm^2/mCi \cdot hr)(60\,mCi)(60.2\,d)(0.25)(e^{-(0.387/cm)(9\,cm)})}{(100\,cm)^2}$$

$$D = 0.107\ rem\ (1.07\ mSv)$$

Therefore, a patient who has received a permanent implant of 60 millicuries (2,220 megabecquerels) of iodine-125 may still be authorized for release. To meet the requirements of 10 CFR 35.75(b), the licensee must provide the patient with instructions and to meet the requirements of 10 CFR 35.75(c), the licensee must maintain a record of the calculation.

Although a correction for attenuation may be calculated, it will usually be simpler to measure the dose rate at 1 meter. If the dose rate is no greater than the rate in column 2 of Table 1, the patient may be released and the record of the survey would serve as the record required by 10 CFR 35.75(c).

3.2 Internal Dose

Internal dose may be a consideration with certain radiopharmaceuticals now being developed, such as radiolabeled antibodies, or those that are developed in the future. Some of the radionuclides used in radiolabeled antibodies are predominantly beta or alpha emitters, which emit few gammas.

A rough estimate of the maximum likely committed effective dose equivalent from internal exposure can then be calculated from the following equation:

$$D_i = Q \bullet 10^{-5} \bullet DCF \qquad \text{(Equation B-11)}$$

Where D_i = the maximum likely internal committed effective dose equivalent to the individual exposed to the patient in rems,

$$D = D_0 e^{-\mu x} \qquad \text{(Equation B-8)}$$

Where D = dose after attenuation,
D_0 = dose before attenuation,
μ = linear attenuation coefficient of tissue,
x = thickness of tissue covering the implant.

Also, the dose before attenuation is, from Equation 2 in the guide:

$$D_0 = \frac{34.6\,\Gamma Q_0 T_e (0.25)}{(100\text{ cm})^2} \qquad \text{(Equation B-9)}$$

Substituting Equation B-9 for D_0 in Equation B-8, the dose after attenuation becomes

$$D = \frac{34.6\,\Gamma Q_0 T_e (0.25)(e^{-\mu x})}{(100\text{ cm})^2} \qquad \text{(Equation B-10)}$$

Example: Calculate the maximum likely dose to an individual exposed to a patient who has received a permanent implant of 60 millicuries (2,220 megabecquerels) of iodine-125. The following factors apply:

Γ = 1.11 R·cm²/mCi·hr,
T_e = 60.2 days,
μ = 0.387/cm (Ref. B-1),
5 HVLs = 9 cm (assume 5 Half Value Layers in soft tissue;
1 Half Value Layer for iodine-125 = 1.8 cm).

There is a significant reduction in the exposure rate from the shielding effects of the source capsule. The Γ of 1.11 R·cm²/mCi·h for iodine-125 already accounts for the reduction in exposure rate from attenuation by the source capsule.

$$D = 0.31 \text{ rem } (3.1 \text{ mSv})$$

Since the dose is no greater than 5 millisievert (0.5 rem), the patient may be released but instructions to the patient are required. Because an occupancy factor less than 0.25 at 1 meter was used, a record of the calculation must be maintained pursuant to 10 CFR 35.75(c).

Example: Calculate the maximum likely dose to an individual exposed to a patient who has received 40 millicuries (1,480 megabecquerels) of iodine-131. The patient requires extensive care because of other medical conditions.

Solution: Since the patient needs extensive care, the exposure factor will have to be increased to account for tho increased time the primary caregiver will spend near the patient. An exposure factor of 0.5 is used in this example:

$$D = \frac{34.6(2.2 \text{ R}\cdot\text{cm}^2/\text{mCi}\cdot\text{hr})(40 \text{ mCi})(8.04 \text{ d})(0.5)}{(100 \text{ cm})^2}$$

$$D = 1.22 \text{ rem } (12.2 \text{ mSv})$$

Since the dose exceeds 5 millisievert (0.5 rem), the licensee may not authorize release. However, when the patient is releasable, 10 CFR 35.75(c) requires a record of the release and 10 CFR 35.75(b) requires instructions to the patient if the dose to an individual from the released patient is likely to exceed 1 millisievert (0.1 rem).

3. OTHER FACTORS

3.1 Attenuation of the Radiation in the Body

Licensees may take into account attenuation of the radiation by the patient. The fraction of the dose that results after attenuation by the body may be calculated using the following equation:

2. EXPOSURE FACTOR

The distance and the time that other individuals will spend in the proximity of the patient may occasionally be taken into account when determining the dose to an individual. If the patient is living alone, will have few if any visits by family or friends, will not be returning to work immediately, and will be generally isolated from other people, the exposure factor can be decreased by a factor of 2 (for example, from the general value of 0.25 to 0.125). This would allow an individual to be released with an activity that is higher than that specified in Table 1 in the regulatory guide. On the other hand, if the patient needs extensive care at home, the exposure factor may have to be increased to account for the increased exposure of the individual caring for the patient.

In general, the NRC does not believe that the exposure factors less than 0.125 can be easily justified because it is not possible to avoid someone being exposed to the patient at all times. Lower values for the exposure factor are not specifically prohibited by the regulation, but must be explicitly justified in the record of the calculation, as the record will be subject to inspection.

Example: Calculate the maximum likely dose to an individual exposed to a patient who has received 40 millicuries (1,480 megabecquerels) of iodine-131. The patient lives alone and will not be working.

Solution: The dose is calculated using Equation B-1:

$$D(t) = \frac{34.6\,\Gamma\,Q_0\,T_p\,E}{r^2}$$

Since the patient lives alone and will not be returning to work, and therefore will not be around the public, the exposure factor can be reduced to 0.125:

$$D(t) = \frac{34.6(2.22\ R\cdot cm^2/mCi\cdot hr)(40\ mCi)(8.05\ d)(0.125)}{(100\ cm)^2}$$

Table B-1. Release Times Post Administration for Therapeutic Iodine-131 Procedures Based on Biological Retention and Elimination

(To be prepared)

$$\frac{34.6(2.2\text{R}\cdot\text{cm}^2/\text{mCi}\cdot\text{h})(0.55)(33\ \text{mCi})(5.8\ \text{d})(0.25)}{(100\ \text{cm})^2}$$

$$D(\infty) = 0.008 + 0.200$$

$$D(\infty) = 0.208\ \text{rem}\ (2.08\ \text{mSv})$$

Therefore, hyperthyroid patients administered 33 millicuries (1,200 megabecquerels) of iodine-131 or less would not have to remain under licensee control and could be released under 10 CFR 35.75.

Release Time Example:

Using Equation B-6, it is possible to calculate doses from which release times can be estimated using a graphical method. This is shown in Table B-1 for the maximum quantities normally administered. The values for hyperthyroidism and thyroid ablation are given for various thyroid retention fractions. The licensee's record required by 10 CFR 35.75(b) should indicate the reason for using the assumed thyroid retention fraction.

Solution: In this example, we will account for elimination of iodine-131 from the body by using the biological half-lives appropriate for hyperthyroidism to calculate the dose. It will be necessary to consider the different biological half-lives for thyroidal and extrathyroidal iodine. The following assumptions are made in this example:

IODINE-131 PARAMETERS FOR HYPERTHYROIDISM EXAMPLE

Physical half-life of iodine-131, T_p	8.0 days
Extrathyroidal fraction, F_1	0.45[1]
Biological half-life of extrathyroidal fraction, T_{b1}	0.33 day[1,2]
Effective half-life of extrathyroidal fraction, T_{1eff}	0.3 day
Thyroidal fraction, F_2	0.55[1]
Biological half-life of thyroidal fraction, T_{b2}	21 days[1]
Effective half-life of thyroidal fraction, T_{2eff}	5.8 days[1]
Specific gamma ray constant, Γ	2.2 R·cm²/mCi·h

[1]Personal communication, M. Pollycove, M.D., Visiting Medical Fellow, U.S. Nuclear Regulatory Commission, Rockville, MD, April 1995.
[2]International Commission on Radiological Protection (ICRP), "Radiation Dose to Patients from Radiopharmaceuticals," ICRP Publication No. 53 (March 1987).

The total dose comprises the doses from the extrathyroidal and thyroidal fractions. The equation is:

$$D(t) = \frac{34.6\,\Gamma F_1 Q_0 T_{1eff}(0.25)(1-e^{-0.693t/T_{1eff}})}{(100\text{ cm})^2} + \frac{34.6\,\Gamma F_2 Q_0 T_{2eff}(0.25)(1-e^{-0.693t/T_{2eff}})}{(100\text{ cm})^2} \qquad \text{(Equation B-6)}$$

Substituting the values from above, the dose to total decay is

$$D(\infty) = \frac{34.6(2.2\text{R·cm}^2/\text{mCi·h})(0.45)(33\text{ mCi})(0.3\text{ d})(0.25)}{(100\text{ cm})^2} +$$

The total dose comprises the doses from the extrathyroidal and thyroidal fractions. The equation is:

$$D(t) = \frac{34.6\,\Gamma F_1 Q_0 T_{1eff}(0.25)(1-e^{-0.693t/T_{1eff}})}{(100\text{ cm})^2} + \frac{34.6\,\Gamma F_2 Q_0 T_{2eff}(0.25)(1-e^{-0.693t/T_{2eff}})}{(100\text{ cm})^2} \qquad \text{(Equation B-6)}$$

Substituting the values from above, the dose to total decay is

$$D(\infty) = \frac{34.6(2.2\text{ R}\cdot\text{cm}^2/\text{mCi}\cdot\text{h})(0.95)(100\text{ mCi})(0.3\text{ d})(0.25)}{(100\text{ cm})^2} + \frac{34.6(2.2\text{ R}\cdot\text{cm}^2/\text{mCi}\cdot\text{h})(0.05)(100\text{ mCi})(7.3\text{ d})(0.25)}{(100\text{ cm})^2}$$

$$D(\infty) = 0.054 + 0.069$$

$$D(\infty) = 0.124\text{ rem (1.24 mSv)}$$

Therefore, thyroid cancer patients administered 100 millicuries (3,700 megabecquerels) of iodine-131 or less would not have to remain under licensee control and could be released under 10 CFR 35.75, assuming that the foregoing assumptions can be justified for the individual patient's case and the patient is given instructions.

In the example above, the thyroidal fraction, $F_2 = 0.05$, is a conservative assumption. For those individuals who have had surgery to remove thyroidal tissue, F_2 is typically smaller and, in some cases, F_2 is known for a specific individual.

Hyperthyroidism Example: Calculate the maximum likely dose to an individual exposed to a patient who has been administered 33 millicuries (1,200 megabecquerels) of iodine-131 for the treatment of hyperthyroidism (i.e., thyroid ablation). The occupancy factor is 0.25 at 1 meter.

Thyroid Cancer Example: Calculate the maximum likely dose to an individual exposed to a patient who has been administered 100 millicuries (3,700 megabecquerels) of iodine-131, 3 to 4 weeks after thyroid cancer surgery, for the treatment of thyroid remnants and metastases. The occupancy factor is 0.25 at 1 meter.

Solution: In this example, we will account for the elimination of iodine-131 from the body by using the biological half-lives appropriate for thyroid cancer to calculate the dose. It is generally recognized that, after surgical removal of the thyroid, the uptake of iodine-131 by the thyroidal remnants and metastases does not exceed 5 percent of the administration. It will be necessary to consider the different biological half-lives for thyroidal and extrathyroidal iodine. The following assumptions are made in this example:

IODINE-131 PARAMETERS FOR THYROID CANCER EXAMPLE

Physical half-life of iodine-131, T_p	8.0 days
Extrathyroidal fraction, F_1	0.95[1]
Biological half-life of extrathyroidal fraction, T_{b1}	0.33 day[2]
Effective half-life of extrathyroidal fraction, T_{1e}	0.3 day
Thyroidal fraction, F_2	0.05[1]
Biological half-life of thyroidal fraction, T_{b2}	80 days[2]
Effective half-life of thyroidal fraction, T_{2e}	7.3 days
Specific gamma ray constant, Γ	2.2 R·cm²/mCi·h

[1]Personal communication, M. Pollycove, M.D., Visiting Medical Fellow, U.S. Nuclear Regulatory Commission, Rockville, MD, April 1995.

[2]International Commission on Radiological Protection (ICRP), "Radiation Dose to Patients from Radiopharmaceuticals," ICRP Publication No. 53, March 1987.

A licensee may take into account the effective half-life of the radioactive material to demonstrate compliance with the dose limits to members of the public stated in 10 CFR 35.75. The effective half-life is defined as:

$$T_{eff} = \frac{T_b \times T_p}{T_b + T_p} \qquad \text{(Equation B-2)}$$

Where T_b = biological half-life of the radionuclide,
T_p = physical half-life of the radionuclide.

using the effective half-life, Equation B-1 becomes:

$$D(t) = \frac{34.6\,\Gamma Q_0 T_{eff} E}{(r)^2} \qquad \text{(Equation B-3)}$$

with the factors defined as above, T_{eff} is the effective half-life.

For radioiodine, the effective half-life comprises the effective half-life of extrathyroidal iodide (i.e., existing outside of the thyroid) and the effective half-life of iodide following uptake by the thyroid. The effective half-life for the extrathyroidal and thyroidal fractions (i.e., F_1 and F_2, respectively) can be calculated with the following equations:

$$T_{1eff} = \frac{T_{b1} \times T_p}{T_{b1} + T_p} \qquad \text{(Equation B-4)}$$

$$T_{2eff} = \frac{T_{b2} \times T_p}{T_{b2} + T_p} \qquad \text{(Equation B-5)}$$

Where T_{b1} = biological half-life for extrathyroidal iodide,
T_{b2} = biological half-life of iodide following uptake by the thyroid,
T_p = physical half-life of iodine-131.

APPENDIX B

PROCEDURES FOR CALCULATING DOSES BASED ON CASE-SPECIFIC FACTORS

In certain situations, a licensee may release a patient with an activity higher than the values listed in Table 1 for a specific radionuclide. Licensees may calculate the potential doses to individuals exposed to patients receiving treatment with radioactive material on a case-by-case basis to account for certain factors specific to an individual.

According to 10 CFR 35.75(b), a record must be kept for 3 years of the basis for the release of the patient if the release of the patient is based on other than standard conservative assumptions. For example, a licensee may use assumptions other than the standard conservative ones, i.e., (1) biological elimination rather than just the physical half-life of the radionuclide, (2) an occupancy factor less than 0.25 at one meter, or (3) the attenuation of radiation by body tissue of the released individual.

The following equation is generally used to calculate doses:

$$D(t) = \frac{34.6\,\Gamma Q_0 T_p E}{(r)^2} \qquad \text{(Equation B-1)}$$

Where $D(t)$ = dose to total decay,

34.6 = conversion factor of 24 hrs/day times the total integration of decay (1.44),

Γ = exposure rate constant,

Q_0 = initial activity at the start of the time interval,

T_p = physical half-life,

E = exposure factor that accounts for the different occupancy times and distances when an individual is around a patient. This value is typically 0.25 when the distance is 100 cm.

r = distance. This value is typically 100 cm.

1. EFFECTIVE HALF-LIFE

Where E_i = the energy of the gamma ray or x-ray i in Mev.

f_i = the probability of decay of gamma rays or x-rays with energy E_i per disintegration. Values for E_i and f_i were taken from: Bernard Shleien, The Health Physics and Radiological Health Handbook, Revised Edition, Scinta, Inc., 1992, pages 294-334. For Re-186, Re-188, and Sn-117m the values for E_i and f_i were taken from: Laurie M. Unger and D. K. Trubey, "Specific Gamma-Ray Dose Constants for Nuclides Important to Dosimetry and Radiological Assessment," ORNL/RSIC-45/R1, 1982.

$\mu_{en,i}$ = the linear energy absorption coefficient in air of photons of energy E_i, taken from Radiological Health Handbook, U. S. Department of Health, Education, and Welfare, 1970, page 135.

ρ = the density of air at standard temperature and pressure, taken to be 0.0012929 gm/cm^3.

The details of the calculation of the exposure rate factors are shown in Table A-2, Appendix A to NUREG-1492.

[3] R. Nath, A.S. Meigooni, and J.A. Meli, "Dosimetry on Transverse Axes of ^{125}I and ^{192}Ir Interstitial Brachytherapy Sources," Medical Physics, Volume 17, Number 6, November/December 1990. The exposure rate constant given is a measured value averaged for several source models and taking into account the attenuation of gamma rays within the implant capsule itself.

[4] Ravinder Nath, Yale University School of Medicine, letter to Dr. U. Hans Behling dated March 31, 1993. The exposure rate constant given is a measured value that takes into account the attenuation of gamma rays within the implant capsule itself.

[5] Not applicable (NA) because release quantities based on beta emission rather than gamma emission.

APPENDIX A

Table A-1. Half-Lives and Exposure Rate Constants of Radionuclides Used in Medicine

Radionuclide	Half-Life (days)[1]	Exposure Rate Constant[2] ($R \cdot cm^2/mCi \cdot h$)	Radionuclide	Half-Life (days)[1]	Exposure Rate Constant[2] ($R \cdot cm^2/mCi \cdot h$)
Ag-111	7.45	0.150	Pd-103 (implants)	16.97	0.86[4]
Au-198	2.696	2.36	Re-186	3.777	0.168
Cr-51	27.704	0.177	Re-188	0.7075	0.337
Cu-64	0.5292	1.10	Sc-47	3.351	0.626
Ga-67	3.261	0.753	Se-75	119.8	2.60
I-123	0.55	1.61	Sm-153	1.9458	0.425
I-125	60.14	1.42	Sn-117m	13.61	1.48
I-125 (implants)	60.14	1.11[3]	Sr-89	50.5	NA[5]
I-131	8.040	2.20	Tc-99m	0.2508	0.756
In-111	2.83	3.15	Tl-201	3.044	0.447
Ir-192	74.02	4.69	Y-90	0.1329	NA[5]
P-32	14.29	NA[5]	Yb-169	32.01	1.83

[1] Keith F. Eckerman, Anthony B. Wolbarst, and Allan C. B. Richardson, Federal Guidance Report No. 11, Limiting Values of Radionuclide Intake and Air Concentration and Dose Conversion Factors for Inhalation, Submersion, and Ingestion, Report # EPA-520/1-88-020, Office of Radiation Programs, U. S. Environmental Protection Agency, Washington, DC, 1988.

[2] The exposure rate factor includes gamma rays and x-rays with an energy above 11.3 keV. The 11.3 keV cutoff is the one used in NCRP Report No. 41, "Specification of Gamma-Ray Brachytherapy Sources," 1974. The exposure rate constant was calculated from the following equation:

$$\Gamma \frac{mR \cdot cm^2}{mCi \cdot hr} = (1.332 \times 10^{14} \frac{dis}{mCi \cdot hr})(\frac{1}{4\pi\,(100\ cm)^2}) \sum_i E_i (\frac{\mu_{a,i}}{\rho}\ \frac{cm^{-1}}{gm \cdot cm^{-3}}) \times$$

$$(\frac{gm \cdot mR}{87.6\ erg})(1.6 \times 10^{-6}\ \frac{erg}{MeV})$$

Except in those cases in which a licensee uses an acceptable alternative method for complying with 10 CFR 35.75, the methods described in this guide will be used in the evaluation of a licensee's compliance with 10 CFR 35.75.

3. RECORDS

3.1 Records of Release

There is no recordkeeping requirement for immediate release of patients based on Table 1. However, if the release of the patient is based on factors other than the standard conservative assumptions on which Table 1 is based, 10 CFR 35.75(c) requires that the licensee maintain, for 3 years, a record of the basis for the release. For example, when the licensee releases a patient with an activity that is greater than the value in the default table, a record of the basis for the release must be maintained for NRC review during inspection.

Records should include (1) the patient's name, (2) the radioactive material, (3) the administered activity, (4) the date and time of administration, (5) the date and time of the patient's release, (6) the case-specific factors that were used in calculating the dose to the individual, and (7) the estimated dose to an individual exposed to the patient. In those instances for which a case-specific calculation applies to more than one patient release, the calculation need not be performed again. The record for a particular patient's release could reference the calculation done for the class of patients.

3.2 Records of Instructions

A record that instructions were provided is required by 10 CFR 35.75(d) if a woman is breast-feeding and failure to interrupt breast-feeding could result in a dose to the beast-feeding child in excess of 5 millisieverts (0.5 rem)

D. IMPLEMENTATION

The purpose of this section is to provide information about the NRC staff's plans for using this regulatory guide.

Tc-99m WBC's	3	15	24 hr for 30 mCi 12 hr for 12 mCi
Ga-67 citrate	0.04	0.2	Complete cessation
Cr-51 EDTA	1.6	8	NA
In-111 WBC's	0.3	1.5	6 hr for 0.5 mCi
Tl-201	1	5	Complete cessation for 3 mCi 48 hr for 1.5 mCi

* NA, meaning "not applicable," is used if the administered activity requiring instructions exceeds the maximum activity normally administered.

- The length of time precautions should be in effect.

The Society of Nuclear Medicine published a pamphlet in 1987 that provides information for patients receiving treatment with radioiodine.[3] This pamphlet was prepared jointly by the Society of Nuclear Medicine and the NRC. The NRC considers the instructions in this pamphlet to be acceptable instructions for patients, provided specific information is given to patients regarding any case-specific factors. However, licensees may develop their own instructions, addressing the items discussed above as appropriate.

Sample instructions for patients who have received permanent implants are given in Appendix C.

2.3 Additional Instructions for Release of Women Who Could be Breast-Feeding after Release

If the patient to be released is a woman who could be breast-feeding after release, Table 2 provides information and instructions on the interruption of breast-feeding for the radiopharmaceuticals commonly used in medical diagnosis and treatment. In order to use this table it will be necessary to determine the breast-feeding status of women patients receiving some administrations.

The purpose of describing the consequences is so that women will understand that breast-feeding after an administration of certain radionuclides could cause harm (e.g., iodine-131 could harm the child's thyroid). In other cases, the guidance could simply address avoidance of any unnecessary radiation exposure to the child from breast-feeding.

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[3] "Guidelines for Patients Receiving Radioiodine Treatment," Society of Nuclear Medicine, 1987. This pamphlet may be obtained from the Society of Nuclear Medicine, 136 Madison Avenue, New York, NY 10016-6760.

2. INSTRUCTIONS

2.1 Activities Requiring Instructions

If the total effective dose equivalent to an individual exposed to a patient is likely to exceed 1 millisievert (0.1 rem), 10 CFR 35.75(b) requires that the released patient be given instructions, including written instructions, on how to maintain doses to other individuals as low as reasonably achievable.

Licensees may use the values in Column 3 or Column 4 of Table 1 to determine when instructions must be given to patients who are not breast-feeding. Column 3 provides activities above which an individual could receive a dose of 1 millisievert (0.1 rem) or more. Column 4 provides corresponding dose rates at 1 meter, based on the activities in Column 3.

If the released patient is a woman who will be breast-feeding after release, licensees may also use Table 2 to determine when additional instructions on the interruption of breast-feeding must be given to the patient to meet the requirements in 10 CFR 35.75(b).

2.2 Content of Instructions

The instructions should be specific to the type of treatment given, such as permanent implants or radioiodine for hyperthyroidism or thyroid carcinoma, or they may include additional information for individual situations. The instructions should include a contact and phone number in case the patient has any questions. The instructions should include, as appropriate

- Maintaining distance from other persons, including separate sleeping arrangements,
- Minimizing time in public places (e.g., public transportation, grocery stores, shopping centers, theaters, restaurants, and sporting events),
- Precautions to reduce the spread of radioactive contamination, and

Y-90	100	4	NA	20	0.8	NA
Yb-169	10	0.4	2	2	0.07	0.4

Table 1. Activities and Dose Rates for Authorizing Patient Release and Giving Instructions[2]

Radio-nuclide	Column 1 Activity At Or Below Which Patients May Be Released (mCi)	(GBq)	Column 2 Dose Rate At 1 meter At Or Below Which Patients May Be Released (mrem/hr)	Column 3 Requiring Instructions If Activity Is Greater Than (mci)	(Gbq)	Column 4 Requiring Instructions If Dose Rates at 1 meter Is Greater Than (mrem/hr)
Ag-111	500	20	8	100	4	2
Au-198	90	3	20	20	0.7	4
Cr-51	100	4	2	20	0.8	0.4
Cu-64	200	9	30	40	2	5
Ga-67	200	9	20	40	2	4
I-123	160	6	20	30	1	4
I-125 (implant)	8.7	0.32	1	1.7	0.06	0.2
I-125	7	0.2	1	1.4	0.5	0.2
I-131	30	1.2	7	6	0.24	1.4
In-111	60	2	20	10	0.4	4
Ir-192	1.6	0.06	0.8	0.3	0.01	0.1
P-32	100	4	NA	20	0.8	NA
Pd-103 implants	40	1.5	3	7.9	0.29	0.7
Re-186	900	30	10	200	7	2
Re-188	600	20	20	100	4	4
Sc-47	300	10	10	50	2	3
Se-75	2	0.07	.5	.4	0.01	0.1
Sm-153	700	30	30	100	5	6
Sn-117m	30	1	4	6	0.2	0.8
Sr-89	100	4	NA	20	0.8	NA
Tc-99m	700	30	50	100	6	10
Tl-201	400	10	20	80	2	4

[2] Values rounded to one significant figure, except in a few instances where it was considered appropriate to use two significant figures. The details of the calculations are shown in NUREG-1492, *Regulatory Analysis on Criteria for the Release of Patients Administered Radioactive Material.*

Appendix B contains procedures for performing case-specific dose calculations, and it describes how various factors may be considered in the calculations.

1.4 Special Consideration for Breast Feeding Women

The release quantities in Table 1 do not include consideration of the dose to a breast-feeding infant from ingestion of radiopharmaceuticals contained in a woman's breast milk. If the patient is a breast-feeding woman it may be necessary to give instructions as described in Section C.2.3 as a condition for release because the activities in Table 1 could cause a dose exceeding 5 millisieverts (0.5 rem) to the breast-feeding infant if there were no interruption of breast-feeding.

C. REGULATORY POSITION

1. RELEASE CRITERIA

1.1 Activities for Release of Patients

Licensees may demonstrate compliance with the dose limit in 10 CFR 35.75(a) for release of patients from licensee control if the activity administered is no greater than the activity in Column 1 of Table 1. In this case, no record of the release is required. If the activity administered exceeds the activity in Column 1 of Table 1, the licensee may hold the patient until the activity in the patient's body is no greater than Column 1 of Table 1 and then authorize release. In this case a record is required by 10 CFR 35.75(c) because the release is based on an activity less than the activity administered.

1.2 Dose Rates for Release of Patients

Licensees may also demonstrate compliance with the dose limit in 10 CFR 35.75(a) for release of patients from licensee control if the dose rate at 1 meter (from the patient centerline) is no greater than the value in Column 2 of Table 1 for that radionuclide. If the release is based on the dose rate at 1 meter, a record of the measured dose rate is required by 10 CFR 35.75(c) because the measurement includes shielding by tissue.

1.3 Releases Based on Case-Specific Factors

Licensees may calculate the maximum likely dose to an individual exposed to the patient on a case-by-case basis to account for factors specific to a patient. In such cases, licensees may be able to release a patient with radioactive material in excess of the activity listed in Table 1 and still demonstrate compliance with the annual dose limit. Licensees may take into account the effective half-life of the radioactive material and other factors that may be relevant to the particular case.

- For radionuclides with half-lives greater than 1 day, it is assumed that the individual likely to receive the highest dose from exposure to the patient would receive a dose of 25 percent of the dose to total decay (0.25 in Equation 2) at a distance of 100 centimeters. Selection of 25 percent of the dose to total decay for estimating the dose is based on measurements indicating that the dose calculated using the factor is conservative in most normal situations.

- For radionuclides with half-lives no greater than 1 day, the factor of 0.25 used in Equation 2 is replaced with a factor of 1.0 to give Equation 3. The factor of 0.25 may not be valid when relatively long-term averaging of behavior cannot be assumed.

Thus, for radionuclides with a half-life greater than 1 day:

$$D(\infty) = \frac{34.6\,\Gamma Q_0 T_p (0.25)}{(100\ \text{cm})^2} \qquad \text{(Equation 2)}$$

For radionuclides with a half-life no greater than 1 day:

$$D(\infty) = \frac{34.6\,\Gamma Q_0 T_p}{(100\ \text{cm})^2} \qquad \text{(Equation 3)}$$

Equations 2 and 3 calculate the dose from external exposure to gamma radiation. The equations do not explicitly include dose from internal intake by household members and members of the public because the dose from intake by other individuals is expected to be small for most radiopharmaceuticals (less than a few percent) relative to the gamma dose (see Section 3.2 of Appendix B). Further, the equations above do not apply to the dose to breast-feeding children who continue to breast-feed. Breast-feeding must be considered separately as described below.

NCRP Report No. 37 uses the following equation to calculate the exposure until time t at a distance r from the patient:

$$D(t) = \frac{34.6\,\Gamma Q_0 T_p (1-e^{-0.693t/T_p})}{r^2} \qquad \text{(Equation 1)}$$

Where $D(t)$ = accumulated exposure at time t, in roentgens,

34.6 = conversion factor of 24 hrs/day times the total integration of decay (1.44),

Γ = specific gamma ray constant for a point source, R/mCi·h at 1 cm,

Q_0 = initial activity of the point source in millicuries, at the time of the release,

T_p = physical half-life in days,

r = distance from the point source to the point of interest in centimeters,

t = exposure time in days.

This guide uses the NCRP equation (Equation 1) in the following manner to calculate the activities at which patients may be released.

- The dose to an individual likely to receive the highest dose from exposure to the patient is taken to be the *dose to total decay*. Therefore, $(1-e^{-0.693t/T_p})$ is set equal to 1.

- It is assumed that 1 roentgen is equal to 1 rem.

- The doses are calculated using the physical half-life of the radionuclides given in Appendix A and do not account for the biological half-life of the radionuclide.

- The gamma ray constants and half-lives for radionuclides typically used in nuclear medicine and brachytherapy procedures are given in Appendix A to this guide.

actions recommended to maintain doses to other individuals as low as reasonably achievable if the total effective dose equivalent to any other individual is likely to exceed 1 millisievert (0.1 rem)."

Section 35.75(c) requires that the licensee maintain "a record of the basis for authorizing the release of a individual for 3 years after the date of release, if the total effective dose equivalent is calculated (1) using an activity less than the activity administered, (2) using an occupancy factor less than 0.25 at 1 meter, (3) using the biological or effective half-life, or (4) considering the shielding by tissue."

Section 35.75(d) requires that the licensee maintain a record "that instructions were provided to a breast-feeding woman if the radiation dose to the infant or child from continued breast-feeding could result in a total effective dose equivalent exceeding 5 millisieverts (0.5 rem)."

Hereafter in this guide the individual to whom the radioactive material has been administered will be called the *patient*.

This guide provides guidance on determining when a licensee may authorize the release of a patient and when instructions must be given and records kept. The guide lists activities for commonly used radionuclides and their corresponding dose rates with which a patient may be released in compliance with the dose limits in 10 CFR 35.75.

The information collections contained in this regulatory guide are covered by the requirements in 10 CFR 35.75, which have been approved by the Office of Management and Budget, Approval No. 3150-0010.

B. DISCUSSION

The activities were calculated by using, as a starting point, the method discussed in National Council on Radiation Protection and Measurements (NCRP) Report No. 37, "Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides."[1]

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[1] National Council on Radiation Protection and Measurements (NCRP), "Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides," NCRP Report No. 37 (October 1, 1970). (Available for sale from the NCRP, 7910 Woodmont Avenue, Suite 800, Bethesda, MD 20814-3095.)

NOTE TO COMMISSION

This guide is a working draft rather than a final draft. It does not have Office concurrence, and it has not yet undergone final editing. It is thus subject to change before publication, but it is expected that the changes will be relatively minor. There should be no difficulty in publishing the final guide before the final rule is effective.

REGULATORY GUIDE 8.39
(Draft was issued as DG-8015)

RELEASE OF PATIENTS ADMINISTERED RADIOACTIVE MATERIALS

A. INTRODUCTION

Section 35.75, "Release of individuals containing radiopharmaceuticals or permanent implants," of 10 CFR Part 35, "Medical Use of Byproduct Material," permits licensees to "authorize the release from its control of any individual who has been administered radiopharmaceuticals or permanent implants containing radioactive material if the total effective dose equivalent to any other individual from exposure to the released individual is not likely to exceed 5 millisieverts (0.5 rem)."

In addition, 10 CFR 35.75(b) requires that the licensee "provide the released individual with instructions, including written instructions, on

ATTACHMENT 2

DRAFT REGULATORY GUIDE 8.39

10. In § 35.415, the introductory text to paragraph (a) and paragraph (a)(1) are revised and paragraph (a)(5) is removed.

§ 35.415 Safety precautions.

(a) For each patient receiving implant therapy and not released from licensee control pursuant to § 35.75 of this part, a licensee shall:

(1) Not quarter the patient or the human research subject in the same room as an individual who is not receiving radiation therapy.

* * * * *

Dated at Rockville, Maryland, this ___ day of _____ , 1996.

For the Nuclear Regulatory Commission.

_____

John C. Hoyle,
Secretary of the Commission.

maintain doses to other individuals as low as is reasonably achievable if the total effective dose equivalent to any other individual is likely to exceed 1 millisievert (0.1 rem). If the dose to a breast-feeding infant or child could exceed 1 millisievert (0.1 rem) assuming there were no interruption of breast-feeding, the instructions shall also include (1) guidance on the interruption or discontinuation of breast-feeding and (2) information on the consequences of failure to follow the guidance.

(c) The licensee shall maintain a record of the basis for authorizing the release of an individual, for 3 years after the date of release, if the total effective dose equivalent is calculated (1) using the retained activity rather than the activity administered, (2) using an occupancy factor less than 0.25 at 1 meter, (3) using the biological or effective half-life, or (4) considering the shielding by tissue.

(d) The licensee shall maintain a record, for 3 years after the date of release, that instructions were provided to a breast-feeding woman if the radiation dose to the infant or child from continued breast-feeding could result in a total effective dose equivalent exceeding 5 millisieverts (0.5 rem).

§ 35.315 [Amended]

9. In § 35.315, paragraph (a)(6) is removed and reserved.

§ 35.315 Safety precautions.

(a) * * *

(6) [Reserved]

* * * * *

Authority: Secs. 81, 161, 182, 183, 68 Stat. 935, 948, 953, 954, as amended (42 U.S.C. 2111, 2201, 2232, 2233); sec. 201, 88 Stat. 1242, as amended (42 U.S.C. 5841).

7. In Section 35.8, paragraph (b) is revised to read as follows:

§ 35.8 Information collection requirements: OMB approval.

* * * * *

(b) The approved information collection requirements contained in this part appear in §§ 35.12, 35.13, 35.14, 35.21, 35.22, 35.23, 35.27, 35.29, 35.13, 35.50, 35.51, 35.53, 35.59, 35.60, 35.61, 35.70, 35.75, 35.80, 35.92, 35.204, 35.205, 35.310, 35.315, 35.404, 35.406, 35.410, 35.415, 35.606, 35.610, 35.615, 35.630, 35.632, 35.634, 35.636, 35.641, 35.643, 35.645, and 35.647.

* * * * *

8. Section 35.75 is revised to read as follows:

§ 35.75 Release of individuals containing radiopharmaceuticals or permanent implants.

(a) The licensee may authorize the release from its control of any individual who has been administered radiopharmaceuticals or permanent implants containing radioactive material if the total effective dose equivalent to any other individual from exposure to the released individual is not likely to exceed 5 millisieverts (0.5 rem).[1]

(b) The licensee shall provide the released individual with instructions, including written instructions, on actions recommended to

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[1]Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials," describes methods for calculating doses to other individuals and contains tables of activities not likely to cause doses exceeding 5 millisieverts (0.5 rem).

(a) Each licensee shall conduct operations so that--

(1) The total effective dose equivalent to individual members of the public from the licensed operation does not exceed 0.1 rem (1 millisievert) in a year, exclusive of the dose contributions from background radiation, from any medical administration the individual has received, from exposure to individuals administered radioactive material and released in accordance with § 35.75, from voluntary participation in medical research programs, and from the licensee's disposal of radioactive material into sanitary sewerage in accordance with § 20.2003, and

(2) The dose in any unrestricted area from external sources, exclusive of the dose contributions from patients administered radioactive material and released in accordance with § 35.75, does not exceed 0.002 rem (0.02 millisievert) in any one hour.

* * * * *

5. In § 20.1903, paragraph (b) is revised to read as follows:

§ 20.1903 Exceptions to posting requirements.

* * * * *

(b) Rooms or other areas in hospitals that are occupied by patients are not required to be posted with caution signs pursuant to § 20.1902 provided that the patient could be released from licensee control pursuant to § 35.75 of this chapter.

* * * * *

PART 35--MEDICAL USE OF BYPRODUCT MATERIAL

6. The authority citation for part 35 continues to read as follows:

3. In § 20.1003, the footnote to the definition of *member of the public* is removed and the definitions of *occupational dose* and *public dose* are revised to read as follows:

§ 20.1003 Definitions.

* * * * *

Occupational dose means the dose received by an individual in the course of employment in which the individual's assigned duties involve exposure to radiation or to radioactive material from licensed and unlicensed sources of radiation, whether in the possession of the licensee or other person. Occupational dose does not include dose received from background radiation, from any medical administration the individual has received, from exposure to individuals administered radioactive material and released in accordance with § 35.75, from voluntary participation in medical research programs, or as a member of the public.

* * * * *

Public dose means the dose received by a member of the public from exposure to radiation or radioactive material released by a licensee, or to any other source of radiation under the control of a licensee. Public dose does not include occupational dose or doses received from background radiation, from any medical administration the individual has received, from exposure to individuals administered radioactive material and released in accordance with § 35.75, or from voluntary participation in medical research programs.

* * * * *

4. In § 20.1301, paragraph (a) is revised to read as follows:

§ 20.1301 Dose limits for individual members of the public.

For the reasons set out in the preamble and under the authority of the Atomic Energy Act of 1954, as amended; the Energy Reorganization Act of 1974, as amended; and 5 U.S.C. 552 and 553; the NRC is adopting the following amendments to 10 CFR parts 20 and 35.

PART 20--STANDARDS FOR PROTECTION AGAINST RADIATION

1. The authority citation for part 20 continues to read as follows:

Authority: Secs. 53, 63, 65, 81, 103, 104, 161, 182, 186, 68 Stat. 930, 933, 935, 936, 937, 948, 953, 955, as amended, sec. 1701, 106 Stat. 2951, 2952, 2953 (42 U.S.C. 2073, 2093, 2095, 2111, 2133, 2134, 2201, 2232, 2236, 2297f), secs. 201, as amended, 202, 206, 88 Stat. 1242, as amended, 1244, 1246 (42 U.S.C. 5841, 5842, 5846).

2. Section 20.1002 is revised to read as follows:

§ 20.1002 Scope.

The regulations in this part apply to persons licensed by the Commission to receive, possess, use, transfer, or dispose of byproduct, source, or special nuclear material or to operate a production or utilization facility under parts 30 through 35, 39, 40, 50, 60, 61, 70, or 72 of this chapter. The limits in this part do not apply to doses due to background radiation, to exposure of patients to radiation for the purpose of medical diagnosis or therapy, to exposure from individuals administered radioactive material and released in accordance with § 35.75, or to exposure from voluntary participation in medical research programs.

XIII. Regulatory Flexibility Certification

As required by the Regulatory Flexibility Act of 1980, 5 U.S.C. 605(b), the NRC certifies that this rule will not have a significant economic impact on a substantial number of small entities. This rule affects medical use of byproduct material licensees. The impact of the final rule will not be significant because the final rule basically represents a continuation of current practice.

XIV. Backfit Analysis

The NRC has determined that the backfit rule, 10 CFR 50.109, does not apply to this rule, and therefore, that a backfit analysis is not required for this rule, because these amendments do not involve any provisions that impose backfits as defined in 10 CFR 50.109(a)(1).

Lists of Subjects in 10 CFR part 20

Byproduct material, Licensed material, Nuclear materials, Nuclear power plants and reactors, Occupational safety and health, Packaging and containers, Penalty, Radiation protection, Reporting and recordkeeping requirements, Special nuclear material, Source material, Waste treatment and disposal.

Lists of Subjects in 10 CFR part 35

Byproduct material, Criminal penalty, Drugs, Health facilities, Health professions, Incorporation by reference, Medical devices, Nuclear materials, Occupational safety and health, Penalty, Radiation protection, Reporting and recordkeeping requirements.

XI. Paperwork Reduction Act Statement

This final rule amends information collection requirements that are subject to the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 et seq.). These requirements were approved by the Office of Management and Budget, approval number 3150-0010.

The public reporting burden for this collection of information is estimated to average 13 hours per licensee per year, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments on any aspect of this collection of information, including suggestions for reducing the burden, to the Information and Records Management Branch (T-6 F33), U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001, or by Internet electronic mail at BJS1@NRC.GOV; and to the Desk Officer, Office of Information and Regulatory Affairs, NEOB-10202, (3150-0010), Office of Management and Budget, Washington, DC 20503.

XII. Regulatory Analysis

The NRC has prepared a final regulatory analysis (NUREG-1492) on this regulation. The analysis examines the benefits and impacts considered by the NRC. The NRC has received public comments regarding the draft regulatory analysis and has addressed the comments (see Comments on the Draft Regulatory Analysis in III. Public Comments on the Proposed Rule). The final regulatory analysis is available for inspection at the NRC Public Document Room at 2120 L Street NW. (Lower Level), Washington, DC. Single copies are available as indicated in the ADDRESSES heading.

requirements that are more stringent than the NRC's requirements, but not less stringent. The recordkeeping requirements in §§ 35.75(c) and (d) are a Division 3 level of compatibility because uniformity in recordkeeping is not considered essential for this rule.

X. Finding of No Significant Environmental Impact: Availability

The NRC has determined under the National Environmental Policy Act of 1969, as amended, and the Commission's regulations in Subpart A of 10 CFR part 51, that the amendments are not a major Federal action significantly affecting the quality of the human environment, and therefore an environmental impact statement is not required. The final amendments clarify the pertinent regulatory language to reflect explicitly the relationship between 10 CFR part 20 and part 35 with respect to release of patients, and the amendments revise the release criteria for patients receiving radioactive material for medical use from an activity-based standard to a dose basis. It is expected that there will be relatively little change in radiation dose to the public or to the environment as a result of the revised regulation.

The final environmental assessment and finding of no significant impact on which this determination is based is available for inspection at the NRC Public Document Room, 2120 L Street NW. (Lower Level), Washington, DC. Single copies of the environmental assessment and the finding of no significant impact are available as indicated in the FOR FURTHER INFORMATION CONTACT heading.

The third statement of the policy reads "The NRC will minimize intrusion into medical judgments affecting patients and into other areas traditionally considered to be a part of the practice of medicine." The rule is consistent with this statement because it places no requirements on the administration of radioactive materials to patients and because the release of patients administered radioactive materials has long been considered a matter of regulatory concern to protect members of the public rather than solely a matter of medical judgment.

Thus, the final rule is considered to be consistent with the 1979 Medical Policy Statement.

IX. Issue of Compatibility for Agreement States

The NRC considers the definitions contained in § 20.1003 and the text in § 20.1301(a) that are modified by this rulemaking are Division 1 levels of compatibility. The definitions and text in these sections must be the same for all NRC and Agreement State licensees so that national consistency can be maintained.

Section 20.1002, "Scope," is a Division 3 level of compatibility because this section by nature is not a regulatory requirement and many States are prohibited by their administrative procedures act from including such sections in their rules. The scope section is a general statement of scope of the rule and does not contain specific requirements that are not presented in other sections of Part 20. Rules at the Division 3 level would be appropriate for Agreement States to adopt, but they do not require any degree of uniformity between NRC and State rules.

Additionally, §§ 35.75(a) and (b) are a Division 2 level of compatibility because the patient release criteria required by the rule are the minimum requirements necessary to ensure adequate protection of the public health and safety. The Agreement States will be allowed to establish

Finally, the requests made by the AMA did not all pertain to the issue of patient release. The final rule grants the request pertaining to patient release, i.e., that the radiation dose limits in 10 CFR 20.1301 should not apply to individuals exposed to the patient and that the dose limit to the individuals should be 500 millirems. The request to change the term "hospitalized" in 10 CFR 35.310(a) and 35.315(a) to the term "confined" was denied for the reasons discussed above. The request not related to the subject of patient release (that it should be clear in Part 20 that Part 20 does not limit the intentional exposure of patients to radiation for the purpose of medical diagnosis or therapy) was addressed in another rulemaking, "Medical Administration of Radiation and Radioactive Materials," which was published as a final rule on September 20, 1995 (60 FR 48623), and became effective on October 20, 1995.

VIII. Consistency with 1979 Medical Policy Statement

On February 9, 1979 (44 FR 8242), the NRC published a Statement of General Policy on the Regulation of the Medical Uses of Radioisotopes. The first statement of the policy reads "The NRC will continue to regulate the medical uses of radioisotopes as necessary to provide for the radiation safety of workers and the general public." The rule is consistent with this statement because its purpose is to provide for the safety of individual members of the public exposed to patients administered radioactive materials.

The second statement of the policy is "The NRC will regulate the radiation safety of patients where justified by the risk to patients and where voluntary standards, or compliance with these standards, are inadequate." This statement is not relevant to the rule because the rule does not affect the safety of patients themselves. The rule instead affects the safety of individuals exposed to patients.

based on NCRP Report No. 37 to relate the dose to the quantity of activity in the patient. Therefore, the wish of the petitioner to have an easy method to determine when the patient may be released is granted in Regulatory Guide 8.39.

(3) Delete 10 CFR 20.1301(d), which requires licensees to comply with provisions of the Environmental Protection Agency's environmental regulations in 40 CFR part 190 in addition to complying with the requirements of 10 CFR part 20. The EPA regulations referenced in 10 CFR 20.1301(d) are contained in 40 CFR part 190, which deals only with doses and airborne emissions from uranium fuel cycle facilities. Part 190 of Title 40 of the Code of Federal Regulations does not apply to hospitals or to the release of patients.

Furthermore, 10 CFR 20.1301(d) does not incorporate the EPA's Clean Air Act standards in 40 CFR part 61 that applies to hospitals. The NRC is separately pursuing actions with the EPA to minimize the impact of dual regulation under the Clean Air Act and to take agreed upon actions that will lead to EPA recision of 40 CFR part 61 for NRC and Agreement State licensees. Because the reference to EPA regulations in 10 CFR 20.1301(d) has nothing to do with the patient release issue, and therefore is outside the scope of this rulemaking. the final rule denies this request.

The requests made by the ACNM and their disposition may be summarized as follows:

(1) Adopt a dose limit of 5 millisieverts (0.5 rem) for individuals exposed to patients who have been administered radiopharmaceuticals. The final rule grants this request.

(2) Permit licensees to authorize release from hospitalization any patient administered a radiopharmaceutical regardless of the activity in the patient by defining "confinement" to include not only confinement in a hospital, but also confinement in a private residence. The final rule denies this request for the reasons described in the discussion on this issue.

radiopharmaceuticals that require this record are described in Regulatory Guide 8.39.

Finally, the NRC is deleting its requirements on written instructions in 10 CFR 35.315(a)(6) and 35.415(a)(5) because those paragraphs are redundant now that 10 CFR 35.75 has requirements for instructions. In addition, 10 CFR 35.415(a) and a(1) are reworded to clarify the original intent of the paragraphs, which was to limit the dose rate at 1 meter from the patient. The ambiguity was introduced when Part 20 was revised and a conforming change was made in 10 CFR 35.415. The conforming change that was made was not fully consistent with the original intended meaning of 10 CFR 35.415(a) and (a)(1).

VII. Disposition of the Petitions for Rulemaking

The three petitions for rulemaking submitted by Dr. Marcus (PRM-20-20), the ACNM (PRM-35-10 and PRM-35-10A), and the AMA (PRM-35-11) requested that the NRC amend the revised 10 CFR part 20 and 10 CFR part 35. These requests and their disposition by this rulemaking are discussed below.

The requests made by Dr. Marcus and their disposition may be summarized as follows:

(1) Raise the annual radiation dose limit in 10 CFR 20.1301(a) for individuals exposed to radiation from patients receiving radiopharmaceuticals for diagnosis or therapy from 1 millisievert (0.1 rem) to 5 millisieverts (0.5 rem). The final rule grants this request.

(2) Amend 10 CFR 35.75(a)(2) to retain the 1,110-megabecquerel (30-millicurie) limit for iodine-131, but provide an activity limit for other radionuclides consistent with the calculational methodology employed in the National Council on Radiation Protection and Measurements (NCRP) Report No. 37, "Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides."[1] The final rule does not contain activity limits, but Regulatory Guide 8.39 uses a calculational methodology

basis for the release, including the assumptions used for the calculations, must also be maintained.

This recordkeeping requirement is a modification of the proposed rule. The proposed rule would have required that a record be maintained of the basis for the patient's release, including all calculations performed, if the total effective dose equivalent to any individual other than the released patient is likely to exceed 1 millisievert (0.1 rem) in a year from a single administration. Under the proposed rule, the major purpose of the record was to provide the basis for limiting the dose to 5 millisieverts (0.5 rem) to individuals exposed to a patient who may receive more than one administration in a year. Upon reconsideration, based on public comments and consultation with the ACMUI, an NRC medical consultant, and the NRC Visiting Medical Fellow, the NRC has decided to delete this requirement. A review of medical treatment practices revealed no routine practice that would result in doses exceeding the 5 millisievert (0.5 rem) limit because of multiple administrations in the same year to the same patient. Without the need to account for the dose from multiple administrations, maintaining records for the many tens of thousands of patients released when their dose to an individual is likely to exceed 1 millisievert (0.1 millisievert) becomes an unnecessary burden. The requirement to retain these records has therefore been deleted. Each patient release is to be treated as a separate event, and licensee knowledge of previous administrations is unnecessary.

The NRC is also adopting a new 10 CFR 35.75(d) to require that the licensee maintain a record that instructions were provided to a breast-feeding woman if the administered activity could result in a total effective dose equivalent to the breast-feeding child exceeding 5 millisieverts (0.5 rem) if the mother did not interrupt or discontinue breast-feeding. Thus, the NRC is requiring records for certain radiopharmaceutical administrations (e.g., therapeutic administrations of iodine-131). The activities of

the retained activity rather than the activity administered, an occupancy factor less than 0.25 at 1 meter, the biological or effective half-life of the radionuclide, or shielding of radiation by the patient's tissue. Thus, records of release are required when the default assumptions are not used as discussed in Regulatory Guide 8.39. Measurements made in several studies indicate that the default assumptions should generally overpredict the dose even when instructions are not given or are not strictly followed. If a licensee administers an activity no greater than the value in the default table of release quantities provided in the regulatory guide as the basis for release, no record of release is required.

Licensees are already required by 10 CFR 35.53 to retain records of the measurement of the activity of each dosage of radioactive material administered to a patient; these records are typically maintained in a patient dose log. In addition, 10 CFR 35.32 requires licensees to retain a written directive and a record of each administered radiation dose or radiopharmaceutical dosage for therapeutic administrations and diagnostic administrations of iodine-125 or iodine-131 sodium iodide greater than 30 microcuries. These records can be used in conjunction with Regulatory Guide 8.39 to demonstrate that patient releases meet the requirements of 10 CFR 35.75(a) when no record is required by 10 CFR 35.75(c). When the licensee determines that the patient must be held to allow the reduction of radioactivity and then released, the licensee will need a record of release time to demonstrate that the release criteria have been met. A licensee may use any existing record to establish the release time. If biological elimination of radioiodine is a basis for release and the licensee uses the information in Regulatory Guide 8.39, a record of the thyroid uptake may be necessary as part of the basis for release because it is one of the nonstandard conservative assumptions listed in 10 CFR 35.75(c). If other case-specific factors are used as the basis for patient release that are in addition to, or modify, the standard conservative assumptions, a record of the

The purpose of describing the consequences is so that women will understand that breast-feeding after an administration of certain radionuclides could cause harm (e.g., iodine-131 could harm the child's thyroid). In other cases, the guidance could simply address avoidance of any unnecessary radiation exposure to the child from breast-feeding.

A requirement for instructions for certain patients was already contained in 10 CFR 35.315(a)(6) and 35.415(a)(5), but the modified requirement for written instructions adds approximately (a) 50,000 patients per year who are administered iodine-131 for the treatment of hyperthyroidism and (b) 27,000 patients per year, among about 8 million administered radiopharmaceuticals, who may be breast-feeding to whom additional written instructions be given. The purpose of the written instructions is to maintain doses to individuals exposed to patients as low as is reasonably achievable. The instructions may be either written only or written plus oral. The NRC believes that written instructions are necessary so that the patient and the patient's family and friends will have a document to refer to rather than having to rely solely on the patient's memory and understanding of the instructions.

The requirement of 10 CFR 35.75(b), requiring a licensee to provide guidance on discontinuation or the interruption period for breast-feeding and the consequences of failing to follow the recommendation, presumes that the licensee will make appropriate inquiry regarding the breast-feeding status of the patient. For breast-feeding women where the dose to the child is likely to exceed 1 millisievert (0.1 rem), the NRC requires that the patient be provided with specific instructions, as described in 10 CFR 35.75(b). There is no specific requirement to maintain a record indicating that breast-feeding status was determined prior to the release of the patient.

The NRC is adopting a new 10 CFR 35.75(c) to require that the licensee maintain a record of the basis for authorizing the release for 3 years if the calculation of the total effective dose equivalent to other individuals uses

The release criteria in 10 CFR 35.75(a) could prevent a woman from being released because of the potential transmission of radioactive materials in breast milk. The dose to the breast-feeding child is controlled by giving the woman guidance, as required by 10 CFR 35.75(b), on the interruption or discontinuation of breast-feeding and information on the consequences of failure to follow the guidance. The expectation is that the woman would follow the instructions and would interrupt or discontinue breast-feeding.

Finally, 10 CFR 35.75(a) includes a footnote to inform licensees that the NRC has made available guidance on rule implementation. The footnote states that Regulatory Guide 8.39, "Release of Patients Administered Radioactive Material," contains tables of activities not likely to cause doses exceeding 5 millisieverts (0.5 rem) and describes methods for calculating doses to other individuals.

The NRC is adopting a new 10 CFR 35.75(b) to require that the licensee provide released patients with instructions, including written instructions, on how to maintain doses to other individuals as low as is reasonably achievable if the total effective dose equivalent to any individual other than the released patient is likely to exceed 1 millisievert (0.1 rem). This also requires giving instructions to breast-feeding women if the dose to the child could exceed 1 millisievert (0.1 rem) assuming there were no interruption of breast-feeding. The instructions must include guidance on discontinuation or the interruption period for breast-feeding and the consequences of failing to follow the recommendation. Regulatory Guide 8.39 contains tables that show temporary interruption periods for various radiopharmaceuticals or discontinuation. The temporary interruption periods were calculated based on the determination that the dose to a child from breast-feeding is unlikely to exceed 1 millisievert (0.1 rem). However, the physician may use discretion in the recommendation, increasing or decreasing the duration of interruption somewhat depending on the woman's concerns about radioactivity or interruption of breast-feeding.

The NRC is amending 10 CFR 20.1903(b) to use the term "licensee control" rather than "confinement" because the latter term no longer applies to 10 CFR 35.75. The conforming change is necessary since the term "licensee control" more clearly reflects the NRC's intent in 10 CFR 35.75.

The NRC is adopting a new 10 CFR 35.75(a) to change the patient release criteria from 30 millicuries of activity in a patient or a dose rate of 5 millirems per hour at 1 meter from a patient to a dose limit of 5 millisieverts (0.5 rem) total effective dose equivalent to an individual from exposure to a released patient. (The dose from the radionuclide involved is taken to be the dose to total decay.) A dose-based limit provides a single limit that can be used to provide an equivalent level of protection from risks from all radionuclides. Also, the changes are supported by the recommendations of the ICRP and NCRP that an individual can receive an annual dose up to 5 millisieverts (0.5 rem) in temporary situations where exposure to radiation is not expected to result in annual doses above 1 millisievert (0.1 rem) for many years. Usually, the only individuals likely to exceed a dose of 1 millisievert (0.1 rem) will be those who are aware of the patient's condition such as the primary care-giver, a family member, or any other individual who spends significant time close to the patient.

This dose-based rule would, in some instances, permit the release of patients with activities greater than currently allowed. This is especially true when case-specific factors are evaluated to more accurately assess the dose to other individuals. The individuals exposed to the patient could receive higher doses than if the patient had been hospitalized longer. These higher doses are balanced by shorter hospital stays and thus lower health care costs. In addition, shorter hospital stays may provide emotional benefits to patients and their families. Allowing earlier reunion of families can improve the patient's state of mind, which in itself may improve the outcome of the treatment and lead to the delivery of more effective health care.

VI. Discussion of Text of Final Rule

This section summarizes the final rule. The NRC is amending 10 CFR 20.1301(a)(1) to state specifically that the dose to individual members of the public from a licensed operation does not include doses received by individuals exposed to patients who were released by the licensed operation under the provisions of 10 CFR 35.75. This is not a substantive change. It is a clarifying change to make clear that the Commission's policy is that patient release is governed by 10 CFR 35.75, not 10 CFR 20.1301.

For the sake of consistency and clarity, the same words are used in § 20.1002, "Scope"; in § 20.1003, "Definitions" (in the definitions of both public dose and occupational dose); and in § 20.1301, "Dose limits for individual members of the public." Also for consistency and clarity, the exclusion of dose from background radiation and from voluntary participation in medical research programs that are now included in §§ 20.1002 and 20.1003 are added to § 20.1301(a). In addition, the definition of "member of the public," as published in 60 FR 36038 on July 13, 1995, is revised by removing the footnote which read, "Except as delineated in other parts of 10 CFR Chapter 1." With the publication of this rule that footnote is no longer needed.

The NRC is amending 10 CFR 20.1301(a)(2) to state specifically that the limit on dose in unrestricted areas does not include dose contributions from individuals administered radioactive material and released in accordance with 10 CFR 35.75. The purpose of this change is to clarify that after a patient has been released under 10 CFR 35.75, licensees are no longer required to control radiation from the patient. The regulation uses the term "individual" to refer to the individual to whom the radioactive material has been administered rather than "patient" to clarify that the regulation refers to anyone receiving a medical administration.

administration of radioactive material and radiation from radioactive material. The NRC staff presented a summary of the comments on the proposed rule to the ACMUI during a public meeting held in Rockville, Maryland, on November 17 and 18, 1994.

Drafts of the final rule and regulatory guide were discussed with ACMUI in Rockville, Maryland, on October 18 and 19, 1995. The ACMUI supported the approach in this rule but suggested some clarifying changes. The NRC staff made all but one of the suggested changes. The ACMUI suggested using the term "rationale" instead of "consequences" in the requirement under the revised 35.75(b), to provide "guidance on the interruption or discontinuation of breast-feeding, and information on the consequences of failure to follow the guidance" for cases where failure to follow the instructions could result in a dose to the infant exceeding 1 millisievert (0.1 rem). Since most of the administrations that would be affected by this requirement are technetium-99m administrations, the ACMUI suggested the change because there was concern that the consequences of low doses of radiation cannot always be explained to the patient without causing unjustified alarm. Also, there was concern that physicians cannot explain with certainty the effects of low doses of radiation, such as would be caused by diagnostic administrations of technetium-99m. The staff did not change the rule in response to the ACMUI comment. The requirement to provide information on the consequences is included primarily to protect the breast-feeding infant from therapeutic administrations of radioiodine, which could cause serious thyroid damage. Regulatory Guide 8.39 will contain guidance on the types of information, including expected consequences, to be provided to patients to meet this requirement. Transcripts of the meetings have been placed in and are available for examination at the NRC Public Document Room, 2120 L Street NW. (Lower Level), Washington, DC.

radioactive material; only radioactive decay was considered. As a consequence, the draft regulatory analysis, in some cases, overestimated the time that patients would need to be retained under licensee control, and therefore the costs of patient retention were too high. The final regulatory analysis corrects the estimates.

The NRC believes that the current cost of $1,000 per day for a hospital room is not an overestimate. Under 10 CFR 35.315(a)(1), licensees are required to provide a private room with a private sanitary facility for each patient receiving radiopharmaceutical therapy and hospitalized for compliance with 10 CFR 35.75. Considering this NRC requirement and the recent reference cited in the final regulatory analysis on the cost of hospitalization, $1,000 per day for a hospital room is a reasonable estimate.

Comment. One commenter said that the description of the measured doses received by family members was not consistent with the reference cited.

Response. The commenter is correct. An incorrect reference was given. The final regulatory analysis provides the correct reference.

IV. Coordination with NRC Agreement States

The NRC staff discussed the status of this rulemaking effort at two public meetings: the Agreement State Managers Workshop held on July 12-14, 1994, and at the All Agreement States Meeting held on October 24-25, 1994. The Agreement States expressed no objections to the approach in this rule.

V. Coordination with the Advisory Committee on Medical Uses of Isotopes

The Advisory Committee on Medical Uses of Isotopes (ACMUI) is an advisory body established to advise the NRC staff on matters that involve the

Response. The Commission recently adopted a value of $2,000 per person-rem as explained in Revision 2 of NUREG/BR-0058, "Regulatory Analysis Guidelines of the U.S. Nuclear Regulatory Commission (November 1995)," Section 4.3.3, "Evaluation of Values and Impacts." (Single copies of NUREG/BR-0058 are available as indicated in the ADDRESSES heading.) The draft regulatory analysis, which was prepared utilizing $1,000 per person-rem, employed a simple computational model using the physical half-life only of radiopharmaceuticals. The regulatory analysis has been revised to include use of $2,000 per person-rem, as well as a more realistic dose model based on biological retention and elimination of the radiopharmaceuticals. The more realistic model with a value of $2,000 continues to demonstrate the cost-effectiveness of the dose-based limit. Specifically, the savings in hospital costs under the earlier release time allowed are estimated at $14 million, whereas the collective dose of 2,740 person-rem (at a value of $2,000 per person-rem) corresponds to a cost of about $5 million.

NUREG-1492 contains a detailed discussion of the model and the benefits and impacts of the dose-based limit. Single copies of the final regulatory analysis are available as indicated in the ADDRESSES heading.

Comment. One commenter said that the benefits of the rule were overestimated because the length of time that a thyroid patient would have to remain in the hospital was overestimated and the cost of a hospital room was overestimated, being $450 per day rather than $1,000 per day as assumed in the draft regulatory analysis.

Response. The commenter is correct that the benefits of the rule were overestimated. The estimates in the draft regulatory analysis of days of hospitalization required did not include biological elimination of the

Response. The NRC believes that there may be some situations for which a case-specific calculation could be done for a class of patients. The record for a particular patient's release could then reference the calculation done for the class of patients. However, depending on a patient's individual status (e.g., lower occupancy factor), there may be cases when the calculation will be done for a specific individual.

Comment. One commenter said that the discussion on radiolabeled antibodies in the draft guide was wrong because antibodies labeled with iodine-131 will be deiodinated in the body and the iodine will behave like other iodine. None of the radiolabeled antibodies now being developed or planned for the future should have an internal dose hazard for the general public.

Response. The NRC agrees with this comment. Statements in Regulatory Guide 8.39 are now modified.

COMMENTS ON THE DRAFT REGULATORY ANALYSIS (DRAFT NUREG-1492)

Comment. One commenter said that the value of a person-rem should be $40 rather than $1,000 as used in the draft regulatory analysis for the purpose of evaluating the costs and benefits of the rule. The commenter cited a 1993 Health Physics Society position paper as a reason that the value should be $40 per person-rem.

guidance on the interruption or discontinuation of breast-feeding should be given. Expanded examples are now given in Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials." The example on thyroid cancer was revised to include more realistic assumptions, and an additional example on hyperthyroidism was added. The NRC believes that the examples provided illustrate the techniques sufficient to perform the whole range of potential calculations.

Comment. One commenter said that the draft regulatory guide did not provide enough information on when and for how long breast-feeding of infants should be interrupted.

Response. Regulatory Guide 8.39 has been greatly expanded with respect to information on the breast-feeding child, including a table on recommendations for the interruption or discontinuation of breast-feeding for specific radiopharmaceuticals.

Comment. One commenter said that the sample instructions in the draft guide concerning implants should include a picture of an implant seed.

Response. The sample instructions were not expanded to include this because of graphics limitations, but licensees may add photos if desired.

Comment. Several commenters asked whether multiple individual calculations have to be done or if a generally applicable calculation could be done once and used for many patients.

Comment. One commenter said that the factor of 10^{-6} used in the draft guide to estimate internal dose is not well supported for nonoccupational exposures. Another commenter said that the calculation of dose to individuals exposed to the patient ignores the potential of radiation dose from the excretion of radioactive material from the patient, and this could present a significant radiological hazard to family members.

Response. It is true that there is not a great deal of information on the use of the factor in nonoccupational settings, but measurements (described in NUREG-1492) have been made in which iodine uptake was measured in people exposed to a patient. These data suggest that the fractional uptake of the administered activity will be on the order of 10^{-6}. Since iodine is among the most soluble and volatile radiopharmaceuticals, it can be expected that the transfer to others of less soluble and less volatile radiopharmaceuticals would be less than that of iodine.

In addition, the NCRP recently concluded that, for individuals exposed to radionuclide therapy patients, the risks of external irradiation and potential contamination are minor from a public health viewpoint; therefore a significant intake from a contamination incident is very unlikely.[2]

Comment. A medical organization commented that the draft guide is not complete and does not provide sufficient comprehensive examples to assist licensees in complying with the rule.

Response. The NRC has expanded the guide to include information and further examples on the biological elimination of iodine-131 and on when

and phosphorous-32. Another commenter said that the table should be expanded to include chromium-51, selenium-75, ytterbium-90, tin-117m, and iridium-192.

Response. Values for the beta emitters strontium-89 and phosphorous-32 have been added to the table of release quantities in Regulatory Guide 8.39. The table of release quantities was also expanded to add values for chromium-51, selenium-75, ytterbium-90, tin-117m, and iridium-192.

Comment. The table of release quantities in the draft regulatory guide should be expanded to include accelerator-produced radioactive materials as an aid to Agreement States.

Response. Several accelerator-produced materials were added to Regulatory Guide 8.39 as an aid to the States and to medical facilities. The NRC has no regulatory authority over the release of patients administered accelerator-produced materials and would not inspect the release of patients administered accelerator-produced materials.

Comment. One commenter said that the regulatory guide should have a table of release quantities based on biological half-life rather than only the physical half-life.

Response. Regulatory Guide 8.39 now provides more information on release quantities for iodine-131 based on biological half-lives.

Response. Draft Regulatory Guide 8.39 discussed situations in which it might be permissible to lower the occupancy factor from 0.25 to 0.125, but did not recommend occupancy factors less than 0.125. Occupancy factors less than 0.125 may be difficult to justify because it is generally not realistic to assume that the patient can avoid all contact with others. However, lower values for the occupancy factor are not prohibited by the regulation, but they must be justified in the record of the calculation, as the record will be subject to inspection.

Comment. Several commenters said that the iodine-131 retention fraction of 0.3 used in the draft guide for treatment of thyroid cancer is too large and that the correct value should be 0.05 or less. Another commenter said that the biological half-life of extrathyroidal iodine should be 0.5 day for both the euthyroid and hyperthyroid condition. One commenter said that the biological half-lives from ICRP Publication No. 53 should be used for thyroid cancer.

Response. The NRC agrees that the commenters raised valid points. In Regulatory Guide 8.39, the iodine retention fraction for thyroid cancer was changed to 0.05. The biological half-life for the extrathyroidal fraction was changed to 0.33 day. In addition, the biological half-lives from ICRP Publication No. 53 were used for the thyroid cancer case.

Comment. One commenter said the table of release quantities in the draft guide should be expanded to include beta emitters such as strontium-89

be used with little consideration of the specific details of a particular patient's release. A review of published information, as described in the regulatory analysis, NUREG-1492, "Regulatory Analysis on Criteria for the Release of Patients Administered Radioactive Material" (1996), finds that measured doses are generally well below those predicted by the methodology used to calculate the table of default release quantities. Thus, the default release quantities are conservative as the NRC intended. However, the licensee is given the option of using case-specific calculations that may be less conservative.

Nevertheless, the NRC agrees that the assumption used in the draft guide of 24-hour nonvoiding in the thyroid cancer example was overly conservative. The revised example uses an excretion half-life of 8 hours as recommended by the ICRP in ICRP Publication 53, "Radiation Dose to Patients from Radiopharmaceuticals."[5]

Comment. One commenter said that the occupancy factor (generally assumed to be 0.25 at 1 meter) should not be left to the discretion of the licensee because low occupancy factors could easily be justified by providing strict safety instructions without any verification that the instructions will be followed. Another commenter liked the flexibility provided by being able to adjust the occupancy factor, but wanted to know if other considerations are allowed and if it is acceptable to use values lower than 0.125.

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[5]International Commission on Radiological Protection (ICRP), "Radiation Dose to Patients from Radiopharmaceuticals," ICRP Publication No. 53 (March 1987). Available for sale from Pergamon Press, Inc., Elmsford, NY 10523.

assumption used in calculating doses is too conservative. As evidence that the calculations are too conservative, several commenters said that the doses measured using dosimeters were much lower than doses calculated using the models in the draft guide.

Response. The NRC has revised the guide to use a phased approach for determining when release can be authorized. While the calculations can sometimes be complex, the results of calculations that use conservative assumptions are given in a table of release quantities in Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials." Of the 8 to 9 million administrations performed annually, in all except about 10,000 cases (radioiodine therapy for thyroid cancer), release can be authorized based on conservative assumptions and using Table 1 with no calculational effort on the part of the licensee and no additional recordkeeping beyond what is already required. For permanent implants, the guide provides dose rates at 1 meter from the patient at which release may be authorized. Thus, for implants, there would be no calculational effort needed. In addition, the guide provides information on iodine therapy for thyroid cancer that can be used for determining release based on retention and elimination. This additional information in the guide will allow the licensee to perform the calculation with relatively little effort.

With regard to the comments that the methodology is too conservative and that measured values are lower than calculated by the methodology, the methodology in the table giving default release quantities is intended to be conservative. The NRC believes it is appropriate and prudent to be conservative when providing generally applicable release quantities that may

Response. The NRC recognizes that the licensee has no control over the patient after the patient has been released. The quantities for release listed in Table 1 of Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials," were calculated using conservative assumptions (for example, by using the physical half-life of the radioactive material rather than the more realistic effective half-life). Thus, the NRC considers it unlikely that the dose to an individual in real circumstances would approach 5 millisieverts (0.5 rem).

In special situations, such as when a released patient would immediately board an airplane and would therefore be in close contact with one or more individuals, it may be necessary to base the release on a more realistic case-specific calculation. Once the patient is released, the responsibility for following the instructions is entirely the patient's, not the licensee's.

COMMENTS ON THE DRAFT REGULATORY GUIDE

Comments were also requested on Draft Regulatory Guide, DG-8015, "Release of Patients Administered Radioactive Materials," associated with this rulemaking. Because the guide is associated with the rule, the comments received on the draft guide are discussed here. Most of the comments concerned the method and the assumptions used to calculate the dose to the individual likely to receive the highest dose.

Comment. Several commenters said that the calculational methodology in the draft guide is too complex and that the assumptions are too conservative. As an example, several commenters said that the assumed 24-hour nonvoiding

based on the licensee's determination that the total effective dose equivalent to an individual from the released patient is not likely to exceed 5 millisieverts (0.5 rem). The dose to the breast-feeding child from breast-feeding is a criterion for release but it can be controlled by giving the woman guidance on the interruption or discontinuation of breast-feeding, as required by the new 10 CFR 35.75. However, the release could be based on the default table of release activities in the regulatory guide or a patient-specific calculation, as required by the new 10 CFR 35.75. The issue of the dose to the breast-feeding child is discussed in NUREG-1492 and Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials."

Comment. One commenter said that the proposed rule did not accurately represent the position of the Advisory Committee on Medical Use of Isotopes.

Response. A review of the transcript for the ACMUI meeting in May 1992 shows that the Federal Register Notice provided an accurate description of the ACMUI position. The final rule was discussed with the ACMUI on October 18, 1995, and the ACMUI, in general, supported the rule. (For ACMUI's comments and NRC's responses, see V. Coordination with the ACMUI.)

Comment. One commenter said that its facility treated many foreign patients with therapeutic pharmaceuticals. These patients frequently may leave the hospital and immediately board a plane to return home. Thus, there is a limit to the amount of control that a licensee has over the patient.

Response. The term "release from licensee control," when read in context, refers to radiation protection considerations and is sufficiently clear that there is no need to define the term.

MISCELLANEOUS COMMENTS ON THE RULE

Comment. Several commenters said that the rule should not be a matter of Agreement State compatibility at any level.

Response. The NRC does not agree. The NRC conducts an assessment of each proposed requirement or rule to determine what level of compatibility will be assigned to the rule. These case-by-case assessments are based, for the most part, on protecting public health and safety. NRC has evaluated the final rule and assigned compatibility designations ranging from level 1 (full compatibility required) to level 3 (uniformity not required) as detailed later in this Federal Register notice.

Comment. Several commenters said that a breast-feeding infant should not be considered as an individual exposed to the patient for the purposes of determining whether patient release may be authorized. These commenters said that consideration of the breast-feeding infant should be under the jurisdiction of the physician, that the issue is a medical issue rather a regulatory issue, and that the NRC should not interfere in medical issues.

Response. The NRC does not agree. The NRC has a responsibility to protect the public health and safety, and that responsibility extends to all individuals exposed to a patient administered licensed radioactive materials, including breast-feeding children. When the release is authorized, it is

However, good health physics practice would be to continue to make efforts to maintain doses to people at the facility as low as is reasonably achievable.

Comment. Commenters also asked how a patient can be confined to his or her house.

Response. These commenters misunderstood the concept of confinement. As explained in the Statement of Considerations for the proposed rule (59 FR 30724), the term "confinement" no longer applies to the revision to 10 CFR 35.75. Instead, the text of the rule uses the phrase "licensee control" to more clearly reflect the NRC's intent.

The NRC believes that there is a distinct difference between a patient being under licensee control in a hospital or other licensee facility (e.g., a hospice or nursing home) and being at home. In a hospital or other area or address of use listed on the NRC license, the licensee has control over access to the patient as well as having trained personnel and instrumentation available for making radiation measurements not typically available at the patient's home. In addition, while under licensee control, a licensee has control over the dose by limiting the amount of time that individuals are in close proximity to the patient. A patient who goes home is released from licensee control.

Comment. One commenter thought that the rule should define the term "release."

that the burden of requiring instructions cannot be justified. Under the final rule, if the dose to any individual exposed to the patient is not likely to exceed 1 millisievert (0.1 rem), instructions are not required but the physician could give any instructions that he or she considers desirable.

CONFINEMENT OF PATIENTS

Comment. Two commenters said that patients cannot be confined against their wishes and that the rule provides no penalty for the patient who leaves confinement in the hospital "against medical advice." Another commenter said that the rule seems to require that the licensee have control of the patient's activities after release.

Response. The NRC recognizes that patients cannot be held against their will. The rule deals with the conditions under which the licensee may authorize release. The NRC would not penalize a licensee for the activities of the patient after release or if the patient were to leave "against medical advice."

Comment. One commenter asked whether a patient who was releasable but was still hospitalized for other reasons would still be considered under the licensee's control.

Response. Once the licensee has authorized the release of the patient, there is no need to keep the patient under licensee control for radiation protection purposes if the patient remains hospitalized for other reasons.

asked how the licensee could verify that the instructions are followed. Another commenter said that a sizable fraction of patients may not follow radiation safety instructions to protect spouses and may be ever less careful about protecting total strangers. This commenter also asked whether it is reasonable to expect that released patients will alter their behavior and limit their activities for the protection of others.

Response. The NRC does not intend to enforce patient compliance with the instructions nor is it the licensee's responsibility. However, it is the responsibility of licensees to provide instructions to the patients. Following the instructions is normally the responsibility of the patient. However, American medical practice routinely depends on patients following instructions, such as instructions on when and how to take medications.

With regard to compliance with the instructions, surveys of patients and their spouses, as discussed in the supporting regulatory analysis, indicate that most will attempt to follow the instructions faithfully, especially with regard to protecting their children, although some patients and their spouses indicated that they might not keep physically distant from their spouse for prolonged periods of time.

Comment. One commenter said that instructions should be given for all administrations of radioactive material, regardless of the quantity administered.

Response. The NRC does not agree. In some cases, particularly in the large number of diagnostic administrations, the potential doses are so small

include in the contents of the written instructions, and is directed at minimizing the risk to the patient's family who have no doctor-patient relations to the prescribing or administering personnel. However, Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials," recommends contents of the written instructions.

Further discussion of the 1979 Medical Policy Statement is presented under the heading, "VIII. Consistency with 1979 Medical Policy Statement."

Comment. Several commenters asked whether written instructions were appropriate if the patient was blind, illiterate, or did not read English. Another commenter said that the instructions should be both written and oral and should be in the primary language of the patient.

Response. The NRC believes that written instructions are useful and should be required. If the patient is blind, illiterate, or does not read English, it is likely that someone else will be able to read the instructions for the patient. NRC considers it too much of a burden to require that the instructions be given in the primary language of the patient, although the regulations do not preclude foreign language written instructions if the licensee chooses to provide them. In most situations, it will be possible to find someone who can translate for the patient if necessary. The requirement that written instructions be given to the patient does not preclude additional oral instructions.

Comment. Several commenters asked how the NRC would enforce implementation of the instructions given to the patient. Another commenter

Response. The NRC believes that providing written instructions has a significant value because often patients will not remember all of the instructions given orally. In addition, written instructions can be read by other family members or care givers. The requirement to provide the instructions in written form was also supported by the ACMUI.

This regulation allows the licensee to determine the form of the written instructions. The NRC believes that for the majority of releases requiring written instructions, the written instructions can be prepared in a generic form. For example, the Society of Nuclear Medicine has prepared a brief pamphlet, "Guidelines for Patients Receiving Radioiodine Treatment," which can be given to patients at nominal cost (less than $1 per patient). However, oral instructions may also be provided in all cases.

Comment. Several commenters said that dictating to a physician how and what he or she must tell a patient is not the purview, mandate, or competence of the NRC and interferes with an essential part of medical practice, which is communication between physician and patient.

Response. In a policy statement published on February 9, 1979 (44 FR 8242), entitled "Regulation of the Medical Uses of Radioisotopes; Statement of General Policy," the NRC made three specific statements. The third statement of the policy is "The NRC will minimize intrusion into medical judgments affecting patients and into other areas traditionally considered to be a part of the practice of medicine." The final rule is consistent with this statement because it does not dictate the choice of medical treatment or diagnosis, does not specify the details of what the physician must say or must

WRITTEN INSTRUCTIONS TO PATIENTS

In general, there was little objection to providing instructions to patients on how to minimize the dose to others, but there was significant opposition to the proposed requirement that the instructions would have to be written.

Comment. One commenter said that the Statement of Considerations for the proposed rule was in error in stating that the existing regulations already required that the instructions to patients be written.

Response. The commenter is correct. The Statement of Considerations was in error on that point. The existing regulations do not specify that instructions have to be in written form.

Comment. A number of commenters said that instructions should not need to be written and that oral instructions should be permissible. Some of these commenters said that oral instructions are more effective and that how the instructions should be given is within the province of the doctor-patient relationship and that the NRC and its regulations should not interfere with that relationship. One commenter said that the physical condition of the patient could lessen the patient's ability to follow the instructions. Another commenter said that the standard written instructions require too much time explaining how each patient varied from the standard instruction sheet. However, one Agreement State and a major health maintenance organization strongly supported the requirement that the instructions be written.

pharmacists to work for the NRC for a period of 1 to 2 years. Both the ACMUI and the current Visiting Medical Fellow, Myron Pollycove, M.D., provided advice to the NRC during the development of this rule. In addition, Barry A. Siegel, M.D., Chairman of the ACMUI, reviewed the patient records at his medical facility for the 1-year period from July 1, 1993, to June 30, 1994 (Mallinckrodt Institute of Radiology, St. Louis, Missouri). Drs. Siegel and Pollycove concluded that no routine nuclear medicine practice, be it diagnostic, therapeutic, or a combination of the two, results in multiple large administrations that would be likely to cause the 5-millisievert (0.5-rem) dose limit to be exceeded because of multiple administrations in a year.

While the proposed requirement to maintain a record of the dose to another individual if the dose is likely to exceed 1 millisievert (0.1 rem) has been deleted, a recordkeeping requirement with a reduced impact has been retained as discussed under the heading, "Discussion of Text of Final Rule."

Comment. Several commenters said that those who pay for health care will put great pressure on physicians to optimize calculations to reduce in-patient days and to justify out-patient treatments.

Response. There is no objection to optimizing calculations to reduce in-patient days as long as the calculations are realistic and the 5-millisievert (0.5-rem) limit in 10 CFR 35.75 is met. Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials," describes examples of calculations that are acceptable to the NRC.

effective dose equivalent greater than 1 millisievert (0.1 rem) are not done to the same patient routinely. Other commenters said that there have been decades of experience unencumbered by any paperwork burden at all with no evidence that a lack of paperwork has resulted in any additional problems. One commenter said that if 0.5 rem is acceptably safe, why have the documentation required at the 0.1 rem level.

Another commenter said that it cannot be a licensee's responsibility to know the details of a radionuclide therapy performed by another licensee in terms of which members of the public received the most radiation dose from that other licensee's therapy procedure.

One commenter said that the excessive recordkeeping cost would be a nonreimbursable cost, and the burden will cause many physicians to stop offering iodine therapy, which would force patients to travel to large medical facilities in cities and cause problems with patient access in sparsely populated areas.

Response. Upon reconsideration, the NRC has decided to delete the requirement to keep records when the dose to the most highly exposed individual is likely to exceed 1 millisievert (0.1 rem). The requirement was proposed so that it would be possible to account for the dose from multiple administrations in the same year to ensure that the total dose to an individual exposed to the patient did not exceed 5 millisieverts (0.5 rem).

The NRC has an advisory committee, the Advisory Committee on the Medical Uses of Isotopes, or "ACMUI," which advises the NRC on rulemakings and other initiatives related to the medical use of byproduct materials. The NRC also has a visiting medical fellows program that recruits selected physicians or

The NRC does not agree that the latter NCRP recommendation should apply in general. The NRC believes that if the dose to another individual is likely to exceed 5 millisieverts (0.5 rem), the patient should remain under the control of the licensee. Licensee control is necessary to provide adequate protection to the individuals exposed to the patient.

RECORDKEEPING

The strongest opposition to the proposed rule was to the proposed requirement to maintain a record of the released patient and the calculated total effective dose equivalent to the individual likely to receive the highest dose if the dose to that person is likely to exceed 1 millisievert (0.1 rem). Under the proposed rule, if a patient had or might have had one or more administrations within the same year, the licensee would use the records to determine the dose from the previous administrations so that the total dose to an individual exposed to a patient from all administrations would not exceed 5 millisieverts (0.5 rem).

Comment. Many commenters indicated that this requirement would cause excessive costs in time, effort, and money to track down records of previous administrations, to perform calculations, and to keep records of all the work and asked that the requirements to make calculations and keep records be removed. The commenters believed that the work would not produce an increased level of safety, that the NRC greatly underestimated the cost, and that the recordkeeping would be unnecessary, inappropriate, and impractical. Some commenters said that multiple administrations that would result in a total

individual exposed to a patient has so little hazard that the NRC should not be concerned with it.

Response. The NRC does not believe that individuals exposed to a patient should, in general, receive doses in excess of 5 millisieverts (0.5 rem). This is consistent with the recommendations of the ICRP in ICRP Publication 60,[3] "1990 Recommendations of the International Commission on Radiological Protection"; and the recommendations of the NCRP in NCRP Report No. 116,[4] "Limitation of Exposure to Ionizing Radiation." Each of these recommendations provides a basis for allowing individuals to receive annual doses up to 5 millisieverts (0.5 rem) under certain circumstances. Both the ICRP and the NCRP recommend that an individual can receive a dose up to 5 millisieverts (0.5 rem) in a given year in situations when exposure to radiation is not expected to result in doses above 1 millisievert (0.1 rem) per year for a long period of time, as would be the case for doses from released patients. In NCRP Commentary No. 11, "Dose Limits for Individuals Who Receive Exposure from Radionuclide Therapy Patients,"[2] the NCRP recommended a dose limit of 5 millisieverts (0.5 rem) annually for members of the patient's family. However, on the recommendation of the treating physician, the NCRP considered it acceptable that members of the patient's family be permitted to receive doses as high as 50 millisieverts (5 rems).

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[3]International Commission on Radiological Protection (ICRP), "1990 Recommendations of the International Commission on Radiological Protection," ICRP Publication No. 60 (November 1990). Available for sale from Pergamon Press, Inc., Elmsford, NY 10523.

[4]National Council on Radiation Protection and Measurements, "Limitation of Exposure to Ionizing Radiation," NCRP Report No. 116 (March 31, 1993). Available for sale from the NCRP, 7910 Woodmont Avenue, Suite 800, Bethesda, MD 20814-3095.

5 millisieverts (0.5 rem). For example, if a licensee uses the default table of release quantities provided in the regulatory guide as the basis for release, a patient administered 1,221 megabecquerels (33 millicuries) or less of iodine-131 could be immediately released and no record of release is required. However, if the licensee wishes to release a patient with an activity that is greater than the value in the default table, the licensee must do a dose calculation using case-specific factors to demonstrate compliance with the release criteria. Furthermore, if the table is used as the basis for release but the administered activity exceeds the value in the table, the licensee must hold the patient until the time at which the retained activity is no greater than the quantity in the table or the dose rate at 1 meter is no greater than the value in the table. When the administered activity is greater than the value in the default table, a record of the basis for the release must be maintained for NRC review during inspection. Regardless of the method used by the licensee to authorize release, the dose limit of 5 millisieverts (0.5 rem) in the revised 10 CFR 35.75 applies. By identifying more than one method for calculating the release of a patient in accordance with 10 CFR 35.75, the NRC provides greater flexibility for licensees to achieve compliance with the new requirement while still providing adequate protection of public health and safety.

Comment. One commenter said that in some cases it should be permissible to authorize the release of a patient even if the dose to a family member might exceed 0.5 rem because the release might be beneficial and acceptable to family members. Another commenter said that a dose of 0.5 rem to an

(0.5-rem) limit that is applied to household members exposed to a patient is a special limit that is appropriate for only occasional use and for use where there is a definite need. This special limit fits the case of doses received by the household members of a released patient, but does not fit the case of people who frequent a hospital on a routine basis. Lastly, in limiting doses, the NRC considers what is reasonably achievable. The mere fact that a home cannot control contamination as well as a hospital does not mean that the contamination control achieved in homes is not adequate. Actual measurements of doses to household members from contamination, as discussed in NUREG-1492, show that the doses from contamination are low, demonstrating that the degree of contamination control that was achieved is adequate.

Comment. One commenter said that the proposed rule did not adequately address the concerns that the Agreement States expressed on the petitions for rulemaking concerning releasing patients with quantities of iodine-131 in excess of 30 millicuries.

Response. In commenting on the petitions, a number of States expressed concerns about releasing patients administered 14.8 gigabecquerels (400 millicuries) of iodine-131, which one of the petitioners had requested. However, the States that commented were generally favorable to the proposed rule limiting the dose to the most exposed individual to 5 millisieverts (0.5 rem), and none of the States indicated that their concerns were misrepresented. In fact, one Agreement State commented that it was pleased that the NRC had considered the comments made by the Agreement States at various meetings with the NRC. The dose-based limit would generally permit releases if the dose to another individual would not be likely to exceed

Regarding the comment on the doubling of risk of developing thyroid cancer, there is no scientific consensus by the United Nations Scientific Committee on the Effects of Atomic Radiation, ICRP, or NCRP to support the suggested increased risk of thyroid cancer following ingestion of iodine-131. Based on the information currently available, the Commission continues to conclude that the benefits outweigh the potential of small increased risks associated with this rule.

Comment. One commenter noted that hospitals now make great efforts to control contamination from patients who are now hospitalized because they contain more than 30 millicuries of iodine-131. This commenter stated that it would not be possible to maintain the same level of contamination control at these patients' homes if these patients were released with more than 30 millicuries of iodine-131.

Response. The NRC agrees that, even though released patients are given instructions on how to limit the hazard from contamination, contamination control in a hospital can be more effective than contamination control out of the hospital. However, the two situations are not really comparable. In the case of the released patient's home, therapeutic administrations almost never occur more than once in a year and only rarely occur more than once in a lifetime; but in the case of a hospital, large therapeutic administrations are done repeatedly on many patients. Therefore, areas in hospitals have the potential for contamination from many patients, and people who frequent the hospital (e.g., clergy or a hospital orderly) have the potential to be exposed to contamination from many patients. In addition, the 5-millisievert

released patients have been measured in several studies and in every case were less than 10 percent of the 5-millisievert (0.5-rem) total effective dose equivalent limit and were most often less than 1 percent of the 5-millisievert (0.5-rem) limit. In addition, the internal doses resulting from contamination were always less and generally far less than the external dose, meaning that contamination was the less important source of radiation exposure. These measurements show that even if the family members repeatedly touched household items touched by the patient, contamination does not cause unacceptably high doses. These findings were true even in the case of a British study where eleven patients volunteered to disregard special precautions against contamination and minimizing spousal and family exposure. These measurements are discussed in NUREG-1492. Also, the NCRP recently addressed the risk of intake of radionuclides from patients' secretions and excreta in NCRP Commentary No. 11, "Dose Limits for Individuals Who Receive Exposure from Radionuclide Therapy Patients," and concluded that, "... a contamination incident that could lead to a significant intake of radioactive material is very unlikely."[2]

In general, the physical reactions (e.g., vomiting) that a patient may experience from the administration of any radiopharmaceutical are rare. Vomiting is seldom an important elimination route for radiopharmaceuticals after the patient has left the medical facility since orally administered radiopharmaceuticals such as iodine-131 are rapidly absorbed, within a half hour, by the gastrointestinal system.

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[2]National Council on Radiation Protection and Measurements, "Dose Limits for Individuals Who Receive Exposure from Radionuclide Therapy Patients," NCRP Commentary No. 11 (February 28, 1995). (Available for sale from the NCRP, 7910 Woodmont Avenue, Suite 800, Bethesda, MD 20814-3095.)

specifies the dose rate at 1 meter of commonly used radionuclides that allow licensees to authorize patient release.

RELEASE QUANTITIES

Using a dose-based system based on a dose to the most highly exposed individual of 5 millisieverts (0.5 rem) would, in some circumstances, allow release of a patient with more than 1,110 megabecquerels (30 millicuries) of activity. Some commenters were opposed to allowing releases with higher activities than are now permitted.

Comment. Several commenters said that the release of patients with more than 30 millicuries of iodine-131 should not be permitted because of concerns about the risk of internal exposure. One commenter said that doses to family members from the patient vomiting were not adequately considered. The same commenter also said that a study indicated that in-home contamination by patients dosed with I-131 could double family members' risk of developing thyroid cancer.

Response. The concern over contamination is not justified by the radiation doses that are likely to be caused by the removal of radionuclides from the patient's body by the pathways of exhaled air, feces, saliva, sweat, urine, and vomit. Measurements from several studies, as discussed in the supporting regulatory analysis, have shown that a relatively small proportion of the radioactive material administered will appear as contamination. Doses to family members exposed to contamination from living in close contact with

NUREG-1492 contains a detailed examination of the benefits and impacts of the final rule that includes dose estimation, recordkeeping, and radiation exposure. Single copies of the final regulatory analysis and Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials," are available as indicated in the ADDRESSES heading.

Comment. A commenter said that the calculational approach in the rule would require the physician to ask many personal questions of the patient.

Response. The commenter is incorrect in believing that the dose-based approach will generally require personal information from the patient. The NRC anticipates that nearly all patients will be released based on default assumptions which do not require any personal information from the patient. A table of release quantities, based on standard conservative assumptions, is provided in Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials." However, the rule does allow the physician to calculate patient-specific dose estimates to allow early release of a patient not otherwise subject to release under the default values in Regulatory Guide 8.39. Personal information may be necessary for such patient-specific cases.

Comment. One commenter said that it should continue to be acceptable to release patients based on the dose rate at 1 meter.

Response. The rule authorizes release of patients based on the dose in a year. However, release quantities based on dose rate and conservative assumptions can be calculated. The table of release quantities in Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials,"

radioactive material in the body of the patient and other factors that vary for different materials. For these reasons, the NRC is establishing a dose limit rather than an activity or dose rate limit.

The NRC is establishing a dose limit of 5 millisieverts (0.5 rem) total effective dose equivalent to an individual from exposure to the released patient for each patient release. This dose limit is consistent with the underlying risk basis of the current 10 CFR 35.75 (50 FR 30627; July 26, 1985), the recommendations of the NCRP and the ICRP, and the provisions in 10 CFR 20.1301(c) pertaining to temporary situations in which there is justification for a dose limit higher than 1 millisievert (0.1 rem).

The NRC believes that the dose-based release limit can and will work well because the associated Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials," can be used to relate the dose to the quantity of activity in the patient. The guide provides conservative estimates of activities for commonly used radionuclides and their corresponding dose rates with which a patient may be released in compliance with the dose limits in the final rule. The approach used in the regulatory guide is based on NCRP Report No. 37, "Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides."[1] In the case of iodine-131, the most significant radionuclide, the release quantity based on the standard conservative assumptions is 1,221 megabecquerels (33 millicuries), which is essentially the same as the current release quantity.

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[1]National Council on Radiation Protection and Measurements (NCRP), "Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides," NCRP Report No. 37 (October 1, 1970). (Available for sale from the NCRP, 7910 Woodmont Avenue, Suite 800, Bethesda, MD 20814-3095.)

The majority of commenters supported the dose-based limit. However, some commenters opposed the dose-based approach.

Comment. A number of commenters said that 10 CFR 35.75 should not be changed and that the 30 millicurie or 5 millirem per hour release criteria should be retained because they are working well. Some commenters said that a dose-based release limit as proposed would cause confusion and potential problems. One commenter said that the Part 20 revision was not intended to alter the status quo for patient release. Commenters objected to the dose-based release limit because they thought the dose estimates to the public would be very inaccurate as these estimates are based on the unreliable method of predicting the anticipated time and proximity to others. Commenters also said that dose estimation and the subsequent recordkeeping would be time consuming and would add to the cost of treatment without a probable significant decrease in radiation exposure.

Response. The NRC is adopting a dose-based limit rather than an activity-based limit because the dose-based limit better expresses the NRC's primary concern for the public's health and safety. A single activity requirement was not retained because different radionuclides with the same activity can give very different doses under identical exposure conditions. Likewise, a single dose rate requirement for all radionuclides was not retained because different radionuclides with the same dose rate, at the time of release, can give very different doses depending upon the half-life of the radionuclide. The total dose depends on the effective half-life of the

steps are taken to reduce the dose to as low as is reasonably achievable. The NRC reaffirms that previous determination in this rulemaking.

In the case of released patients, it would be unlikely for a single individual exposed to a patient to receive a dose in a year of over 1 millisievert (0.1 rem) because large therapeutic doses (greater than 3,700 megabecquerels (100 millicuries)) are rarely administered more than once to the same patient in a given year.

Comment. One commenter said that the NRC should change the 0.1 rem dose limit for the public in 10 CFR 20.1301(a)(1) to 0.5 rem for all licensed activities because a dose limit of 0.5 rem offers adequate protection and is a dose that has no proven effects.

Response. This issue of the general public dose limit is outside the scope of this rulemaking. The issue was dealt with when 10 CFR part 20 was recently revised (56 FR 23360; May 21, 1991). That rulemaking explained the NRC's rationale for adopting the 1-millisievert (0.1-rem) dose limit in 10 CFR 20.1301(a)(1).

ACTIVITY-BASED VS. DOSE-BASED RELEASE LIMIT

The issue is whether to retain the current patient release limit in 10 CFR 35.75, which is expressed as an activity limit together with an alternative but approximately equivalent limit on dose rate at 1 meter, or to express the release limit as a dose to an individual exposed to the patient.

low as is reasonably achievable, a dose limit of 1 millisievert (0.1 rem), or a dose limit of 5 millisieverts (0.5 rem) in certain special circumstances, provides adequate protection. The revised Part 20 is based, in part, upon the recommendations of the International Commission on Radiological Protection (ICRP) and the recommendations of the National Council on Radiation Protection and Measurements (NCRP). The NCRP recommends public dose limits of 1 millisievert (0.1 rem) for continuous or frequent exposure and 5 millisieverts (0.5 rem) for infrequent exposure.

The ICRP recommends that the limit for public exposure should be expressed as an effective dose of 1 millisievert (0.1 rem) in a year, except that, in special circumstances, the dose could be higher in a single year provided the average over 5 years does not exceed 1 millisievert (0.1 rem) per year. In ICRP Publication 60, in defining medical exposure, ICRP stated that medical exposure includes "exposures (other than occupational) incurred knowingly and willingly by individuals helping in the support and comfort of patients undergoing diagnosis or treatment." Furthermore, in explaining dose limits in medical exposure, the ICRP stated in the same publication that "the Commission therefore recommends that dose limits should not be applied to medical exposures." Thus, in ICRP's opinion, family members who are helping in the support and comfort of patients would not be restricted under the dose limit stated above.

The revision of Part 20 incorporated the long-term objective as the dose limit and included a provision (§ 20.1301(c)) to allow for alternative limits on an occasional basis. Section 20.1301(c) provides that an annual dose of up to 5 millisieverts (0.5 rem) is acceptable if there is a need for it and if

III. Public Comments on the Proposed Rule

A total of 63 comment letters were received on the proposed rule, the draft regulatory guide, and the draft regulatory analysis. A majority of the comment letters were from medical practitioners and medical organizations, but there were also comment letters from private individuals, public-interest groups, and regulatory agencies in Agreement States. Overall, the majority of comment letters supported a dose limit of 5 millisieverts (0.5 rem) for individuals exposed to patients released with radioactive material. However, about one-fourth of the comment letters opposed the proposed recordkeeping requirement. The significant comments are discussed below, arranged by subject.

EXCLUSION OF PATIENT RELEASE FROM § 20.1301(a)

All the commenters except one supported governing patient release by the regulations in 10 CFR 35.75 and excluding the dose to individuals exposed to a released patient from 10 CFR 20.1301(a).

Comment. One commenter, representing a public-interest group, objected to any exposure of a member of the general public who has not consented freely to the dosage. They said that such exposure would lead to widespread morbidity and mortality.

Response. In its revision of 10 CFR part 20 (56 FR 23360; May 21, 1991), the NRC determined that, while doses should be maintained as

calculated total effective dose equivalent to the individual likely to receive the highest dose if the total effective dose equivalent to any individual other than the released patient is likely to exceed 1 millisievert (0.1 rem) in a year from a single administration. The major purpose was to provide a record to allow licensees to assess the need to limit the dose to individuals exposed to a patient who may receive more than one administration in a year.

Finally, the NRC proposed to amend its requirements on instructions in 10 CFR 35.315(a)(6) and 35.415(a)(5). These regulations already required instructions (not necessarily written) in certain cases, but the phrase "if required by § 35.75(b)" was added to each. The purpose of this change was to make Part 35 consistent as to when instructions must be given.

In addition, the NRC concurrently issued an associated draft regulatory guide and supporting draft regulatory analysis for public comment. The draft regulatory guide, DG-8015, "Release of Patients Administered Radioactive Materials," proposed guidance on determining the potential doses to an individual likely to receive the highest dose from exposure to a patient and established appropriate activities and dose rates for release of a patient. The draft guide also proposed guidelines on instructions for patients on how to maintain doses to other individuals as low as is reasonably achievable and it described recordkeeping requirements. The draft regulatory analysis, NUREG-1492, "Regulatory Analysis on Criteria for the Release of Patients Administered Radioactive Material" (May 1994), examined the benefits and impacts of the proposed rule considered by the NRC.

The NRC proposed to adopt a new 10 CFR 35.75(a) to change the patient release criteria from 1,110 megabecquerels (30 millicuries) of activity in a patient or a dose rate of 0.05 millisievert (5 millirems) per hour at 1 meter from a patient to a total effective dose equivalent not to exceed 5 millisieverts (0.5 rem) in any 1 year to an individual from exposure to a released patient. A dose-based limit provides a single limit that could be used to provide an equivalent level of risks from all radionuclides. Also, the proposed changes were supported by the recommendations of the ICRP and the NCRP that an individual could be allowed to receive an annual dose up to 5 millisieverts (0.5 rem) in temporary situations when exposure to radiation is not expected to result in annual doses above 1 millisievert (0.1 rem) for long periods of time.

The NRC proposed to adopt a new 10 CFR 35.75(b)(1) to require that the licensee provide released patients with written instructions on how to maintain doses to other individuals as low as is reasonably achievable if the total effective dose equivalent to any individual other than the released patient is likely to exceed 1 millisievert (0.1 rem) in any 1 year. A requirement to give instructions to certain patients was already contained in 10 CFR 35.315(a)(6) and 35.415(a)(5), but the proposed requirement would also require instructions for an additional 50,000 individuals who are administered iodine-131 for the treatment of hyperthyroidism and another 27,000 individuals who are breast-feeding and administered various diagnostic and therapeutic radioactive materials. The purpose of the instructions is to maintain doses to individuals exposed to patients as low as is reasonably achievable.

The NRC proposed to adopt a new 10 CFR 35.75(b)(2) to require that licensees maintain, for 3 years, a record of the released patient and the

On June 15, 1994 (59 FR 30724), in response to the first two petitions, the NRC published a proposed rule on criteria for the release of patients administered radioactive material. The proposed rule discussed the public comment letters received on the first two petitions. Three additional comment letters were received on the third petition (PRM-35-11). These letters each supported the petition but did not contain any additional information not covered by the letters on the first two petitions.

The NRC proposed to amend 10 CFR 20.1301(a)(1) to specifically state that the dose to individual members of the public from a licensed operation does not include doses received by individuals exposed to patients who were released by the licensed operation under the provisions of 10 CFR 35.75. This was to clarify that the Commission's policy is that patient release is governed by 10 CFR 35.75, not 10 CFR 20.1301.

The NRC proposed to amend 10 CFR 20.1301(a)(2) to specifically state that the limit on dose in unrestricted areas does not include dose contributions from patients administered radioactive material and released in accordance with 10 CFR 35.75. The purpose was to clarify that licensees would not be required to control areas (such as waiting rooms) simply because of the presence of a patient released pursuant to 10 CFR 35.75. If a patient has been released from licensee control pursuant to 10 CFR 35.75, licensees would not be required to limit the radiation dose from a patient to members of the public (e.g., visitors in a waiting room) to 0.02 millisievert (2 millirems) in any 1 hour. Patient waiting rooms or hospital rooms would need only be controlled for those patients not meeting the release criteria in 10 CFR part 35.

comment on, a petition for rulemaking (PRM-20-20) from Dr. Carol S. Marcus. In addition, Dr. Marcus submitted a letter dated June 12, 1992, further characterizing her position.

On March 9, 1992 (57 FR 8282), the NRC published a notice of receipt and request for comment in the Federal Register on another petition for rulemaking (PRM-35-10) on patient release criteria from the American College of Nuclear Medicine (ACNM). On May 18, 1992 (57 FR 21043), the NRC published in the Federal Register notice of an amendment submitted by the ACNM to its original petition (PRM-35-10A).

In addition, a third petition (PRM-35-11) dealing, in part, with these same issues was submitted by the American Medical Association (AMA). That petition was noticed in the Federal Register on July 26, 1994 (59 FR 37950). The main point raised in the petition was that the radiation dose limits in 10 CFR part 20 should not apply to individuals exposed to the patient and that the dose limit to the individuals should be 500 millirems per year. The AMA believed that 10 CFR 20.1301 would have an adverse impact on the availability and the cost of treatment of thyroid disease, which would outweigh the advantages of reduced radiation exposure to the public. The AMA stated that treatment of up to 10,000 cancer patients annually for thyroid carcinoma would require the hospitalization of the patients under the revised regulation (10 CFR 20.1301), reducing both early release of patients and the treatment of patients at home.

II. Publication of the Proposed Rule

hereinafter referred to as "patients." These patients can expose others around them to radiation until the radioactive material has been excreted from their bodies or the radioactivity has decayed away.

NRC's current patient release criteria in 10 CFR 35.75, "Release of patients or human research subjects containing radiopharmaceuticals or permanent implants," are as follows:

"(a) A licensee may not authorize release from confinement for medical care any patient or human research subject administered a radiopharmaceutical until either: (1) The measured dose rate from the patient or human research subject is less than 5 millirems per hour at a distance of 1 meter; or (2) The activity in the patient or human research subject is less than 30 millicuries; (b) A licensee may not authorize release from confinement for medical care of any patient or human research subject administered a permanent implant until the measured dose rate from the patient or human research subject is less than 5 millirems per hour at a distance of 1 meter."

On May 21, 1991 (56 FR 23360), the NRC published a final rule that amended 10 CFR part 20, "Standards for Protection Against Radiation." The rule contained limits on the radiation dose for members of the public in 10 CFR 20.1301. However, when 10 CFR part 20 was issued, there was no discussion in the supplementary information on whether or how the provisions of 10 CFR 20.1301 were intended to apply to the release of patients.

Some licensees were uncertain about what effect the revised 10 CFR part 20 would have on patient release criteria, and two petitions for rulemaking were received on the issue. On June 12, 1991 (56 FR 26945), the NRC published in the Federal Register a notice of receipt of, and request for

ADDRESSES: Copies of Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials"; the final regulatory analysis, NUREG-1492, "Regulatory Analysis on Criteria for the Release of Patients Administered Radioactive Material" (1996); Revision 2 of NUREG/BR-0058, "Regulatory Analysis Guidelines of the U.S. Nuclear Regulatory Commission" (1996); and the public comments received on the proposed rule may be examined and copied for a fee in the Commission's Public Document Room at 2120 L Street NW. (Lower Level), Washington, DC. Single copies of Regulatory Guide 8.39 may be obtained free of charge by writing the Office of Administration, Attn: Distribution and Services Section, USNRC, Washington, DC 20555, or by fax at (301) 415-2260. Single copies of NUREG-1492 and NUREG/BR-0058 may be purchased at current rates from the U.S. Government Printing Office, P.O. Box 37082, Washington, DC 20402-9328 (telephone (202) 512-1800); or from the National Technical Information Service at 5285 Port Royal Road, Springfield, VA 22161.

FOR FURTHER INFORMATION CONTACT: Stewart Schneider or Stephen A. McGuire, Office of Nuclear Regulatory Research, U.S. Nuclear Regulatory Commission, Washington, DC 20555, telephone (301) 415-6225.

I. Background

Each year in the United States, radioactive pharmaceuticals or compounds or radioactive implants are administered to approximately 8 to 9 million individuals for the diagnosis or treatment of disease or for human research. These individuals to whom radioactive materials have been administered are

[7590-01-P]

NUCLEAR REGULATORY COMMISSION

10 CFR Parts 20 and 35

RIN 3150-AE41

Criteria for the Release of Individuals Administered Radioactive Material

AGENCY: Nuclear Regulatory Commission.

ACTION: Final rule.

SUMMARY: The Nuclear Regulatory Commission (NRC) is amending its regulations concerning the criteria for the release of patients administered radioactive material. The new criteria for patient release are based on the potentia dose to other individuals exposed to the patient. The new criteria are consistent with the recommendations of the National Council on Radiation Protection and Measurements (NCRP) and the International Commission on Radiological Protection (ICRP). This final rule requires the licensee to provide written instructions to patients on how to maintain the doses to others as low as is reasonably achievable if the total effective dose equivalent to any other individual exposed to the released patient is likely to exceed 1 millisievert (0.1 rem). This final rule responds to three petitions for rulemaking regarding the criteria for release of patients administered radioactive material.

EFFECTIVE DATE: _____ (120 days following publication in the Federal Register).

ATTACHMENT 1

FEDERAL REGISTER NOTICE

3. Notes:

a. The final rule will become effective 120 days after publication in the Federal Register.

b. A final regulatory guide will be published, for use, before the final rule becomes effective (Attachment 2).

c. A final regulatory analysis will be available in the Public Document Room (Attachment 3).

d. A final environmental assessment and a finding of no significant impact have been prepared (Attachment 4).

e. The Chief Counsel for Advocacy of the Small Business Administration will be informed of the certification regarding economic impact on small entities and the reasons for it as required by the Regulatory Flexibility Act.

f. The appropriate Congressional Committees will be informed (Attachment 5);

g. A public announcement will be issued (Attachment 6).

h. The rule contains information collection requirements that are subject to review by the Office of Management and Budget. Upon Commission approval, the OMB supporting statement (Attachment 7) will be submitted to OMB for approval.

i. Copies of the Federal Register notice of final rulemaking and the associated regulatory guide will be distributed to all NRC medical licensees and each Agreement State. The notice will be sent to other interested parties upon request.

James M. Taylor
Executive Director
for Operations

Attachments: As Stated (7)

Second, the ACMUI suggested using the phrase "the retained activity rather than the activity administered" instead of "an activity other than the activity administered" in the requirement under 10 CFR 35.75(c), to maintain a record of the basis for authorizing the release of an individual, if the total effective dose equivalent is calculated. The ACMUI was concerned that the meaning was not clear, and in addition, the requirement was already implicit in the remainder of the recordkeeping requirements in 10 CFR 35.75(c). The staff changed the rule in response to the ACMUI comment. This information would be needed for cases where a patient would be held for some time period prior to release. Such cases would not be covered in the default release table that appears in the regulatory guide. In this case, a record is needed to confirm that the licensee has released the individual in accordance with the limit in Part 35. Regulatory Guide 8.39 will provide guidance on cases where such records will be needed for release.

Third, the ACMUI suggested that the term "discontinuation" should be used in conjunction with "interruption" in the requirement to provide "guidance on the interruption of breast-feeding" if failure to follow the instructions could result in a dose to the infant exceeding 1 millisievert (0.1 rem). The ACMUI suggested the change because they said that there is a distinct difference between the two terms. The staff changed the rule in response to the ACMUI comment. As stated in the Federal Register notice, "the instructions must include guidance on the interruption period for breast-feeding." Table 2 in the guide gives interruption periods for various radiopharmaceuticals which can be temporary (48 hours or less) in some cases, or discontinuation (no resumption) when necessary.

Finally, the ACMUI recommended that the Commission proceed with the rule as promptly as possible.

RESOURCES:

Resources needed to conduct and implement this rulemaking are included in the FY 1995-1999 Five-Year Plan.

COORDINATION:

The Office of the General Counsel has no legal objection to this paper.

RECOMMENDATION:

That the Commission:

1. Approve the notice of final rulemaking for publication (Attachment 1).

2. Certify that this rule will not have a significant economic impact on a substantial number of small entities; such certification will satisfy requirements of the Regulatory Flexibility Act, 5 U.S.C. 605(b).

The regulatory guide will contain interruption periods that keep the dose from breast-feeding to less than 1 millisievert (0.1 rem). The purpose of describing the consequences is so that women will understand that breast-feeding after an administration of certain radionuclides could cause harm (e.g., iodine-131 could harm the child's thyroid). In other cases, the guidance could simply address avoidance of any unnecessary radiation exposure to the child from breast-feeding. The regulatory analysis indicates the basis for selecting the option of enhancing communications and instructions to breasting-feeding women.

6. The amendments make it clear that the limit on dose in unrestricted areas presented in 10 CFR 20.1301(a)(2) does not include dose contributions from patients administered radioactive material and released in accordance with 10 CFR 35.75. The purpose of this change is to clarify that licensees are not responsible for doses outside of their restricted areas from radiation sources not under their control. The comments supported this position.

The final amendments represent a partial granting of the regulatory relief requested by the petitioners. The request to delete 10 CFR 20.1301(d) was denied because the reference to the Environmental Protection Agency's regulations in 10 CFR 20.1301(d) has nothing to do with the patient release issue. Also, the request to permit licensees to authorize release from hospitalization any patient administered a radiopharmaceutical regardless of the activity in the patient by defining "confinement" to include not only confinement in a hospital, but also confinement in a private residence, was denied. The staff considers it inadvisable to use a patient's home for the purpose of confinement when the activity in the patient is expected to result in a dose exceeding 5 millisieverts (0.5 rem) to another individual.

At its last meeting, held on October 18 and 19, 1995, the ACMUI passed several motions suggesting changes to three aspects of the rule.

First, the ACMUI suggested using the term "rationale" instead of "consequences" in the requirement, under 10 CFR 35.75(b), to provide "guidance on the interruption of breast feeding, and information on the consequences of failure to follow the guidance" for cases where failure to follow the instructions could result in a dose to the infant exceeding 1 millisievert (0.1 rem). Since most of the administrations that would be affected by this requirement are technetium-99m administrations, the ACMUI suggested the change because there was concern that the consequences of low doses of radiation cannot always be explained to the patient without causing unjustified alarm. Also, there was concern that physicians cannot explain with certainty the effects of low doses of radiation, such as would be caused by diagnostic administrations of technetium-99m. The staff did not change the rule in response to the ACMUI comment because the requirement to provide information on the consequences is included primarily to protect the breast-feeding infant from therapeutic administrations of radioiodine, which could cause serious thyroid damage. Regulatory Guide 8.39 will contain guidance on the types of information, including expected consequences, to be provided to patients to meet this requirement.

Overall, a substantial majority of all comments supported an explicit dose limit of 5 millisieverts (0.5 rem) for individuals exposed to patients released with radioactive material in their bodies. In addition, ACMUI and the Agreement States supported the criterion based on a dose limit. A few commenters who thought that the present criteria were working well and were adequate opposed allowing the release of patients with quantities of radioactive material greater than that permitted under the current regulations.

4. The proposed rule would have required licensees to maintain, for 3 years, a record of the basis for the patient's release and the total effective dose equivalent if any individual is likely to receive a dose in excess of 1 millisievert (0.1 rem) in a year from a single administration. This requirement was proposed so that records would be available to calculate the dose if a patient received multiple administrations in a year.

   This proposed recordkeeping requirement met a great deal of opposition. Commenters were especially concerned about having to retrieve records of previous administrations, sometimes from another medical facility. Upon reconsideration, it was decided to delete this requirement because a review of nuclear medicine procedures indicated that there was no significant likelihood of exceeding a 5-millisievert (0.5-rem) annual dose because of multiple administrations.

   In place of the deleted recordkeeping requirement, the final rule contains requirements to maintain: (1) a record for the basis of the release for a limited number of certain radiopharmaceutical administrations (e.g., therapeutic administrations of iodine-131) and (2) a record that instructions were provided to a breast-feeding woman if the administered activity could result in a total effective dose equivalent to the breast-feeding child exceeding 5 millisieverts (0.5 rem) if the woman did not interrupt breast-feeding. The requirements (in 10 CFR 35.75(c) and (d)) would affect about 20,000 of the 8 to 9 million administrations done annually.

5. The amendments require that the patient be given instructions, including written instructions, on how to maintain doses to others as low as is reasonably achievable if the dose to an individual is likely to exceed 1 millisievert (0.1 rem). In general, most commenters agreed with this requirement, although a few did not think that instructions should necessarily have to be written.

   The proposed rule had a requirement to provide instructions which would include guidance on breast-feeding children, but some commenters wanted information on when instructions would have to be given and what the instructions should say about interruption or cessation of breast-feeding. The final rule requires that guidance regarding interruption of breast-feeding and consequences be provided if the released individual may be breast-feeding an infant or child and the total effective dose equivalent is likely to exceed 1 millisievert (0.1 rem).

1. The major changes to the final rulemaking are: (1) significant expansion of the discussion on breast-feeding in the Statement of Considerations and the regulatory analysis and (2) explicit use of the term "breast-feeding" in the final rule text to make it clear that breast-feeding women are a class of patients requiring additional records and instructions to limit the dose to the breast-feeding child. The subject of breast-feeding was mentioned in the Statement of Considerations to the proposed rule but not in the proposed rule text.

2. The amendments make it clear that patient release is governed by 10 CFR 35.75 rather than by 10 CFR 20.1301(a). There was very broad agreement with this position in the comment letters, with ACMUI, and with the Agreement States.

3. The amendments revise the criteria for release of patients administered radioactive material for medical use under 10 CFR 35.75 to permit a maximum likely total effective dose equivalent of 5 millisieverts (0.5 rem), excluding background or any occupational exposure, to an individual exposed to the patient.

   Specifying the release criterion in terms of radiation dose requires that the NRC provide an acceptable method that relates the quantity of radioactivity administered to that dose. That relationship will be included in a regulatory guide. A working draft of that guide is attached (Attachment 2); the staff is still reviewing the guide, but will publish it in final form before the final rule becomes effective.

   The guide presents two methods to relate dose to quantity of radioactivity administered. The first method is the use of a default table of release quantities and release dose rates based on conservative assumptions. For the radioactive material of greatest significance, iodine-131, the default table is essentially equivalent to the release criteria in the current regulations. The staff anticipates that nearly all patients will be released based on the default table of activities.

   The second method is to perform a case-specific dose calculation using the method described in the guide. The case-specific method can be less conservative than the default table because it permits a more realistic estimate of how quickly the radioactive material leaves the patient's body. Thus, use of this method would, in some cases, permit the release of patients containing several times more radioactive material than the current regulations permit or allowed with use of the default table.

   The authorization to release a patient is based on the licensee's determination that the total effective dose equivalent to an individual from the released patient is not likely to exceed 5 millisieverts (0.5 rem). The dose to the breast-feeding child from breast-feeding is not necessarily a criterion for release since it can be controlled by giving the woman guidance on the interruption of breast-feeding, as required by the amendments (see No. 5).

NRC's current patient release criteria are contained in 10 CFR 35.75, "Release of patients or human research subjects containing radiopharmaceuticals or permanent implants." That section states: "(a) A licensee may not authorize release from confinement for medical care any patient or human research subject administered a radiopharmaceutical until either: (1) The measured dose rate from the patient or human research subject is less than 5 millirems per hour at a distance of 1 meter; or (2) The activity in the patient or human research subject is less than 30 millicuries; (b) A licensee may not authorize release from confinement for medical care of any patient or human research subject administered a permanent implant until the measured dose rate from the patient or the human research subject is less than 5 millirems per hour at a distance of 1 meter."

Some licensees were uncertain about the effect that the revised 10 CFR Part 20 would have on patient release criteria, and three petitions for rulemaking were received on the issue.[2] To resolve this uncertainty, two steps were taken.

The short-term resolution was to inform licensees of the NRC's position that 10 CFR 35.75 governed patient release. The Commission was informed in SECY-94-01 of the staff's recommendation that 10 CFR 35.75 governs patient release. Information Notice No. 94-09 was issued on February 3, 1994, to inform licensees of this position in accordance with a Staff Requirements Memorandum (SRM) dated January 28, 1994.

The longer term resolution was to address this issue through rulemaking, and a proposed rule was published for comment on June 15, 1994 (59 FR 30724). The proposed rule was transmitted to the Commission in SECY-94-054 and responses to questions raised by the Office of the Inspector General are contained in SECY-94-054A.

DISCUSSION:

The final rule (Attachment 1) takes into consideration the recommendations of the Agreement States, as well as the comment letters received on the proposed rule and the petitions. In all, 232 comment letters were received on the three petitions, and 63 comment letters were received on the proposed rule. The rule was also discussed with the Advisory Committee on Medical Uses of Isotopes (ACMUI) at several public meetings, the last on October 18 and 19, 1995.

The following summarizes the main features of the amendments:

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[2] One commenter raised an issue about contacts allegedly relating to this rulemaking between one of the petitioners and the Office of the Chairman. The staff notes that the final rule is based on the public record associated with the rulemaking and that the NRC decision maker with whom contact was made is no longer with the Commission. The staff has not included any further comment with respect to this issue in the final rulemaking package.

FOR: The Commissioners

FROM: James M. Taylor
Executive Director for Operations

SUBJECT: FINAL AMENDMENTS TO 10 CFR PARTS 20 AND 35 ON CRITERIA FOR THE RELEASE OF INDIVIDUALS ADMINISTERED RADIOACTIVE MATERIAL

PURPOSE:

To obtain Commission approval to publish a notice of final rulemaking in the Federal Register.

BACKGROUND[1]:

On May 21, 1991 (56 FR 23360), the NRC published a final rule that amended 10 CFR Part 20, "Standards for Protection Against Radiation." The rule contained a dose limit of 1 millisievert (0.1 rem) total effective dose equivalent for members of the public in 10 CFR 20.1301(a). When 10 CFR Part 20 was issued, there was no discussion in the supplemental information on whether or how the provisions of 10 CFR 20.1301 were intended to apply to the release of patients.

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[1] The subject paper was submitted to the Commission on November 30, 1995 (SECY-95-286). Subsequently, the staff requested withdrawal of the paper to revise the regulatory analysis (RA) to conform with the new RA guidelines. In a Staff Requirements Memorandum dated December 21, 1995, the Commission granted the request. The staff revised the RA (a summary of major changes is attached to the RA) and made conforming changes to the Federal Register Notice (FRN) and the Environmental Assessment (EA). These revisions did not affect the content of this staff paper except in Items 1 and 5 of the DISCUSSION in which the staff mentioned the expanded discussions of breast-feeding women in the RA.

CONTACTS:
Stewart Schneider, RES
415-6225

Stephen A. McGuire, RES
415-6204

CONTENTS

ABSTRACT

The Nuclear Regulatory Commission (NRC) has received three petitions to amend its regulations in 10 CFR Parts 20 and 35 as they apply to doses received by members of the public exposed to patients released from a hospital after they have been administered radioactive material. While the three petitions are not identical, they all request that the NRC establish a dose limit of 5 millisieverts (0.5 rem) per year for individuals exposed to patients who have been administered radioactive materials. This Regulatory Analysis evaluates three alternatives. Alternative 1 is for the NRC to amend its patient release criteria in 10 CFR 35.75 to use the more stringent dose limit of 1 millisievert (0.1 rem) per year in 10 CFR 20.1301(a) for its patient release criteria. Alternative 2 is for the NRC to continue using the existing patient release criteria in 10 CFR 35.75 of 1,110 megabecquerels (30 millicuries) of activity or a dose rate at 1 meter from the patient of 0.05 millisievert (5 millirems) per hour. Alternative 3 is for the NRC to amend the patient release criteria in 10 CFR 35.75 to specify a dose limit of 5 millisieverts (0.5 rem) for patient release.

The evaluation demonstrates that diagnostic procedures are unaffected by the choice of alternative. Only some therapeutic administrations of radioactive material could be affected by the choice of alternative. The evaluation indicates that Alternative 1 would cause a large increase in the national health care cost from retaining patients in a hospital longer and would cause significant personal and psychological costs to patients and their families. The choice of Alternatives 2 or 3 would affect only thyroid cancer patients and some hyperthyroid patients treated with iodine-131. For those patients, Alternative 3 would result in less hospitalization than Alternative 2. Alternative 3 has a potential decrease in national health care cost of $13,700,000 per year but would increase the potential collective dose from released therapy patients by about 2,740 person-rem per year, mainly to family members. Alternative 3 would also have personal and psychological benefits for the patients and their families.

§35.8 Information collection requirements: OMB approval

(b) The approved information collection requirements contained in this part appear in §§ 35.12, 35.13, 35.14, 35.21, 35.22, 35.23, 35.29, 35.31, 35.50, 35.51, 35.52, 35.53, 35.59, 35.60, 35.61, 35.70, 35.75, 35.80, 35.92, 35.204, 35.205, 35.310, 35.315, 35.404, 35.406, 35.410, 35.415, 35.606, 35.610, 35.615, 35.630, 35.632, 35.634, 35.636, 35.641, 35.643, 35.645, 35.647, 35.980, and 35.981.

Attachment 1

PAPERWORK REDUCTION ACT STATEMENT

This final rule (or final policy statement) amends information collection requirements that are subject to the Paperwork Reduction Act of 1980 (44 U.S.C. 3501 et seq.). These requirements were approved by the Office of Management and Budget, approval number 3150-0010.

The public reporting burden for this collection of information is estimated to average _____ hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to the Information and Records Management Branch (T-6 F33), U.S. Nuclear Regulatory Commission, Washington, DC 20555-0001, and to the Desk Officer, Office of Information and Regulatory Affairs, NEOB-10202, (3150-0010), Office of Management and Budget, Washington, DC 20503.

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

June 8, 1995

MEMORANDUM TO: Michael T. Lesar, Chief
Rules Review Section
Rules Review and Directives Branch
Division of Freedom of Information and
Publications Services
Office of Administration

FROM: Brenda Jo. Shelton, Chief
Information and Records Management Branch
Office of Information Resources Management

SUBJECT: REQUEST FOR COMMENT AND CONCURRENCE ON THE FINAL RULE, 10 CFR 35, CRITERIA FOR THE RELEASE OF INDIVIDUALS ADMINISTERED RADIOACTIVE MATERIALS

In response to your subject memorandum, the Information and Records Management Branch (IRMB) provides the following:

____ The Paperwork Reduction Act Statement (PRAS) is correct.

__X__ Change the PRAS to Attachment 1. done

____ The "Information Collection Requirements: OMB Approval" section is correct.

__X__ Change the "Information Collection Requirements: OMB Approval" section to Attachment 2. done

__X__ Do not publish the "Federal Register Notice" until further notice.

____ The "Federal Register Notice" can be published.

____ Enclosed is a copy of the IRMB memorandum to the program office addressing our concerns.

____ A copy of the IRMB memorandum to the program office addressing our concerns will be forwarded at a later date.

__X__ An IRMB memorandum to the program office is not required.

Attachments:
As stated

cc: S. McGuire, RES
J. Glenn, RES

~~9708150206 3pp~~

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

June 9, 1995

MEMORANDUM TO: David L. Morrison, Director
Office of Nuclear Regulatory Research

FROM: James Lieberman, Director
Office of Enforcement

SUBJECT: OFFICE REVIEW AND CONCURRENCE ON A FINAL RULE - CRITERIA FOR THE RELEASE OF INDIVIDUALS ADMINISTERED RADIOACTIVE MATERIALS

The Office of Enforcement has no objection to the subject draft final rule. Attached are three pages with miscellaneous edits that you may wish to consider.

Enclosure:
As stated

9508150192 1p.

Suggested Changes - Final Rule On Patient Release Criteria

1. Page 24, Miscellaneous comments on the Rule

We suggest the response to the first statement be revised as follows:

Response: The NRC does not agree. NRC conducts an assessment of each proposed requirement or rule to determine what level of compatibility will be assigned to the rule. These case-by-case assessments are based, for the most part, on protecting public health and safety.

2. Page, 34, IV. Coordination with NRC Agreement States

We suggest the paragraph be revised as follows:

The staff discussed the status of this rulemaking effort at two public meetings; the Agreement State Managers Workshop held on July 12-14, 1994 and at the All Agreement States Meeting held on October 24-25, 1994. The Agreement States expressed no objections to the approach in this rule.

3. Page 39, VIII. Issues of Compatibility for Agreement States

10 CFR 20.1002 Scope.

Office of State Programs Internal Procedure B.7 entitled, "Criteria for Compatibility Determinations", states that "Scope" in 10 CFR Part 20 is a Division III item of compatibility. Therefore, the wording regarding 20.1002 "scope" should be designated as a Division III matter of compatibility rather than Division II. Division III rules would be appropriate for Agreement States to adopt, but do not require any degree of uniformity between NRC and State rules.

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

May 3, 1995

MEMORANDUM TO: Bill M. Morris, Director
Division of Regulatory Applications, RES

FROM: Richard L. Bangart, Director
Office of State Programs

SUBJECT: TECHNICAL REVIEW: DRAFT FINAL RULE - CRITERIA FOR THE RELEASE OF PATIENTS ADMINISTERED RADIOACTIVE MATERIALS

This is in response to your April 12, 1995 memorandum on the subject document.

We have reviewed the draft final rule as it applies to the Agreement States through compatibility requirements. Attached are several suggested changes relating to staff's interaction with the Agreement States.

We have no objection to proceeding with this rulemaking effort.

If you have any questions, please contact me or Lloyd Bolling of my staff.

Attachment:
As stated

9708150148 2pp.

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

June 12, 1995

cc: Morris
Glenn
Schneider
McGuire
file

dm

MEMORANDUM TO: David L. Morrison, Director
Office of Nuclear Regulatory Research

FROM: Richard L. Bangart, Director
Office of State Programs

SUBJECT: OFFICE REVIEW AND CONCURRENCE: DRAFT FINAL RULE - CRITERIA FOR THE RELEASE OF INDIVIDUALS ADMINISTERED RADIOACTIVE MATERIALS

This is in response to your May 31, 1995 memorandum on the subject document.

We have reviewed the draft final rule as it applies to the Agreement States through compatibility requirements. In a meeting between Lloyd Bolling of my staff and Stewart Schneider, RES on Wednesday June 7, 1995, the scope section in 10 CFR Part 20.1002 was revised to a Division III item of compatibility for Agreement States.

Based on this revision and our previous comments (see attached memorandum dated May 3, 1995), we concur in the rule.

Attachment:
As stated

9508150195 1p.

From: Shelly L. Shortt (SLS)
To: SAM2, SXS4
Date: Thursday, June 8, 1995 11:21 am
Subject: FINAL AMEND TO 10 CFR PARTS 20 AND 35

Stewart Schneider, RES
Stephen McGuire, RES

As requested by DMorrison's memorandum of May 31, 1995, OC has reviewed the Draft Final Rule on the Criteria for the Release of Individuals Administered Radioactive Materials.

By this e-mail I am providing you with office concurrence.

Please contact me on 415-6032 if you have any questions.

Thanks.
Shelly Shortt

CC: eah1

9708160444 1P.

To assist you in preparing the list of documents centrally relevant to the final rule that is required by NRC's regulatory history procedures, you should place the designator "AE41" in the upper right-hand corner of each document concerning the rule that you forward to the Nuclear Documents System.

If you have any questions concerning this matter, please have a member of your staff contact Michael T. Lesar, 415-7163, Rules Review Section, Division of Freedom of Information and Publications Services.

Attachment:
As stated

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

June 5, 1995

MEMORANDUM TO: David L. Morrison, Director
Office of Nuclear Regulatory Research

FROM: David L. Meyer, Chief
Rules Review and Directives Branch
Division of Freedom of Information and
Publications Services
Office of Administration

SUBJECT: OFFICE CONCURRENCE ON A FINAL RULE PACKAGE REGARDING REGARDING CRITERIA FOR THE RELEASE OF INDIVIDUALS ADMINISTERED RADIOACTIVE MATERIAL

The Office of Administration concurs, subject to the comments provided, on the final rule package regarding the criteria for the release of individuals administered radioactive material. We have attached a marked copy of the package that presents additional editorial comments.

The Statement of Considerations for the final rule must contain a clear statement that indicates the final disposition of the petitions for rulemaking that the rule addresses (PRMs 20-20, 35-10 and 10A, and 35-11). If the statement in the proposed rule remains valid, the final rule should indicate that these petitions are partially granted, specify the aspects of the petitions that have been granted, indicate that the remaining portions of the petitions are denied, and state that the final rule completes action on the petitions.

We have adjusted the amendatory instruction for the authority citation to Part 20 and provided the currently effective text of that authority citation.

When these documents are forwarded for signature and publication, please have a member of your staff include a 3.5-inch diskette that contains a copy of the document in WordPerfect 5.0 or 5.1 as part of the transmittal packages. The diskettes will be forwarded to the Office of the Federal Register and the Government Printing Office for their use in typesetting the documents.

Please note that the information collection requirements contained in the final rule must be approved by the Office of Management and Budget before the final rule may be submitted for signature and publication. Please contact the Information and Records Management Branch, Office of Information Resources Management, concerning the paperwork management aspects of this rulemaking action.

9708150178 2PP.

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

OFFICE OF THE
GENERAL COUNSEL

June 15, 1995

MEMORANDUM TO: David L. Morrison, Director
Office of Nuclear Regulatory Research

FROM: Stuart A. Treby
Associate General Counsel for
Rulemaking and Fuel Cycle

Stuart A Treby

SUBJECT: DRAFT FINAL RULE - PATIENT RELEASE CRITERIA

We have reviewed the final version of the draft final rule addressing release of individuals administered radioactive materials. The revisions have satisfactorily addressed our earlier comments and we have no legal objection to this rulemaking package.

CONTACT: Bradley W. Jones, OGC
415-1628

9708150183 1p.

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

June 13, 1995

MEMORANDUM TO: David L. Morrison, Director
Office of Nuclear Regulatory Research

FROM: Carl J. Paperiello, Director
Office of Nuclear Material
Safety and Safeguards

Carl J Paperiello

SUBJECT: OFFICE REVIEW AND CONCURRENCE: DRAFT FINAL RULE - CRITERIA FOR THE RELEASE OF INDIVIDUALS ADMINISTERED RADIOACTIVE MATERIALS

This Office has reviewed the rulemaking package for "Final Amendments to 10 CFR Parts 20 and 35 on Criteria for the Release of Individuals Administered Radioactive Material" and we concur. As you requested in your memorandum dated May 31, 1995, we are not providing comments or concurrence on the draft Regulatory Guide at this time.

Contact: Patricia K. Holahan, NMSS
(301) 415-7847

9508160182 1p.

b. A final regulatory analysis will be available in the Public Document Room (Attachment 3);

c. A final environmental assessment and a finding of no significant impact have been prepared (Attachment 4);

d. The Chief Counsel for Advocacy of the Small Business Administration will be informed of the certification regarding economic impact on small entities and the reasons for it as required by the Regulatory Flexibility Act;

e. The rule contains information collection requirements that are subject to review by OMB. Upon Commission approval, the OMB supporting statement (Attachment 7) will be submitted to OMB for approval.

f. The appropriate Congressional Committees will be informed (Attachment 5);

g. A public announcement will be issued (Attachment 6); and

h. Copies of the Federal Register Notice of final rulemaking and the associated regulatory guide will be distributed to all Commission medical licensees and each Agreement State. The notice will be sent to other interested parties upon request.

James M. Taylor
Executive Director
for Operations

Attachments: As Stated (7)

RECORD NOTE: A draft of the final rule was sent to OIG for information on May 31, 1995.

Offc:	RPHEB:DRA	RPHEB:DRA	RPHEB:DRA	D:DRA:RES	D:NMSS	D:SP	ADM
Name:	SSchneider	SMcGuire	JGlenn	BMorris	CPaperiello	RBangart	WOliu
Date:	6/8/95	6/8/95	6/9/95	6/15/95	6/13/95	6/13/95	6/5/95
Offc:	D:IRM	OC	OGC	D:OE	D:RES	EDO	
Name:	GCranford	PScroggins	MMalsch	JLieberman	DMorrison	JMTaylor	
Date:	6/7/95	6/8/95	6/8/95	6/6/95	6/14/95	/ /95	

OFFICIAL RECORD COPY

d. A final environmental assessment and a finding of no significant impact have been prepared (Attachment 4).

e. The Chief Counsel for Advocacy of the Small Business Administration will be informed of the certification regarding economic impact on small entities and the reasons for it as required by the Regulatory Flexibility Act.

f. The appropriate Congressional Committees will be informed (Attachment 5);

g. A public announcement will be issued (Attachment 6).

h. The rule contains information collection requirements that are subject to review by the Office of Management and Budget. Upon Commission approval, the OMB supporting statement (Attachment 7) will be submitted to OMB for approval.

i. Copies of the Federal Register notice of final rulemaking and the associated regulatory guide will be distributed to all NRC medical licensees and each Agreement State. The notice will be sent to other interested parties upon request.

Original Signed By Hugh L. Thompson, Jr.

for James M. Taylor
Executive Director
for Operations

Attachments: As Stated (7)

RECORD NOTE: A draft of the final rule was sent to OIG for information on May 31, 1995.

* see previous concurrence

Offc:	RPHEB:DRA	RPHEB:DRA	RPHEB:DRA	D:DRA:RES	D:NMSS	D:SP	ADM
Name:	SSchneider	SMcGuire	JGlenn	BMorris	CPaperiello	RBangart	WOliu
Date:	6/08/95*	6/08/95*	6/09/95*	6/14/95*	6/13/95*	6/13/95*	6/05/95*

Offc:	D:IRM	OC	OGC	D:OE	D:RES	EDO
Name:	GCranford	PScroggins	MMalsch	JLieberman	DMorrison	JMTaylor
Date:	6/07/95*	6/08/95*	6/08/95*	6/06/95*	6/14/95*	6/13/95

OFFICIAL RECORD COPY RES FILE NO.3A-3

3. Notes:

a. The final rule will become effective 120 days after publication in the Federal Register.

b. A final regulatory guide will be published, for use, before the final rule becomes effective (Attachment 2).

c. A final regulatory analysis will be available in the Public Document Room (Attachment 3).

d. A final environmental assessment and a finding of no significant impact have been prepared (Attachment 4).

e. The Chief Counsel for Advocacy of the Small Business Administration will be informed of the certification regarding economic impact on small entities and the reasons for it as required by the Regulatory Flexibility Act.

f. The appropriate Congressional Committees will be informed (Attachment 5);

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h. The rule contains information collection requirements that are subject to review by the Office of Management and Budget. Upon Commission approval, the OMB supporting statement (Attachment 7) will be submitted to OMB for approval.

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James M. Taylor
Executive Director
for Operations

Attachments: As Stated (7)

RECORD NOTE: A draft of the final rule was sent to OIG for information on May 31, 1995. * see previous conc.

Offc:	RPHEB:DRA	RPHEB:DRA	RPHEB:DRA	D:DRA:RES	D:NMSS	D:SP	ADM
Name:	SSchneider	SMcGuire	JGlenn	BMorris	CPaperiello	RBangart	WOliu
Date:	3/11/96	3/11/96	3/11/96	3/11/96	3/11/96	6/13/95*	6/05/95*

Offc:	D:IRM	OC	OGC	D:OE	D:RES	EDO
Name:	GCranford	PScroggins	STreby	JLeiberman	DMorrison	JMTaylor
Date:	6/07/95*	6/08/95*	3/11/96	6/06/95*	3/11/96	/ /96

OFFICIAL RECORD COPY RES FILE NO. 3A-3

SECY PAPER DISTRIBUTION Rev. 07/11/95

____ POLICY ____ MEETING SECY-95-_____

____ RULEMAKING ___✓___ AFFIRMATION

____ ADJUDICATORY ____ NOTATION Reviewed By _____

____ NEGATIVE CONSENT NOTE: Classified - (1) to each Commission office, OGC (2), SECY (3), & Central Files (1)

____ INFORMATION

CLASSIFICATION _____

CHAIRMAN JACKSON (3) (2 for INFO)	___	EXECUTIVE DIRECTOR FOR OPERATIONS (3)	3
COMMISSIONER ROGERS (3)	_____	DEPUTY EXECUTIVE DIRECTORS (2)	2
COMMISSIONER (3)	_____	[illegible] ( ) (2)*	2
COMMISSIONER (3)	_____	[illegible]	4
COMMISSIONER (3)	_____	IRM (3) (4)*	4
SECY (10-14) (80 For Mtg)	_____	AEOD (5)	_____
OGC (17) (7 For ADJ)	_____	NRR (12)	5
OFFICE OF CAA (1/4)	_____	NMSS (5)	5
OIG (3)	_____	RES (12)	5
PA (2)	_____	OE (1)	1
IP (5)	_____	OI (2)	_____
CA (2)	_____	SP (3)	3
ACRS (20)	_____	OP (2)	_____
ACNW (10)	_____	SBCR (1)	_____
ASLBP (4)	_____	DOCUMENT CONTROL DESK (1)	1
		FILES CENTER (1)	1

Page Counted 3/9708150209

REGIONAL OFFICES: (C&R BRANCH, SECY)

RI - King of Prussia (2) _____

RII - Atlanta (2) _____

RIII - Chicago (2) _____

RIV - Dallas (2) _____

TOTAL NUMBER OF COPIES _____

*If Rulemaking RETURN ORIGINAL TO: _____

Table 1.

Reporting Requirements

Section	No. of Procedures Requiring Written Instructions Per Year	Hours Per Procedure	Total Burden Hours
35.75(b)			
exceeding 0.1 rem	62,000[1]	1/6	10,333
breast-feeding mothers	27,000[2]	1/6	4,500

Recordkeeping Requirements

Section	No. of Procedures Requiring Records Per Year	Hours Per Licensee	Total Burden Hours
35.75(c)	10,000[3]	2/15	1,333
35.75(d)	7,200[4]	2/15	960

Total burden = 17,126 hours or 13 hours per licensee (17,126 ÷ 1,350) at a cost of $2,277,758 ($133 x 17,126).

---

[1]50,000 iodine administrations for thyroid ablation + 10,000 iodine administrations for thyroid cancer + 2,000 iodine permanent implants = 62,000.

[2]8,000,000 administrations x 0.5 fraction of the administrations potentially requiring instructions x 0.135 fraction of females of child bearing age (from Table 4.3 of NUREG-1492) x 0.05 breast-feeding = 27,000.

[3]Iodine treatment for thyroid cancer patients.

[4](60,000 iodine + 1,000,000 technetium-99m pertechnetate) x 0.135 fraction of females of child bearing age x 0.05 breast feeding = 7,200.

In addition, the estimated burden on the Agreement States to review records is estimated to be 1 hour per Agreement State licensee per year, or 900 hours for all Agreement State licensees. At a cost of $133 per hour, the annual cost to Agreement States is $119,700 annually.

12. Estimate of Burden

The total burden to provide instructions and maintain release records is estimated to be about 13 hours per licensee annually, or a total of approximately 17,126 hours annually for all 1,350 NRC and Agreement State medical use of byproduct material licensees. See attached table for details.

13. Reasons for Change in Burden

The amendment adds recordkeeping and reporting requirements to 10 CFR 35.75 to protect individuals likely to be exposed to patients administered radiopharmaceuticals or permanent implants, for demonstrating compliance with the annual limit for individuals due to the release of patients administered radioactive material. The final rule reflects a burden decrease from that of the proposed rule from 19 to 13 hours per licensee. The proposed rule required records for releases if the total effective dose equivalent to any individual other than the released patient exceeded 0.1 rem. The final rule requires records only for exceptions to standard assumptions and when instructions were provided to a breast-feeding woman if the dose to the child from continued breast-feeding could result in a total effective dose equivalent exceeding 5 millisieverts (0.5 rem).

14. Publication for Statistical Use

There is no application to statistics in the information collected. There is no publication of this information.

B. COLLECTIONS OF INFORMATION EMPLOYING STATISTICAL METHODS

Not applicable.

4. Effort to Identify Duplication and Use Similar Information

There is no similar information available to the NRC. The Information Requirements Control Automated System (IRCAS) was searched for duplication, and none was found.

5. Effort to Reduce Small Business Burden

The NRC believes that there is no way to reduce the burden on small businesses by less frequent or less complete records while maintaining the required level of safety.

6. Consequences of Less Frequent Collection

The consequences of less frequent recordkeeping and reporting would be that there would be no basis for demonstrating compliance with the required level of safety through the NRC inspection program.

7. Circumstances Which Justify Variation from OMB Guidelines

There are no variations from OMB guidelines.

8. Consultation Outside the Agency

A public meeting to discuss the concepts and approaches of a previous version of the proposed rule with representatives of the Agreement States was held in July 1992 and October 1993. In addition, a draft rule package was sent to the Agreement States for their review and comment in July 1993. The final rule was discussed with the States at a meeting in October 1994. The proposed rule was also discussed with the Advisory Committee on Medical Uses of Isotopes (ACMUI) during public meetings held in October 1992, May 1993, and November 1993. The final rule was discussed with the ACMUI in November 1994, May 1995, and October 1995. The Agreement States and the ACMUI were generally supportive of the approach in the rule.

9. Confidentiality of Information

No information normally considered confidential is requested.

10. Justification of Sensitive Information

No sensitive information is requested under these regulations.

11. Estimated Annual Cost to the Federal Government

The estimated burden on the NRC to review records is estimated to be 1 hour per NRC licensee per year, or 450 hours for all NRC licensees. At a cost of $133 per hour, the annual cost to NRC is $59,850 annually. This cost is fully recovered through fee assessments to NRC licensees pursuant to 10 CFR Part 171.

exceed 1 millisievert (0.1 rem). In those cases where the released individual may be a breast-feeding woman, paragraph (b) also requires the instructions to include guidance on the interruption or discontinuation of breast-feeding and information on the consequences of failure to follow the guidance. The instructions should be specific to the type of treatment given and may include additional information regarding individual situations. The instructions should include a contact and phone number in case the patient has any questions. Instructions should include, as appropriate: (1) maintaining distance from other individuals, including sleeping arrangements and the need to minimize use of public transportation; (2) the interruption period for breast-feeding and the consequences to the breast-feeding child upon failure to follow the guidance, if applicable; (3) minimizing time in public places (such as grocery stores, shopping centers, restaurants, and sporting events); (4) hygiene; and (5) the length of time precautions should be taken. Written instructions are needed to provide a reference available after the patient's release, if questions regarding patient care arise, and to reduce the chance of misunderstanding the licensee's instructions as verbal instructions may not be properly conveyed to persons not present at the time of release. The written instructions are also necessary to permit the NRC to verify the type of instructions generally given to patients.

Paragraph (c) of this section requires licensees to maintain, for 3 years, a record of the basis for the release if the release is authorized using other than standard assumptions. The records are necessary so that the NRC inspector can review the method for calculating the dose to determine that the method is adequate to show that the requirements in paragraph (a) were met.

Paragraph (d) of this section requires licensees to maintain, for 3 years, a record that instructions were provided to a breast-feeding woman if the administered activity could result in a total effective dose equivalent to the breast-feeding infant exceeding 5 millisieverts (0.5 rem) if the woman did not interrupt or discontinue breast-feeding. The records are necessary so that the NRC inspector can verify that instructions were given to the breast-feeding woman to inform her of the need to interrupt or discontinue breast-feeding.

2. Agency Use of Information

Records kept, and written instructions provided by the licensee, will be used by NRC inspectors to evaluate compliance with NRC regulations to assure that the public health and safety are protected.

3. Reduction of Burden Through Information Technology

No responses are submitted to NRC. NRC encourages licensees to utilize any technology which would reduce the burden of recordkeeping and reporting. Archival storage of (1) surveys and prospective evaluations and (2) the content of written instructions lend themselves readily to the use of automated information technology.

OMB SUPPORTING STATEMENT FOR 10 CFR PART 35,
"Criteria for the Release of Individuals
Administered Radioactive Material"
(3150-0010)

Description of Information Collection

This clearance package covers the recordkeeping and reporting requirements of amendments to 10 CFR Part 35, "Medical Use of Byproduct Material," § 35.75, "Release of individuals containing radiopharmaceuticals or permanent implants." The existing § 35.75 contains no information collection requirements. The revision to § 35.75 incorporates the information collection required below.

The information collection requirements in the proposed rule were submitted to OMB and approved under OMB control number 3150-0010. The entire collection is being resubmitted at the final rule stage because of some major changes in the information collections.

A. JUSTIFICATION

The amenument to § 35.75 revises the criteria for authorizing the release of individuals administered radioactive material under 10 CFR Part 35 to permit a maximum annual dose of 5 millisieverts (0.5 rem) to an individual member of the public, requires written instruction on how to maintain doses to others as low as is reasonably achievable if the dose to an individual exposed to a released patient is likely to exceed 1 millisievert (0.1 rem). In those cases where the released individual may be a breast-feeding woman, the instructions must also include guidance on the interruption or discontinuation of breast-feeding and information on the consequences of failure to follow the guidance. The amendment also establishes recordkeeping requirements when the release is authorized using other than standard assumptions or when instructions were provided to a breast-feeding woman because the dose to the child from continued breast-feeding could result in a total effective dose equivalent exceeding 5 millisieverts (0.5 rem).

1. Need for tne Collection of Information

The information collection requirements of the amendments to 10 CFR Part 35 are identified below.

§ 35.75 Release of individuals containing radiopharmaceuticals or permanent implants.

Paragraph (b) of this section requires licensees to provide, upon release, the patient with written instructions on how to maintain doses to other individuals as low as reasonably achievable if the total effective dose equivalent to any individual other than the released patient is likely to

Comments and questions can be directed by mail to the OMB reviewer:

Peter Francis

Office of Information and Regulatory Affairs

(3150-0010)

NEOB-10202

Office of Management and Budget

Washington, DC 20503

Comments may also be communicated by telephone at (202) 395-3084.

The NRC Clearance Officer is Brenda Jo. Shelton, (301) 415-7230.

Dated at Rockville, Maryland, this _____ day of _____, 1996.

For the Nuclear Regulatory Commission.

_____

Gerald F. Cranford, Designated Senior Official for Information Resources Management.

written instructions on how to maintain doses to other individuals as low as is reasonably achievable if the dose to an individual exposed to the patient is likely to exceed 0.1 rem. In those cases where the released individual may be a breast-feeding woman, the instructions must also include guidance on the interruption or discontinuation of breast-feeding and information on the consequences of failure to follow the guidance. The amendment also requires the licensee to maintain a record of the basis for the release if the release is authorized using other than standard assumptions or that instructions were provided to a breast-feeding woman if the dose to the child from continued breast-feeding could result in a total effective dose equivalent exceeding 0.5 rem. These requirements are necessary to ensure adequate protection of the public health and safety and that doses to other individuals are maintained as low as reasonably achievable.

Copies of the submittal may be inspected or obtained for a fee from the NRC Public Document Room, 2120 L Street NW. (Lower Level), Washington, DC.

4. How often is the collection required: On occasion; when the release of a patient is based on other than standard assumptions or requires interruption or discontinuation of breast-feeding to meet the 5-millisievert (0.5-rem) dose limit.

5. Who will be required or asked to report: Medical licensees administering radiopharmaceuticals and permanent implants and releasing patients under the provisions of 10 CFR 35.75.

6. An estimate of the number of respondents: Approximately 1,350 NRC and Agreement State licensees.

7. An estimate of the number of hours annually needed to complete the requirement or request: 17,126 hours (includes NRC and Agreement State licensees).

8. The average annual burden per respondent: 13 hours.

9. An indication of whether Section 3504(h), Pub. L. 96-511 applies: Applicable.

10. Abstract: The Nuclear Regulatory Commission (NRC) is amending the criteria for release of individuals administered radioactive material under 10 CFR Part 35. The amendment requires the licensee to provide the patient with

[7590-01]

NUCLEAR REGULATORY COMMISSION

Documents Containing Reporting or Recordkeeping Requirements; Office of Management and Budget (OMB) Review

AGENCY: Nuclear Regulatory Commission (NRC).

ACTION: Notice of the OMB review of information collection.

SUMMARY: The Nuclear Regulatory Commission has recently submitted to OMB for review the following proposal for collection of information under the provisions of the Paperwork Reduction Act of 1980 (44 U.S.C. Chapter 35).

1. Type of submission, new, revised, or extension: Revision.

2. The title of the information collection: Final amendments to 10 CFR 35.75, "Criteria for the Release of Individuals Administered Radioactive Material."

3. The form number if applicable: Not applicable.

ATTACHMENT 7

FEDERAL REGISTER NOTICE AND SUPPORTING STATEMENT FOR OMB REVIEW

Release of patients containing radioactivity is instead governed by the more explicit requirements of revised medical use regulations, which include, in addition to the 500-millirem per year limit, a requirement that, if the annual dose to an individual exposed to the patient is likely to exceed 100 millirems, the licensee must provide the patient with written instructions on how to maintain doses to other individuals as low as reasonably achievable. If the released individual may be breast-feeding an infant or child, the instructions must also include guidance on the interruption or discontinuation of breast-feeding and information on the consequences of failure to follow the guidance.

The revisions partially grant three petitions for rulemaking on criteria for release of patients who have been administered radioactive material. On June 12, 1991, March 9, 1992, May 18, 1992, and July 26, 1994, the NRC published Federal Register notices concerning receipt of the petitions from Dr. Carol S. Marcus, the American College of Nuclear Medicine and the American Medical Association.

A proposed rule on this subject was published in the Federal Register on June 15, 1994. The final rule reflects public comments received.

The rule will be effective _____ (120 days after publication of a Federal Register notice on _____).

###

NRC REVISES REGULATIONS ON RELEASE

OF PATIENTS ADMINISTERED BYPRODUCT MATERIAL

The Nuclear Regulatory Commission is amending its regulations governing the release of patients from a hospital or other licensed medical facility after they have received radioactive material for treatment or diagnostic purposes. The revisions respond to three petitions received on this subject.

Radioactive pharmaceuticals or radioactive implants are administered to approximately 8 to 9 million patients in the United States each year for diagnosis or treatment of disease. These patients can expose other persons around them to radiation until the radioactive material has been excreted from their bodies or has become less intense due to radioactive decay.

Under the final rule, licensees may not authorize the release of patients if the estimated dose, to the individual likely to receive the highest dose from exposure to the patient, would be greater than 500 millirems. (Typical natural background radiation in the United States is 300 millirems per year.) The new criteria are consistent with recommendations of the International Commission on Radiological Protection and the National Council on Radiation Protection and Measurements.

Under current NRC medical use regulations, licensees are not permitted to authorize the release of patients to whom nuclear material has been administered until either (1) the measured dose rate from the patient is less than 5 millirems per hour at a distance of 1 meter or (2) the radiopharmaceutical content of the patient is less than 30 millicuries.

The final rule amends the general radiation protection regulations in 10 CFR Part 20 to exclude doses to individuals exposed to released patients.

ATTACHMENT 6

DRAFT PUBLIC ANNOUNCEMENT

DRAFT CONGRESSIONAL LETTER

Dear Mr. Chairman:

Enclosed for the information of the Subcommittee are copies of a public announcement and a final amendment to 10 CFR Parts 20 and 35 dealing with criteria for the release of patients administered radioactive materials. Roughly 8 to 9 million medical diagnostic and therapeutic administrations of radioactive material are performed in the United States each year.

The rule is largely in response to three petitions for rulemaking that were submitted by the medical community because of concerns that the NRC's recent amendments of its regulations in Part 20, "Standards for Protection Against Radiation," would require medically unnecessary hospitalization of patients administered radioactive materials for the treatment of disease and would thus increase national health care costs.

The rule makes it clear that the release of patients administered radioactive materials continues to be regulated by the requirements in NRC's Part 35, "Medical Use of Byproduct Material." While the comments of the medical community on the proposed rule were generally supportive, they objected strongly to one of the recordkeeping requirements contained in the proposed rule. Upon reconsideration, the NRC has deleted the recordkeeping requirement in question after concluding that the records were not necessary to provide for adequate protection of public health and safety.

Sincerely,

Dennis K. Rathbun, Director
Office of Congressional Affairs

Enclosures:
1. Public Announcement
2. Federal Register Notice

cc: Representative _____

Attachment 5

ATTACHMENT 5

DRAFT CONGRESSIONAL LETTER

M. Rosenstein, Ph.D., Food and Drug Administration, Center for Devices and Radiology Health, Rockville, MD

J. St.Germain, Radiation Safety Officer, Memorial Sloan Kettering, New York City, NY

B.A. Siegel, M.D. (Chairman, NRC Advisory Committee on Medical Use of Isotopes), Director, Division of Nuclear Medicine, Mallinckrodt Institute of Radiology, Washington University Medical Center, St. Louis, MO

M.G. Stabin, Ph.D., CHP, Radiation Internal Dose Information Center, Oak Ridge Institute for Science and Education, Oak Ridge, TN

D. Steidley, Ph.D., CHP, Medical Health Physicist, Department of Oncology, St. Barnabas Medical Center, Livingston, NJ

J. Stubbs, Ph.D., Radiation Internal Dose Information Center, Oak Ridge Institute for Science and Education, Oak Ridge, TN

K. Suphanpharian, Ph.D., President, Best Industries, Springfield, VA

R.E. Toohey, Ph.D., Director, Radiation Internal Dose Information Center, Oak Ridge Institute for Science and Education, Oak Ridge, TN

10/18/95 Rockville, MD Advisory Committee on the Medical Uses of
10/19/95 Isotopes (ACMUI)

Much of the statistical and technical information required for this assessment is not available in the open literature. In such instances, information was obtained directly from technical experts. The following individuals are acknowledged for their cooperation and contribution of technical information and data:

R. Atcher, Ph.D., Radiation and Cellular Oncology Department, University of Chicago, Chicago, IL

K. Behling, S. Cohen and Associates, McLean, VA

U. H. Behling, S. Cohen and Associates, McLean, VA

D. Flynn, M.D. (NRC Advisory Committee on Medical Use of Isotopes), Massachusetts General Hospital, Boston, MA

D. Goldin, S. Cohen and Associates, McLean, VA

W.R. Hendee, Ph.D., Dean of Research, Medical College of Wisconsin, Milwaukee, WI

P. Holahan, Ph.D., U.S. Nuclear Regulatory Commission, Washington, DC

C. Jacobs, President, Theragenics, Norcross, GA

F.A. Mettler, M.D., Department of Radiology, University of New Mexico, School of Medicine, Albuquerque, NM

K.L. Miller, CHP, Professor of Radiology and Director, Division of Health Physics, Milton Hershey Medical Center, Hershey, PA

R. Nath, Ph.D., Professor of Yale University, School of Medicine, and past President of the American Association of Physicists in Medicine, New Haven, CT

M.P. Nunno, Ph.D., CHP, Cooper Hospital, University Medical Center, Camden, NJ

P. Paras, Ph.D., Food and Drug Administration, Center for Devices and Radiology Health, Rockville, MD

M. Pollycove, M.D., Visiting Medical Fellow, U.S. Nuclear Regulatory Commission, Washington, DC

G.E. Powers, Ph.D., Office of Nuclear Regulatory Research, U.S. Nuclear Regulatory Commission, Washington, DC

V. FINDING OF NO SIGNIFICANT IMPACT

The Commission has determined under the National Environmental Policy Act of 1969, as amended, and the Commission's regulations in Subpart A of 10 CFR Part 51, that the amendments are not a major Federal action significantly affecting the quality of the human environment, and therefore an environmental impact statement is not required. The amendments establish new criteria for patient release that are based on the potential radiation dose to other individuals exposed to the patient. Furthermore, the amendments require the licensee to provide written instructions to patients on how to maintain the doses to others as low as is reasonably achievable. It is expected that there will be no significant impact to the environment.

VI. LIST OF AGENCIES AND PERSONS CONSULTED

The NRC has held public meetings concerning the release criteria for patients receiving radioactive material for medical use. Appropriate suggestions from the meetings have been incorporated in the proposed amendments. The following table lists the date, location, and the groups represented at each meeting.

Public Meetings Held

Date	Location	Groups Represented
07/15/92 07/16/92	Atlanta, GA	Agreement States: AL, AR, AZ, CA, CO, FL, GA, IL, KS, KY, LA, MD, NC, ND, NE, NH, NV, NY, OR, SC, TX, UT, WA, and NY City
10/24/92 10/25/92 10/26/92 10/27/92	Tempe, AZ	Agreement States: AL, AR, AZ, CA, CO, FL, GA, IA, IL, KY, LA, MD, MS, NC, ND, NE, NH, NV, OR, RI, SC, TN, TX, UT, WA, and NY City
10/24/94 10/25/94	Portland, ME	Agreement States: AL, AR, IL, KS, LA, NH, NV, NY, PA, RI, TX, UT, WA, and NY City
10/22/92 10/23/92	Rockville, MD	Advisory Committee on the Medical Uses of Isotopes (ACMUI)
05/03/93 05/04/93	Bethesda, MD	Advisory Committee on the Medical Uses of Isotopes (ACMUI)
11/01/93	Reston, VA	Advisory Committee on the Medical Uses of Isotopes (ACMUI)
11/18/94	Rockville, MD	Advisory Committee on the Medical Uses of Isotopes (ACMUI)
05/12/95	Rockville, MD	Advisory Committee on the Medical Uses of Isotopes (ACMUI)

Included within this range of options was the option to enhance communication between the licensee and woman regarding instructions to interrupt or discontinue breast-feeding before the woman is released from the hospital, which is the option adopted in this rulemaking. As discussed in the Regulatory Analysis, the other options were dismissed as ineffective or impractical due to a variety of reasons: the option of a woman remaining in a hospital was dismissed due to psychological impacts to the woman and breast-feeding infants, impacts on the practice of medicine, and health care costs; the option of maintaining status quo was dismissed due to lack of assurance that instructions will be provided to a breast-feeding woman. Therefore, the option to enhance communication is selected as the preferred option.

To enhance communications and reduce the probability of a mother breast-feeding after administration of large quantities of iodine-131, amended 10 CFR 35.75(b) will require licensees to provide guidance on the interruption or discontinuation of breast-feeding and information on the rationale for following the guidance. Compliance with the regulation provides NRC with confidence that the licensee will give the instructions to breast-feeding women and it is expected that almost all women will follow instructions to interrupt or discontinue breast-feeding to protect their children from potentially harmful effects. The NRC is not aware of any instances where instructions were given to the woman but she ignored the warning and continued breast-feeding a child.

The decision to require instructions as shown in column 5 of Table B.5 of the Regulatory Analysis (NUREG-1492) is based on both the external and internal dose to the nursing infant. It can be seen from column 4 that for some radiopharmaceuticals the external dose from breast-feeding can be a significant part of the total dose. The duration of the interruption shown in column 6 is selected to reduce the maximum dose to a newborn infant to less than 1 millisievert (0.1 rem). However, the actual doses that would be received by most infants for the recommended interruption periods shown should be a small fraction of 1 millisievert (0.1 rem) due to the conservatism of the analysis. The conservative factors are based on: (1) the maximum measured level of activity in breast milk, (2) the longest biological half-life, and (3) the lowest body weight (i.e., the newborn).

It is expected that there will be no effect from breast-feeding on collective dose due to therapeutic administrations, although there may be a small effect from more infants having an opportunity to have contact with a woman sent home from hospital (i.e., cancer patients). However, instructions providing guidance, such as to maintain distance from other persons, should aid in minimizing this effect. In the case of diagnostic administrations of iodine-131 sodium iodide, it is currently normal practice to recommend interruption of breast-feeding. Thus, this rule is expected to have little or no effect on collective dose due to diagnostic administrations. In sum, the environmental impact is not considered significant.

iodine-131 sodium iodide for thyroid cancer (see Tables 4.10 and 4.11 of NUREG-1492); whereas, 1 person-sievert (100 person-rem) is associated with exposure to released patients (about 1,000) administered more than 1,110 megabecquerels (30 millicuries) of iodine-131 sodium for thyroid ablation (see Tables 4.10 and 4.11 of NUREG-1492). Based on the assumption that each patient could expose about seven family members and friends (including the primary care-provider), the increase in dose to an affected individual in a year is about 0.00037 sievert (37 millirem) for thyroid cancer and about 0.00014 sievert (14 millirem) for thyroid ablation. The increase in risk to the affected individual could vary from zero (if a dose threshold exists) to 1.8×10^{-5} per year (if the linear no threshold hypotheses is valid and a risk factor of about 5×10^{-4} per person-rem is used). When compared with the incidence of cancer of 0.20 from natural causes, the potential cancer risk for a family member or other person who has close contact with a thyroid cancer or thyroid ablation patient is small. Thus, the environmental impact is not considered significant.

Breast-feeding Infant

There are specific issues associated with the administration of iodine-131 sodium iodide in that following both diagnostic and therapeutic administrations, the dose to a breast-feeding child could exceed 5 millisieverts (0.5 rem) if there was no interruption of breast-feeding. In particular, if the woman does not cease breast-feeding after administration of millicurie quantities of iodine-131 sodium iodide, the internal dose to the breast-feeding infant could be large enough to cause the infant's thyroid to be severely damaged resulting in hypothyroidism. If hypothyroidism were undiagnosed in very young children, severe mental retardation may occur. However, if the patient was provided instructions to discontinue breast-feeding, as well as being advised of the consequences of not following the instructions, the NRC believes that the probability of a woman failing to cease breast-feeding after being administered iodine-131 sodium iodide is small. For example, in 1990 an administered dosage of 185 megabecquerels (5 millicuries) of iodine-131 sodium iodide to a patient resulted in her breast-fed infant receiving an unintended radiation dose of 300 grays (30,000 rads) to the infant's thyroid gland. This dose would result in ablation of the infant's thyroid. This situation was recognized in 2 days which allowed prompt action to be taken thereby reducing potential consequences such as mental retardation. The NRC is aware of two other cases that occurred during 1991 and 1995. In each of these cases, there was a breakdown in communications, rather than lack of intent to prevent breast-feeding.

Although instructions to keep doses to household members and the public as low as is reasonably achievable are currently required for radiopharmaceutical therapy in 10 CFR 35.315(a)(6), there is no requirement specific to the dose from breast-feeding. In some cases, instructions to interrupt or discontinue breast-feeding may not be effectively communicated. To deal with this issue, the NRC considered a range of options which varied from maintaining the status quo to the extreme option of a woman remaining in the hospital for a period of time after administration of millicurie quantities of I-131 sodium iodide to ensure her milk production has stopped.

$412,000,000 per year, mostly because of increased national health care costs. In view of this, Alternative 1 may be dismissed.

3. Alternative 3 relative to Alternative 2 has a net value of about $9,000,000 per year, mostly due to lower health care costs. Also, Alternative 3 has psychological benefits to patients and their families. Thus, Alternative 3 is cost-effective in comparison with Alternative 2.

4. Basing the patient release criteria in 10 CFR 35.75 on the dose to individuals exposed to a patient provides a consistent, scientific basis for such decisions that treats all radionuclides on a risk-equivalent basis. The dose delivered by an initial activity of 30 millicuries or a dose rate at 1 meter of 5 millirems per hour varies greatly from one radionuclide to another. Thus, while the values in the current 10 CFR 35.75 may be appropriate for iodine-131, they are too high for some other radionuclides and too low for others.

5. A dose-based rule no longer restricts patient release to a specific activity, and therefore would permit the release of patients with activities that are greater than currently allowed. This is especially true when case-specific factors are evaluated to more accurately assess the dose to other individuals. For the case of thyroid cancer, in those occasional cases where multiple administrations in a year of 1,110 millisieverts (30 millicuries) or less of iodine-131 are now administered to a patient, it may be possible to give all of the activity in a single administration. This would reduce the potential for repeated exposures to hospital staff and to those providing care to the released patient. Additionally, this would provide physicians with the flexibility to not have to fractionate doses to avoid hospitalization to meet the current requirements, which may lead to a more effective treatment.

6. Shorter hospital stays provide emotional benefits to patients and their families. Allowing earlier reunion of families can improve the patient's state of mind, which in itself may improve the outcome of the treatment and lead to the delivery of more effective health care.

IV. ENVIRONMENTAL IMPACTS OF THE PROPOSED ACTION AND THE ALTERNATIVES

Family Members or Other Persons

For the purpose of evaluating the environmental impact of the proposed action, the proposed action (Alternative 3) is compared to the impact of the existing patient release criteria, the status quo (Alternative 2). The impacts can be seen in Table 1 above. The estimated change in the collective dose when comparing Alternative 3 to Alternative 2 is an increase of about 27 person-sievert (2,700 person-rem). Most of the increase, about 26 person-sievert (2,600 person-rem), is received by the primary care-providers and family members exposed to released patients (about 10,000) administered

- Alternative 2: ≤ 1,110 megabecquerels (30 millicuries) or ≤ 0.05 millisievert (5 millirems)/hr at 1 meter

In this alternative, the existing patient release criteria in 10 CFR 35.75 are evaluated as the controlling requirements for determining when a patient may be released.

- Alternative 3: 5 millisieverts (0.5 rem) total effective dose equivalent)

In this alternative, a dose limit of 5 millisieverts (0.5 rem) for determining when a patient may be released is evaluated.

The alternatives were evaluated in the regulatory analysis done for the rulemaking (*Regulatory Analysis on Criteria for the Release of Patients Administered Radioactive Materials, Final Report*, Stewart Schneider and Stephen A. McGuire, NRC report NUREG-1492, 1996).

The regulatory analysis found that there would be no need to retain patients because of any diagnostic procedure under any of the alternatives. Only about 62,000 therapeutic procedures per year, mostly using iodine-131, would be potentially affected. The costs of the alternatives for the affected therapeutic procedures are presented in Table 1. For details of how the results were calculated, the regulatory analysis should be consulted.

Table 1 Annual Attributes of Alternatives 1, 2, and 3

			Cost Estimates			
Alternative	Collective Dose (person-rem)	Hospital Retention (days)	Hospitalization cost $ (millions)	Value of lost time $ (millions)	Records & Instructions $ (millions)	Psychological cost (relative)
1	18,100	427,000	427	25.62	0	High
2	29,840	16,000	16	0.96	0	Moderate
3	32,580	0	0	0	2.3	Low

As set forth in more detail in the Regulatory Analysis, Alternative 3 is favored for the following reasons:

1. All of the alternatives are acceptable according to generally accepted radiation protection principles, as those expressed by NRC, NCRP, and ICRP, as discussed in Section 4.4 of the Regulatory Analysis.

2. Alternative 1 is considerably more expensive to the public compared to Alternative 2 (the status quo) or Alternative 3. Even neglecting the psychological costs, which have not been expressed in dollar terms, the additional cost of Alternative 1 relative to Alternative 2 is about

information on whether or how the provisions of 10 CFR 20.1301 were intended to apply to the release of patients.

Because some licensees were uncertain about what effect the revised 10 CFR Part 20 would have on patient release criteria, three petitions were received on the issue. On June 12, 1991 (56 FR 26945), the NRC published in the Federal Register a notice of receipt of, and request for comment on, a petition for rulemaking (PRM-20-20) from Dr. Carol S. Marcus. The petition requested the NRC to amend the revised Part 20 and 10 CFR 35.75 to raise the annual radiation dose limits to members of the public from 1 millisievert (0.1 rem) to 5 millisieverts (0.5 rem) from patients administered radioactive materials. In addition, Dr. Marcus submitted a letter dated June 12, 1992, further characterizing her position. On March 9, 1992 (57 FR 8282) the NRC published a notice of receipt and request for comment in the Federal Register for a similar petition for rulemaking (PRM-35-10) from the American College of Nuclear Medicine (ACNM). On May 18, 1992 (57 FR 21043), the NRC published in the Federal Register notice of an amendment submitted by the ACNM to its original petition (PRM-35-10A). In addition, the ACNM submitted two letters dated September 24, 1991, and October 8, 1991, on the issues in their petition. On July 26, 1994 (59 FR 37950) the NRC published in the Federal Register a petition from the American Medical Association requesting that patient release be regulated by Part 35 rather than Part 20.

On June 15, 1994, the NRC published a proposed rule on criteria for the release of patients administered radioactive material in response to the petitions (59 FR 30724). The Federal Register Notice for the proposed rule discussed the public comment letters received on the first two petitions. Three comment letters, each supporting the petition, were received on the third petition (PRM-35-11), but these letters did not contain any additional information not covered by the letters on the first two petitions.

The NRC proposed to amend 10 CFR 20.1301(a)(1) to specifically state that the dose to individual members of the public from a licensed operation does not include doses received by individuals exposed to patients who were released by the licensed operation under the provisions of 10 CFR 35.75. This was to clarify that the Commission's policy is that patient release is governed by 10 CFR 35.75, not 10 CFR 20.1301.

III. ALTERNATIVES CONSIDERED

To evaluate the issues raised by the petitioners and the members of the public who commented on the requests made by the petitioners and the proposed rule, the NRC has determined that the following alternatives merit evaluation:

- Alternative 1: 1 millisievert (0.1 rem) total effective dose equivalent

  In this alternative, the 1 millisievert (0.1 rem) per year dose limit in 10 CFR 20.1301(a) is evaluated as the controlling criterion for determining when a patient may be released from the licensee's control.

ENVIRONMENTAL ASSESSMENT AND FINDING OF NO SIGNIFICANT IMPACT

ON

AMENDMENTS OF 10 CFR PARTS 20 AND 35 ON "CRITERIA FOR THE RELEASE OF PATIENTS ADMINISTERED RADIOACTIVE MATERIAL"

Stewart Schneider and Stephen A. McGuire
Office of Nuclear Regulatory Research
U. S. Nuclear Regulatory Commission
April 1996

I. THE PROPOSED ACTION

The Nuclear Regulatory Commission (NRC) is amending its regulations in 10 CFR Parts 20 and 35 concerning criteria for the release of patients administered radioactive material. The amendments permit licensees to authorize the release from licensee control of patients administered radiopharmaceuticals or permanent implants only if the dose to total decay to an individual exposed to the released patient is not likely to exceed 5 millisieverts (0.5 rem).

II. NEED FOR THE RULEMAKING ACTION

This action is necessary to respond to three petitions for rulemaking. The petitions were submitted by Dr. Carol S. Marcus, by the American College of Nuclear Medicine (ACNM), and by the American Medical Association (AMA).

NRC's current patient release criteria in 10 CFR 35.75, "Release of Patients or Human Subjects Containing Radiopharmaceuticals or Permanent Implants," are as follows: "(a) A licensee may not authorize release from confinement for medical care any patient or human research subject administered a radiopharmaceutical until either: (1) The measured dose rate from the patient or human research subject is less than 5 millirems per hour at a distance of one meter; or (2) The activity in the patient or human research subject is less than 30 millicuries; (b) A licensee may not authorize release from confinement for medical care of any patient or human research subject administered a permanent implant until the measured dose rate from the patient or the human research subject is less than 5 millirems per hour at a distance of one meter."

On May 21, 1991 (56 FR 23360), the NRC published a final rule that amended 10 CFR Part 20, "Standards for Protection Against Radiation." The rule contained a dose limit of 1 millisievert (0.1 rem) (total effective dose equivalent) for members of the public in 10 CFR 20.1301(a). When 10 CFR part 20 was issued, there was no discussion in the supplemental

ATTACHMENT 4

ENVIRONMENTAL ASSESSMENT

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Table B.5 Potential Doses to Breast-Feeding Infants from Radiopharmaceuticals Administered to a Woman if No Interruption of Breast-Feeding and Recommendations on Interruption of Breast-Feeding (Continued)

Radio-pharmaceutical	Maximum Administered Activity[1] (mCi) (MBq)	Internal Dose to Infant if No Interruption of Breast-Feeding[2] (mrem)	External Dose to Infant if No Interruption of Breast-Feeding[3] (mrem)	Instructions Required?[4]	Recommendation on Interruption of Breast-Feeding[5]
Tc-99m MAG3	10 (370)	0.2-2	30	no	None
Tc-99m White Blood Cells	5 (185)	20-800	10	yes	Interruption for about 24 hours
Ga-67 Citrate	5 (185)	300-10,000	NA[6]	yes	Complete cessation
Cr-51 EDTA	0.05 (1.85)	<0.01	2	no	None
In-111 White Blood Cells	0.5 (18.5)	20-100	60	yes	Interruption for about 24 hours
Tl-201 Chloride	3 (111)	100-200	NA[6]	yes	Complete cessation

1. Maximum activity normally administered.

2. Doses were calculated using the maximum administered activities shown in column 2. If smaller activities were to be administered, the doses would be proportionally smaller. The doses were calculated for newborn infants; doses to one-year-old infants would be less than half the doses shown. If a dose range is shown, the range is due to individual variability and measurement variability as indicated by different measurements of concentrations in breast milk as shown in Table B.2. All values have been rounded to one significant figure. The external dose, typically small relative to the internal dose, is considered separatley under column 4.

3. Dose to the infant from external radiation only during breast-feeding assuming no interruption of breast-feeding. Doses were calculated using an occupancy factor of 0.16 and an effective distance from source to receptor tissue of 0.2 meter. All values have been rounded to one significant figure.

4. The decision on whether instructions are required by 10 CFR 35.75 is based on the sum of the maximum value of the internal dose range for the newborn infant plus the external dose assuming no interruption of breast-feeding.

5. The duration of interruption is selected to reduce the maximum dose to a newborn infant to less than 0.1 rem. The actual doses that would be received by most infants would be far below 0.1 rem. The physician may use discretion in the recommendation, increasing or decreasing the duration of interruption somewhat depending on the woman's concerns about radioactivity or interruption of breast-feeding.

6. Not applicable (NA) because complete cessation of breast-feeding is assumed.

Table B.5 Potential Doses to Breast-Feeding Infants from Radiopharmaceuticals Administered to a Woman if No Interruption of Breast-Feeding and Recommendations on Interruption of Breast-Feeding

Radio-pharmaceutical	Maximum Administered Activity[1] (mCi) (MBq)	Internal Dose to Infant if No Interruption of Breast-Feeding[2] (mrem)	External Dose to Infant if No Interruption of Breast-Feeding[3] (mrem)	Instructions Required?[4]	Recommendation on Interruption of Breast-Feeding[5]
I-131 NaI	150 (5,550)	very large	N A[6]	yes	Complete cessation is necessary to avoid thyroid ablation in the infant
I-123 NaI	0.4 (14.8)	60	5	no	None
I-123 OIH	2 (74)	4-30	30	no	None
I-123 mIBG	10 (370)	300	100	yes	Interruption for about 24 hours
I-125 OIH	0.01 (0.37)	0.2	10	no	None
I-131 OIH	0.3 (11.1)	3-20	70	no	None
Tc-99m DTPA	20 (740)	0.3-6	50	no	None
Tc-99m MAA	4 (148)	4-300	10	yes	Interruption for about 12 hours
Tc-99m O4 (Pertechnetate)	30 (1,110)	20-800	80	yes	Interruption for about 24 hours
Tc-99m DISIDA	8 (300)	4-20	20	no	None
Tc-99m Glucoheptonate	20 (740)	2-5	50	no	None
Tc-99m HAM	8 (300)	20-50	20	no	None
Tc-99m MIBI	30 (1,110)	1-10	80	no	None
Tc-99m MDP	20 (740)	4-5	50	no	None
Tc-99m PYP	20 (740)	5-20	50	no	None
Tc-99m RBC In Vivo Labeling	20 (740)	0.3-100	50	yes	Interruption for about 6 hours
Tc-99m RBC In Vitro Labeling	20 (740)	1-2	50	no	None
Tc-99m Sulfur Colloid	12 (444)	9-100	30	yes	Interruption for about 6 hours
Tc-99m DTPA Aerosol	1 (37)	0.02-0.3	3	no	None

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
Tl-201 Chloride	3	minimum	3	1.22E−02	4.08E−01	1.84E+02	1.04E+02
			12	9.72E−03	3.24E−01	1.46E+02	8.26E+01
			24	7.49E−03	2.50E−01	1.12E+02	6.36E+01
			48	4.92E−03	1.64E−01	7.38E+01	4.18E+01
			96	2.45E−03	8.17E−02	3.68E+01	3.08E+01
			120	1.76E−03	5.86E−02	2.64E+01	1.50E+01
			168	9.10E−04	3.03E−02	1.36E+01	7.74E+00
			336	9.11E−05	3.04E−03	1.37E+00	7.74E−01
			672	9.13E−07	3.04E−05	1.37E−03	7.76E−03
		maximum	3	2.37E−02	7.91E−01	3.55E+02	2.01E+02
			12	2.12E−02	7.08E−01	3.18E+02	1.80E+02
			24	1.86E−02	6.21E−01	2.79E+02	1.58E+02
			48	1.51E−02	5.04E−01	2.26E+02	1.28E+02
			96	1.16E−02	3.88E−01	1.74E+02	9.86E+01
			120	1.07E−02	3.56E−01	1.60E+02	9.10E+01
			168	9.41E−03	3.14E−01	1.41E+02	8.00E+01
			336	6.71E−03	2.24E−01	1.01E+02	5.70E+01
			672	3.53E−03	1.18E−01	5.30E+01	3.00E+01

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
Tc-99m Sulfur Colloid	12	minimum	3	1.26E−02	1.05E−01	9.33E+00	4.57E+00
			12	3.74E−03	3.11E−02	2.76E+00	1.35E+00
			24	7.38E−04	6.15E−03	5.46E−01	2.68E+01
			48	2.88E−05	2.40E−04	2.13E−02	1.05E−02
			96	4.40E−08	3.67E−07	3.26E−05	1.60E−05
			120	1.72E−09	1.43E−08	1.27E−06	6.23E−07
			168	2.62E−12	2.19E−11	1.94E−09	9.51E−10
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maximum	3	1.76E−01	1.47E+00	1.30E+02	6.38E+01
			12	8.30E−02	6.92E−01	6.14E+01	3.01E+01
			24	3.05E−02	2.54E−01	2.26E+01	1.11E+01
			48	4.11E−03	3.42E−02	3.04E+00	1.49E+00
			96	7.47E−05	6.22E−04	5.53E−02	2.71E−02
			120	1.01E−05	8.39E−05	7.45E−03	3.65E−03
			168	1.83E−07	1.53E−06	1.35E−04	6.64E−05
			336	1.48E−13	1.23E−12	1.09E−10	5.36E−11
			672	0.00E+00	0.00E+00	0.00E+02	0.00E+00
Tc-99m White Blood Cells*	30	minimum	3	4.78E−02	1.59E−01	1.95E+01	9.02E+00
			12	5.10E−03	1.70E−02	2.08E+00	9.63E−01
			24	2.58E−04	8.61E−04	1.05E−01	4.88E−02
			48	6.63E−07	2.21E−06	2.70E−04	1.25E−04
			96	4.36E−12	1.45E−11	1.77E−09	8.23E−10
			120	1.11E−14	3.69E−14	4.50E−12	2.09E−12
			168	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maximum	3	2.03E+00	6.76E+00	8.25E+02	3.83E+02
			12	6.54E−01	2.18E+00	2.66E+02	1.23E+02
			24	1.44E−01	4.81E−01	5.88E+01	2.73E+01
			48	7.05E−03	2.35E−02	2.87E+00	1.33E+00
			96	1.68E−05	5.61E−05	6.84E−03	3.17E−03
			120	8.21E−07	2.74E−06	3.34E−04	1.55E−04
			168	1.96E−09	6.53E−09	7.97E−07	3.69E−07
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00

* The dose estimates for Tc-99m labeled white blood cells are actually the dose estimates for Tc-99m pertechnetate, as it was assumed that activity released in breast milk from this product would be in the form of pertechnetate.

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
Tc-99m RBC In Vitro Labeling	20	minimum	3	3.53E−03	1.76E−02	1.10E+00	4.83E−01
			12	1.58E−03	7.92E−03	4.93E−01	2.17E−01
			24	5.46E−04	2.73E−03	1.70E−01	7.47E−02
			48	6.47E−05	3.24E−04	2.01E−02	8.86E−03
			96	9.10E−07	4.55E−06	2.83E−04	1.25E−04
			120	1.08E−07	5.39E−07	3.35E−05	1.48E−05
			168	1.52E−09	7.58E−09	4.71E−07	2.08E−07
			336	4.95E−16	2.48E−15	1.54E−13	6.78E−14
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	6.06E−03	3.03E−02	1.88E+00	8.30E−01
			12	3.03E−03	1.52E−02	9.42E−01	4.15E−01
			24	1.20E−03	6.01E−03	3.74E−01	1.65E−01
			48	1.90E−04	9.48E−04	5.89E−02	2.59E−02
			96	4.70E−06	2.35E−05	1.46E−03	6.44E−04
			120	7.41E−07	3.71E−06	2.30E−04	1.01E−04
			168	1.84E−08	9.20E−08	5.72E−06	2.52E−06
			336	4.43E−14	2.22E−13	1.38E−11	6.07E−12
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Tc-99m RBC In Vivo Labeling	20	minimum	3	9.49E−04	4.75E−03	2.88E−01	1.30E−01
			12	3.79E−04	1.90E−03	1.15E−01	5.19E−02
			24	1.12E−04	5.58E−04	3.39E−02	1.53E−02
			48	9.67E−06	4.84E−05	2.94E−03	1.32E−03
			96	7.26E−08	3.63E−07	2.20E−05	9.94E−06
			120	6.29E−09	3.15E−08	1.91E−06	8.62E−07
			168	4.73E−11	2.36E−10	1.43E−08	6.47E−09
			336	4.57E−19	2.28E−18	1.39E−16	6.25E−17
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	4.38E−01	2.19E+00	1.33E+02	5.99E+01
			12	1.80E−01	8.98E−01	5.45E+01	2.46E+01
			24	5.48E−02	2.74E−01	1.66E+01	7.50E+00
			48	5.09E−03	2.54E−02	1.54E+00	6.96E−01
			96	4.39E−05	2.20E−04	1.33E−02	6.01E−03
			120	4.08E−06	2.04E−05	1.24E−03	5.59E−04
			168	3.52E−08	1.76E−07	1.07E−05	4.82E−06
			336	1.47E−15	7.33E−15	4.45E−13	2.01E−13
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
Tc-99m O_4 (Pertechnetate)	30	minimum	3	4.78E−02	1.59E−01	1.95E+01	9.02E+00
			12	5.10E−03	1.70E−02	2.08E+00	9.63E−01
			24	2.58E−04	8.61E−04	1.05E−01	4.88E−02
			48	6.63E−07	2.21E−06	2.70E−04	1.25E−04
			96	4.36E−12	1.45E−11	1.77E−09	8.23E−10
			120	1.11E−14	3.69E−14	4.50E−12	2.09E−12
			168	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	2.03E+00	6.76E+00	8.25E+02	3.83E+02
			12	6.54E−01	2.18E+00	2.66E+02	1.23E+02
			24	1.44E−01	4.81E−01	5.88E+01	2.73E+01
			48	7.05E−03	2.35E−02	2.87E+00	1.33E+00
			96	1.68E−05	5.61E−05	6.84E−03	3.17E−03
			120	8.21E−07	2.74E−06	3.34E−04	1.55E−04
			168	1.96E−09	6.53E−09	7.97E−07	3.69E−07
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Tc-99m PYP	20	minimum	3	1.73E−02	8.66E−02	4.81E+00	2.05E+00
			12	2.92E−03	1.46E−02	8.10E−01	3.46E−01
			24	2.72E−04	1.36E−03	7.55E−02	3.22E−02
			48	2.36E−06	1.18E−05	6.54E−04	2.79E−04
			96	1.77E−10	8.87E−10	4.92E−08	2.10E−08
			120	1.54E−12	7.70E−12	4.27E−10	1.82E−10
			168	8.05E−17	4.02E−16	2.23E−14	9.53E−15
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmumum	3	8.73E−02	4.37E−01	2.42E+01	1.03E+01
			12	3.49E−02	1.74E−01	9.68E+00	4.13E+00
			24	1.03E−02	5.14E−02	2.85E+00	1.22E+00
			48	8.90E−04	4.45E−03	2.47E−01	1.05E−01
			96	6.68E−06	3.34E−05	1.85E−03	7.91E−04
			120	5.79E−07	2.90E−06	1.61E−04	6.86E−05
			168	4.35E−09	2.17E−08	1.21E−06	5.15E−07
			336	4.20E−17	2.10E−16	1.17E−14	4.97E−15
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
Tc-99m MDP	20	minimum	3	8.94E−03	4.47E−02	3.64E+00	1.39E+00
			12	1.51E−03	7.53E−03	6.13E−01	2.34E−01
			24	1.40E−04	7.02E−04	5.71E−02	2.18E−02
			48	1.22E−06	6.09E−06	4.95E−04	1.89E−04
			96	9.16E−11	4.58E−10	3.73E−08	1.42E−08
			120	7.94E−13	3.97E−12	3.23E−10	1.23E−10
			168	4.15E−17	2.08E−16	1.69E−14	6.45E−15
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	1.20E−02	5.98E−02	4.87E+00	1.86E+00
			12	3.53E−03	1.76E−02	1.44E+00	5.48E−01
			24	6.92E−04	3.46E−03	2.82E−01	1.08E−01
			48	2.67E−05	1.33E−04	1.09E−02	4.14E−03
			96	3.96E−08	1.98E−07	1.61E−05	6.15E−06
			120	1.52E−09	7.62E−09	6.20E−07	2.37E−07
			168	2.26E−12	1.13E−11	9.20E−10	3.51E−10
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Tc-99m MIBI	30	minimum	3	2.23E−03	7.44E−03	1.16E+00	5.37E−01
			12	5.59E−04	1.86E−03	2.90E−01	1.34E−01
			24	8.83E−05	2.94E−04	4.57E−02	2.12E−02
			48	2.20E−06	7.34E−06	1.14E−03	5.30E−04
			96	1.37E−09	4.56E−09	7.09E−07	3.29E−07
			120	3.41E−11	1.14E−10	1.77E−08	8.21E−09
			168	2.12E−14	7.08E−14	1.10E−11	5.11E−12
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	1.97E−02	6.56E−02	1.02E+01	4.73E+00
			12	7.76E−03	2.59E−02	4.02E+00	1.87E+00
			24	2.24E−03	7.47E−03	1.16E+00	5.39E−01
			48	1.87E−04	6.24E−04	9.70E−02	4.51E−02
			96	1.31E−06	4.36E−06	6.77E−04	3.14E−04
			120	1.09E−07	3.64E−07	5.66E−05	2.63E−05
			168	7.62E−10	2.54E−09	3.95E−07	1.83E−07
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
Tc-99m MAA	4	minimum	3	6.66E−03	1.66E−01	4.19E+00	1.70E+00
			12	7.11E−04	1.78E−02	4.47E−01	1.81E−01
			24	3.60E−05	9.00E−04	2.26E−02	9.19E−03
			48	9.23E−08	2.31E−06	5.81E−05	2.36E−05
			96	6.07E−13	1.52E−11	3.82E−10	1.55E−10
			120	1.54E−15	3.85E−14	9.69E−13	3.93E−13
			168	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	4.78E−01	1.19E+01	3.01E+02	1.22E+02
			12	1.47E−01	3.68E+01	9.27E+01	3.76E+01
			24	3.07E−02	7.68E−01	1.93E+01	7.84E+00
			48	1.33E−03	3.33E−02	8.38E−01	3.40E−01
			96	2.51E−06	6.28E−05	1.58E−03	6.41E−04
			120	1.09E−07	2.73E−06	6.86E−05	2.78E−05
			168	2.06E−10	5.14E−09	1.29E−07	5.25E−08
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Tc-99m MAG3	10	minimum	3	1.29E−03	1.29E−02	1.52E−01	6.66E−02
			12	1.74E−04	1.74E−03	2.07E−02	9.04E−03
			24	1.22E−05	1.22E−04	1.44E−03	6.30E−04
			48	5.92E−08	5.92E−07	7.00E−06	3.06E−06
			96	1.40E−12	1.40E−11	1.66E−10	7.25E−11
			120	6.80E−15	6.80E−14	8.05E−13	3.52E−13
			168	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	2.39E−02	2.39E−01	2.83E+00	1.24E+00
			12	6.88E−03	6.88E−02	8.15E−01	3.56E−01
			24	1.31E−03	1.31E−02	1.55E−01	6.77E−02
			48	4.72E−05	4.72E−04	5.58E−03	2.44E−03
			96	6.14E−08	6.14E−07	7.27E−06	3.18E−06
			120	2.22E−09	2.22E−08	2.62E−07	1.15E−07
			168	2.89E−12	2.89E−11	3.42E−10	1.50E−10
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested		Effective Dose Equivalent (mrem)	
				(mCi)	(%)	Newborn	1-Yr-Old
Tc-99m Glucoheptonate	20	minimum	3	1.48E−02	7.41E−02	2.30E+00	5.38E+00
			12	2.63E−03	1.31E−02	4.08E−01	9.52E−01
			24	2.61E−04	1.31E−03	4.06E−02	9.48E−02
			48	2.59E−06	1.29E−05	4.02E−04	9.38E−04
			96	2.53E−10	1.27E−09	3.94E−08	9.19E−08
			120	2.51E−12	1.25E−11	3.90E−10	9.10E−10
			168	2.21E−16	1.11E−15	3.44E−14	8.03E−14
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	3.02E−02	1.51E−01	4.70E+00	1.10E+01
			12	6.37E−03	3.19E−02	9.90E−01	2.31E+00
			24	7.99E−04	3.99E−03	1.24E−01	2.90E−01
			48	1.25E−05	6.27E−05	1.95E−03	4.55E−03
			96	3.10E−09	1.55E−08	4.81E−07	1.12E−06
			120	4.87E−11	2.43E−10	7.56E−09	1.76E−08
			168	1.19E−14	5.97E−14	1.86E−12	4.33E−12
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Tc-99m HAM	8	minimum	3	3.60E−02	4.50E−01	2.00E+01	8.13E+00
			12	4.51E−03	5.64E−02	2.50E+00	1.02E+00
			24	2.83E−04	3.54E−03	1.57E−01	6.38E−02
			48	1.11E−06	1.39E−05	6.17E−04	2.51E−04
			96	1.72E−11	2.14E−10	9.52E−09	3.87E−09
			120	6.73E−14	8.42E−13	3.74E−11	1.52E−11
			168	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	8.95E−02	1.12E+00	4.97E+01	2.02E+01
			12	3.67E−02	4.59E−01	2.04E+01	8.29E+00
			24	1.12E−02	1.40E−01	6.21E+00	2.53E+00
			48	1.04E−03	1.30E−02	5.77E−01	2.35E−01
			96	8.98E−06	1.12E−04	4.98E−03	2.03E−03
			120	8.35E−07	1.04E−05	4.63E−04	1.88E−04
			168	7.21E−09	9.01E−08	4.00E−06	1.63E−06
			336	3.00E−16	3.75E−15	1.66E−13	6.76E−14
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
Tc-99m DTPA	20	minimum	3	2.57E−03	1.29E−02	3.23E−01	1.43E−01
			12	3.49E−04	1.74E−03	4.39E−02	1.94E−02
			24	2.43E−05	1.22E−04	3.06E−03	1.35E−03
			48	1.18E−07	5.92E−07	1.49E−05	6.57E−06
			96	2.80E−12	1.40E−11	3.52E−10	1.55E−10
			120	1.36E−14	6.80E−14	1.71E−12	7.55E−13
			168	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maximum	3	4.78E−02	2.39E−01	6.02E+00	2.65E+00
			12	1.38E−02	6.88E−02	1.73E+00	7.64E−01
			24	2.61E−03	1.31E−02	3.29E−01	1.45E−01
			48	9.43E−05	4.72E−04	1.19E−02	5.24E−03
			96	1.23E−07	6.14E−07	1.55E−05	6.82E−06
			120	4.43E−09	2.22E−08	5.58E−07	2.46E−07
			168	5.77E−12	2.89E−11	7.26E−10	3.23E−10
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Tc-99m DTPA Aerosol	1	minimum	3	5.14E−05	5.14E−03	1.43E−02	6.09E−03
			12	6.98E−06	6.98E−04	1.94E−03	8.26E−04
			24	4.87E−07	4.87E−05	1.35E−04	5.76E−05
			48	2.37E−09	2.37E−07	6.57E−07	2.80E−07
			96	5.60E−14	5.60E−12	1.55E−11	6.63E−12
			120	2.72E−16	2.72E−14	7.55E−14	3.22E−14
			168	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maximum	3	9.93E−04	9.93E−02	2.76E−01	1.18E−01
			12	2.86E−04	2.86E−03	7.93E−02	3.38E−02
			24	5.43E−05	5.43E−03	1.51E−02	6.43E−03
			48	1.96E−06	1.96E−04	5.44E−04	2.32E−04
			96	2.55E−09	2.55E−07	7.08E−07	3.02E−07
			120	9.21E−11	9.21E−09	2.56E−08	1.09E−08
			168	1.20E−13	1.20E−11	3.33E−11	1.42E−11
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
In-111 White Blood Cells	0.5	minimum	3	6.21E−04	1.24E−01	2.04E+01	8.04E+00
			12	5.77E−04	1.15E−01	1.90E+01	7.47E+00
			24	5.23E−04	1.05E−01	1.72E+01	6.77E+00
			48	4.30E−04	8.60E−02	1.42E+01	5.57E+00
			96	2.91E−04	5.82E−02	9.58E+00	3.77E+00
			120	2.39E−04	4.78E−02	7.88E+00	3.10E+00
			168	1.62E−04	3.23E−02	5.32E+00	2.09E+00
			336	4.11E−05	8.22E−03	1.35E+00	5.32E−01
			672	2.66E−06	5.31E−04	8.75E−02	3.44E−02
		maximum	3	3.10E−03	6.19E−01	1.02E+02	4.01E+01
			12	2.96E−03	5.92E−01	9.75E+01	3.83E+01
			24	2.79E−03	5.58E−01	9.19E+01	3.61E+01
			48	2.48E−03	4.95E−01	8.16E+01	3.21E+01
			96	1.95E−03	3.91E−01	6.43E+01	2.53E+01
			120	1.73E−03	3.47E−01	5.71E+01	2.25E+01
			168	1.37E−03	2.74E−01	4.50E+01	1.77E+01
			336	5.95E−04	1.19E−01	1.96E+01	7.71E+00
			672	1.13E−04	2.26E−02	3.72E+00	1.46E+00
Tc-99m DISIDA	8	minimum	3	5.64E−03	7.05E−02	4.80E+00	2.30E+00
			12	1.07E−03	1.34E−02	9.12E−01	4.36E−01
			24	1.17E−04	1.46E−03	9.95E−02	4.76E−02
			48	1.39E−06	1.74E−05	1.18E−03	5.67E−04
			96	1.97E−10	2.47E−09	1.68E−07	8.03E−08
			120	2.35E−12	2.94E−11	2.00E−09	9.57E−10
			168	3.21E−16	4.02E−15	2.73E−13	1.31E−13
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maximum	3	2.25E−02	2.82E−01	1.92E+01	9.17E+00
			12	1.13E−02	1.42E−01	9.66E+00	4.62E+00
			24	4.55E−03	5.69E−02	3.87E+00	1.85E+00
			48	7.32E−04	9.15E−03	6.23E−01	2.98E−01
			96	1.89E−05	2.36E−04	1.61E−02	7.70E−03
			120	3.04E−06	3.80E−05	2.59E−03	1.24E−03
			168	7.86E−08	9.83E−07	6.69E−05	3.20E−05
			336	2.18E−13	2.73E−12	1.86E−10	8.89E−11
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
I-131 OIH	0.3	minimum	3	2.62E−03	8.73E−01	2.91E+00	1.16E+00
			12	1.49E−04	4.96E−02	1.65E−01	6.61E−02
			24	3.26E−06	1.09E−03	3.61E−03	1.45E−03
			48	1.56E−09	5.19E−07	1.73E−06	6.91E−07
			96	3.48E−16	1.16E−13	3.86E−13	1.54E−13
			120	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			168	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	1.50E−02	4.99E+00	1.66E+01	6.65E+00
			12	5.13E−03	1.71E+00	5.69E−00	2.29E+00
			24	1.23E−03	4.09E−01	1.36E−00	5.45E−01
			48	7.05E−05	2.35E−02	7.82E−02	3.13E−02
			96	2.32E−07	7.73E−05	2.58E−04	1.03E−04
			120	1.33E−08	4.44E−06	1.48E−05	5.91E−06
			168	4.38E−11	1.46E−08	4.86E−08	1.95E−08
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
I-131 Sodium Iodide (NaI)	150	minimum	3	1.06E+00	7.07E−01	2.08E+07*	1.53E+07*
			12	4.52E−01	3.01E−01	8.86E+06*	6.52E+06*
			24	1.45E−01	9.66E−02	2.84E+06*	2.09E+06*
			48	1.49E−02	9.94E−03	2.92E+05*	2.15E+05*
			96	1.58E−04	1.05E−04	3.10E+03*	2.28E+03*
			120	1.62E−05	1.08E−05	3.18E+02*	2.33E+02*
			168	1.71E−07	1.14E−07	3.35E+00*	2.47E+00*
			336	1.92E−14	1.28E−14	3.76E−07*	2.77E−07*
			672	0.00E+00	0.00E+00	0.00E+00*	0.00E+00*
		maxmimum**	3	7.50E+01	5.00E+01	1.47E+09*	1.08E+09*
			12	7.50E+01	5.00E+01	1.47E+09*	1.08E+09*
			24	7.50E+01	5.00E+01	1.47E+09*	1.08E+09*
			48	7.50E+01	5.00E+01	1.47E+09*	1.08E+09*
			96	7.50E+01	5.00E+01	1.47E+09*	1.08E+09*
			120	7.50E+01	5.00E+01	1.47E+09*	1.08E+09*
			168	7.06E+01	5.00E+01	1.47E+09*	1.08E+09*
			336	1.88E+01	1.25E+01	3.69E+08*	2.71E+08*
			672	7.68E−01	5.12E−01	1.51E+07*	1.11E+07*

* Dose to the infant thyroid, mrad.

** The values under Total Activity Ingested and Effective Dose Equivalent for interruption times 3 to 168 hours show no change with time because the total fraction of administered activity excreted in the breast milk exceeded the upper limit (or cap) of 0.50 (see B.1 CALCULATIONAL METHOD).

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radiopharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
I-123 NaI	0.4	minimum	3	1.03E−02	2.58E+00	6.11E+01	4.20E+01
			12	3.53E−03	8.83E−01	2.09E+01	1.44E+01
			24	8.45E−04	2.11E−01	5.00E+00	3.44E+00
			48	4.84E−05	1.21E−02	2.87E 01	1.97E−01
			96	1.59E−07	3.98E−05	9.42E−04	6.48E−04
			120	9.12E−09	2.28E−06	5.40E−05	3.71E−05
			168	3.00E−11	7.49E−09	1.77E−07	1.22E−07
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	1.08E−02	2.70E+00	6.40E+01	4.40E+01
			12	3.70E−03	9.25E−01	2.19E+01	1.51E+01
			24	8.86E−04	2.22E−01	5.25E+00	3.61E+00
			48	5.08E−05	1.27E−02	3.01E−01	2.07E−01
			96	1.67E−07	4.17E−05	9.88E−04	6.79E−04
			120	9.56E−09	2.39E−06	5.66E−05	3.89E−05
			168	3.14E−11	7.85E−09	1.86E−07	1.28E−07
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
I-125 OIH	0.01	minimum	3	2.52E−04	2.52E+00	2.24E−01	9.04E−02
			12	6.84E−05	6.84E−01	6.07E−02	2.45E−02
			24	1.20E−05	1.20E−01	1.07E−02	4.31E−03
			48	3.72E−07	3.72E−03	3.30E−04	1.33E−04
			96	3.55E−10	3.55E−06	3.15E−07	1.27E−07
			120	1.10E−11	1.10E−07	9.75E−09	3.94E−09
			168	1.05E−14	1.05E−10	9.32E−12	3.77E−12
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	2.52E−04	2.52E+00	2.24E−01	9.04E−02
			12	6.84E−05	6.84E−01	6.07E−02	2.54E−02
			24	1.20E−05	1.20E−01	1.07E−02	4.31E−03
			48	3.72E−07	3.72E−03	3.30E−04	1.33E−04
			96	3.55E−10	3.55E−06	3.15E−07	1.27E−07
			120	1.10E−11	1.10E−07	9.75E−09	3.94E−09
			168	1.05E−14	1.05E−10	9.32E−12	3.77E−12
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules (Continued)

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
I-123 mIBG	10	minimum	3	5.41E−02	5.41E−01	3.20E+02	2.20E+02
			12	3.13E−02	3.13E−01	1.86E+02	1.28E+02
			24	1.51E−02	1.51E−01	8.96E+01	6.16E+01
			48	3.53E−03	3.53E−02	2.09E+01	1.44E−01
			96	1.92E−04	1.92E−03	1.14E+00	7.82E−01
			120	4.48E−05	4.48E−04	2.65E−01	1.82E−01
			168	2.44E−06	2.44E−05	1.44E−02	9.92E−03
			336	9.15E−11	9.15E−10	5.42E−07	3.73E−07
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maximum	3	5.41E−02	5.41E−01	3.20E+02	2.20E+02
			12	3.13E−02	3.13E−01	1.86E+02	1.28E+02
			24	1.51E−02	1.51E−01	8.96E+01	6.16E+01
			48	3.53E−03	3.53E−02	2.09E+01	1.44E−01
			96	1.92E−04	1.92E−03	1.14E+00	7.82E−01
			120	4.48E−05	4.48E−04	2.65E−01	1.82E−01
			168	2.44E−06	2.44E−05	1.44E−02	9.92E−03
			336	9.15E−11	9.15E−10	5.42E−07	3.73E−07
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
I-123 OIH	2	minimum	3	1.63E−02	8.13E−01	3.85E+00	1.62E+00
			12	2.76E−03	1.38E−01	6.54E−01	2.76E−01
			24	2.60E−04	1.30E−02	6.16E−02	2.60E−02
			48	2.31E−06	1.15E−04	5.47E−04	2.31E−04
			96	1.82E−10	9.08E−09	4.30E−08	1.82E−08
			120	1.61E−12	8.06E−11	3.82E−10	1.61E−10
			168	8.79E−17	4.40E−15	2.08E−14	8.78E−15
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maximum	3	1.24E−01	6.18E+00	2.93E+01	1.24E+01
			12	4.18E−02	2.09E+00	9.91E+00	4.18E+00
			24	9.86E−03	4.93E−01	2.33E+00	9.85E−01
			48	5.48E−04	2.74E−02	1.30E−01	5.47E−02
			96	1.69E−06	8.45E−05	4.00E−04	1.69E−04
			120	9.38E−08	4.69E−06	2.22E−05	9.37E−06
			168	2.89E−10	1.45E−08	6.85E−08	2.89E−08
			336	0.00E+00	0.00E+00	0.00E+00	0.00E+00
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00

Table B.4 Total Activity Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk Under Different Interruption Schedules

Radio-pharmaceutical	Administered Activity (mCi)	Concentration	Interruption Time (hr)	Total Activity Ingested (mCi)	Total Activity Ingested (%)	Effective Dose Equivalent (mrem) Newborn	Effective Dose Equivalent (mrem) 1-Yr-Old
Cr-51 EDTA	0.05	minimum	3	7.71E−06	1.54E−02	8.85E−04	3.71E−04
			12	3.14E−06	6.27E−03	3.60E−04	1.51E−04
			24	9.44E−07	1.89E−03	1.08E−04	4.54E−05
			48	8.55E−08	1.71E−04	9.81E−06	4.11E−06
			96	7.02E−10	1.40E−06	8.06E−08	3.38E−08
			120	6.37E−11	1.27E−07	7.30E−09	3.06E−09
			168	5.23E−13	1.05E−09	6.00E−11	2.51E−11
			336	1.56E−20	3.12E−17	1.79E−18	7.50E−19
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
		maxmimum	3	3.37E−05	6.75E−02	3.87E−03	1.62E−03
			12	1.37E−05	2.74E−02	1.57E−03	6.60E−04
			24	4.13E−06	8.26E−03	4.74E−04	1.99E−04
			48	3.74E−07	7.48E−04	4.29E−05	1.80E−05
			96	3.07E−09	6.15E−06	3.53E−07	1.48E−07
			120	2.79E−10	5.57E−07	3.19E−08	1.34E−08
			168	2.29E−12	4.58E−09	2.62E−10	1.10E−10
			336	6.82E−20	1.36E−16	7.82E−18	3.28E−18
			672	0.00E+00	0.00E+00	0.00E+00	0.00E+00
Ga-67 Citrate	5	minimum	3	4.09E−02	8.17E−01	2.72E+02	1.04E+02
			12	2.76E−02	5.52E−01	1.84E+02	7.05E+01
			24	1.64E−02	3.28E−01	1.09E+02	4.18E+01
			48	5.77E−03	1.15E−01	3.84E+01	1.47E+01
			96	7.14E−04	1.43E−02	4.76E+00	1.82E+00
			120	2.51E−04	5.03E−03	1.67E+00	6.42E−01
			168	3.11E−05	6.23E−04	2.07E−01	7.95E−02
			336	2.08E−08	4.17E−07	1.39E−04	5.32E−05
			672	9.27E−15	1.85E−13	6.17E−11	2.37E−11
		maxmimum	3	1.99E+00	3.98E+01	1.33E+04	5.08E+03
			12	1.81E+00	3.62E+01	1.20E+04	4.62E+03
			24	1.59E+00	3.18E+01	1.06E+04	4.06E+03
			48	1.23E+00	2.47E+01	8.21E+03	3.15E+03
			96	7.40E−01	1.48E+01	4.93E+03	1.89E+03
			120	5.73E−01	1.15E+01	3.82E+03	1.46E+03
			168	3.44E−01	6.88E+00	2.29E+03	8.78E+02
			336	5.76E−02	1.15E+00	3.83E+02	1.47E+02
			672	1.61E−03	3.23E−02	1.07E+01	4.12E+00

Table B.3 Biological and Physical Parameters Used to Calculate the Total Activty Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk (Contiuned)

Radiopharmaceutical	Administered Activity (mCi)	Excretion Fraction[1]		Biological Half-Life for Excretion[2]	
		Lowest α_1	Highest α_2	Shortest T_{b1} (hr)	Longest T_{b2} (hr)
Cr-51 EDTA	0.05	3.2E-7	1.4E-6	7	7
Tc-99m Sulfur Colloid	12	2.8E-6	2.6E-5	35	(8.3)
Tc-99m White Blood Cells	30	6.7E-6	1.7E-4	5.2	66
Tl-201 Chloride	3	1.7E-6	2.2E-6	13	43
		9.5E-7	1.9E-7	43	(362)

[1] "Lowest" and "Highest" in this table refer to the lowest and highest concentration observed at peak for a given radiopharmaceutical by any author (see Table B.2 for references). These are combined with the shortest and longest biological half-lives for that radiopharmaceutical reported by any author. A given concentration and half-life combined to produce a supposedly best case or worst case scenario did *not* necessarily come from the same study.

[2] For some radiopharmacueticals, T_{b1} and/or T_{b2} may be negative (i.e., values shown in parentheses) because these were the unusual cases reported in the literature in which the the effective half-life was greater than the radionuclide's physical half-life (i.e., effective half-life > T_p indicates continued activity accumulation). In these cases, the effective half-life was used to perform the analysis.

Table B.3 Biological and Physical Parameters Used to Calculate the Total Activty Ingested and Internal Radiation Doses Received from the Intake of Radiopharmaceuticals in Breast Milk

Radiopharmaceutical	Administered Activity (mCi)	Excretion Fraction[1]		Biological Half-Life for Excretion[2]	
		Lowest α_1	Highest α_2	Shortest T_{b1} (hr)	Longest T_{b2} (hr)
Cr-51 EDTA	0.05	3.2E-7	1.4E-6	7	7
Ga-67 Citrate	5	8.0E-6	1.0E-4	20	390
I-123 mIBG	10	7.2E-6	7.2E-6	85	85
I-123 OIH	2	2.9E-5	1.5E-4	4.8	10.2
I-123 Sodium Iodide (NaI)	0.4	6.2E-5	6.5E-5	10.4	10.4
I-125 OIH	0.01	7.1E-5	7.1E-5	4.8	4.8
I-131 OIH	0.3	4.3E-5	1.2E-4	2.2	8.0
I-131 Sodium Iodide (NaI)	150	1.4E-5	6.7E-4	7.6	117
In-111 White Blood Cells	0.5	2.4E-7	7.3E-7	(85)	(140)
Tc-99m DISIDA	8	2.4E-6	4.6E-6	10	(9.1)
Tc-99m DTPA	20	5.0E-7	6.5E-6	6.5	30
Tc-99m DTPA Aerosol	1	2.0E-7	2.7E-6	6.5	30
Tc-99m Glucoheptonate	20	2.6E-6	4.9E-6	9	12
Tc-99m HAM	8	1.8E-5	2.3E-5	6	(7)
Tc-99m MAA	4	7.0E-6	3.1E-4	5.2	45
Tc-99m MAG3	10	5.0E-7	6.5E-6	6.5	30
Tc-99m MDP	20	1.6E-6	1.6E-6	8.4	34
Tc-99m MIBI	30	2.2E-7	1.4E-6	18	(6.7)
Tc-99m O_4 (Pertechnetate)	30	6.7E-6	1.7E-4	5.2	66
Tc-99m PYP	20	3.1E-6	9.2E-6	8.4	(6.8)
Tc-99m RBC - In Vitro Labeling	20	3.3E-7	5.0E-7	(7.8)	(9)
Tc-99m RBC - In Vivo Labeling	20	1.0E-7	4.5E-5	(6.8)	(7)

Table B.2 Excretion Fractions and Biological Half-Lives for Radiopharmaceuticals Excreted in Breast Milk (Continued)

Radiopharmaceutical	Measured Excretion Fractions*	Biological Half-Life for Excretion T_b (hr)	Reference
Tc-99m RBC - In Vivo Labeling	6.0E-3§§ - 1.0E-2§§	(7.7)††	RO90
	4.5E-5 (8)	(6.8)††	RO90
	~1.0E-7 (~4)	(7)††	AH85
Tc-99m Sulphur Colloid	1.6E-3§§ - 1.5E-2§§	35-(8.3)††	RU94
Tc-99m White Blood Cells	Treated as Tc-99m pertechnetate, as fraction of free Tc-99m is highly variable.		
Tl-201 Chloride	2.2E-6	43	MU89 (2 compartment model)
	1.9E-7	(362)††	
	1.7E-6	13	JO95 (2 compartment model)
	9.5E-7	164	
Xe-133 Gas	Insignificant Dose to the breast-feeding infant.		

* Peak fraction per milliliter of milk. All values corrected to the time of activity administration. The number in parenthesis is the time (hr) at which this maximum was observed. If data from more than one patient are reported, data are presented as a range.

** Pooled data from 4 patients.

† Patient admitted for study of enlarged thyroid.

‡ Conservative value chosen due to anecdotal report (n=1) (see addendum of MO84).

§ Data in Table 1 of RU91 recalculated due to possible errors in derived values for the percent excreted in milk.

§§ Total fraction excreted - milk concentrations not given.

†† Effective half-life > T_p indicates continued activity accumulation.

* Speciation tests indicated that the activity excreted was most likely in the form of NaI, not mIBG.

Table B.2 Excretion Fractions and Biological Half-Lives for Radiopharmaceuticals Excreted in Breast Milk (Continued)

Radiopharmaceutical	Measured Excretion Fractions* α	Biological Half-Life for Excretion T_b (hr)	Reference
Tc-99m DTPA	7.2E-7 (2.2)	15	MO84‡
	6.0E-7 (2.8)	15	MO85
	5.0E-4§§ - 2.4E-3§§	6.5-30	RU94
	~5.0E-7 (~3)	9.6	AH85
Tc-99m DTPA Aerosol	Fraction of administered aerosol assumed to reach bloodstream (0.406) treated as Tc-99m DTPA.		
Tc-99m Glucoheptonate	1.4E-3§§	9.0	RU94
	2.6E-6	12	MO87
Tc-99m HAM	8.8E-3§§ - 1.1E-2§§	6.0-(7.0)††	RU94
Tc-99m MAA	1.4E-4 (2.2)	20	MO84
	7.1E-6 (5) - 3.1E-4 (7)	5.2-45	MA81
	2.4E-5 (4)	5.3	BE73
	1.4E-4 (3.5)	12**	CR85
	7.0E-6 (6)	~12	HE79
	4.0E-3§§ - 5.2E-2§§	7.3-18	AH85
Tc-99m MAG3	Treated as Tc-99m DTPA (renal agent for which data exist).		
Tc-99m MDP/HDP	~1.6E-6 (~4)	8.4-34	AH85
Tc-99m MIBI	1.4E-6 (3.3)	23	RU91§
	1.0E-4§§ - 3.0E-4§§	18-(6.7)††	RU94
Tc-99m O_4 (Pertechnetate)	~6.7E-6 (8.5)		RU78
	2.6E-5 (10) - 6.4E-5 (2)	9-66	WY73
	1.4E-4 (22)	20	VA71
	~1.3E-5 (3)		PI79
	7.19E-3 (2.4) - 1.7E-2 (2)		OG83†
	~5.0E-4 (~5)	6.9	AH85
	1.7E-4 (8.2)	6	MO87
	1.4E-4 (~3)	5.2	HE86
Tc-99m PYP	1.5E-3§§ - 4.4E-3§§	8.4-(6.8)††	RU94
Tc-99m RBC - In Vitro Labeling	2.0E-4§§ - 3.0E-4§§	(7.8-9.0)††	RU94

Table B.2 Excretion Fractions and Biological Half-Lives for Radiopharmaceuticals Excreted in Breast Milk

Radiopharmaceutical	Measured Excretion Fractions* α	Biological Half-Life for Excretion T_b (hr)	Reference
Cr-51 EDTA	1.5E-4§§ - 6.5E-4§§	5.0-7.0	AH85
Ga-67 Citrate	9.5E-5 (72)	216	TO76
	2.7E-5 (38) - 3.7E-5 (58)	82-385	RU94
	5.6E-5 (96)		LA71
	1.0E-4 (88)		GR83
	4.3E-5 (48)		WE94
	3.16E-2§§ - 9.9E-2§§	20-390	RU94
I-123 mIBG*	7.2E-6 (8)	85	KE94
I-123 OIH	6.0E-5	4.8	MO89b
	1.2E-02§§ - 3.5E-2§§	8.1-10.2	RO90
	1.5E-4 (4)	8.3	RO90
I-123 Sodiun Iodide (NaI)	2.6E-2§§	10.4	HE86
	6.5E-5	10.4	HE86
I-125 OIH	2.4E-2§§	4.8	AH85
I-131 OIH	1.8E-2§§ - 4.9E-2§§	2.2-6.0	AH85
I-131 Sodiun Iodide (NaI)	1.4E-5 (24) - 4.0E-5 (6)	~9.9	NU52
	6.7E-4 (6)		WE60
	6.6E-4	12	DY88 (2 comp
	1.6E-5	526	model)
	3.0E-2 (18)	~9.4	RU88
	~5.0E-4	13	RO94 (diag.)
		11	RO94 (ther.
		235	2 comp model)
	2.3E-1§§	117	RU94
	2.5E-1§§ - 4.6E-1§§	7.6-12	MO89a
In-111 White Blood Cells	3.3E-7 (13)	(85.3)††	MO85
	7.3E-7 (16)	(140)††	HE88
	2.4E-7 (20)		BU86
Tc-99m DISIDA	1.0E-3§§ - 2.8E-3§§	10-(9.1)††	RU94

Table B.1 Effective Dose Equivalents to Newborns and One-Year-Olds from Infant's Intake of Radiopharmaceuticals

Radiopharmaceutical	Effective Dose Equivalent[1] (rem/mCi)	
	Newborn	One-Year-Old
Cr-51 EDTA	0.11	0.048
Ga-67 Citrate	6.7	2.6
I-123 mIBG[2]	5.9	4.1
I-123 OIH	0.24	0.10
I-123 Sodium Iodide (NaI)	5.9	4.1
I-125 OIH	0.89	0.36
I-131 OIH	1.1	0.44
I-131 Sodium Iodide (NaI)	20,000[3]	14,000[3]
In-111 White Blood Cells	33	13
Tc-99m DISIDA	0.85	0.41
Tc-99m DTPA	0.13	0.056
Tc-99m DTPA Aerosol	0.28	0.12
Tc-99m Glucoheptonate	0.16	0.36
Tc-99m HAM	0.56	0.23
Tc-99m MAA	0.63	0.26
Tc-99m MAG3	0.12	0.052
Tc-99m MDP	0.41	0.16
Tc-99m MIBI	0.52	0.24
Tc-99m O_4 (Pertechnetate)	0.41	0.19
Tc-99m PYP	0.28	0.12
Tc-99m RBC - In Vitro Labeling	0.31	0.14
Tc-99m RBC - In Vivo Labeling	0.30	0.14
Tc-99m Sulfur Colloid	0.74	0.36
Tc-99m White Blood Cells[4]	0.41	0.19
Tl-201 Chloride	15	8.5

[1] Effective dose equivalent to the infant per unit activity administerted intravenously to the infant (except in the case of Tc-99m DTPA Aerosol).

[2] Specification tests indicated that the activity was most likely in the form of NaI, not mIBG.

[3] Dose to the infant's thyroid per unit activity administered intravenously (or orally) to the infant (rad/mCi).

[4] The values shown are actually the dose estimates for Tc-99m pertechnetate, as it was assumed that activity released in breast milk from this product would be in the form of pertechnetate.

reference. Most papers reported an effective half-life for excretion of radiopharmaceuticals in breast milk and these values were converted to biological half-lives. Several values of the reported effective half-life for excretion were larger than the physical half-life of the radionuclide (e.g., T_{eff} = 9 hours for Technetium-99m RBCs (RU94)) indicating continued accumulation in the breast milk of the radiopharmaceutical over time. These values are denoted in the table in *parentheses*. Several publications reported cumulative excretion fractions (denoted by the symbol §§) and these values were used to estimate the concentrations of the radiopharmaceutical in breast milk as described above (see Section B.1 CALCULATIONAL METHOD"). When data for a single subject were reported, the reported/derived value of excretion fraction per milliliter of breast milk was considered to be "highest", for that publication, and no "lowest" value was listed. In some cases, the breast milk peak concentration was estimated from graphical information in an article; these estimates are shown with a "~" symbol.

inson et al. (RO94) reported a concentration excretion half-life for a diagnostic dose of ne-131 sodium iodide and also reported that the same patient exhibited biphasic excretion of the iodine-131 administered in a therapeutic study. Murphy et al. (MU89) reported that thallium-201 chloride exhibited biphasic clearance. All other radiopharmaceuticals seemed to follow monophasic clearance patterns, except for two case studies involving iodine-131 sodium iodide. This radiopharmaceutical was nonetheless modeled with a monophasic clearance pattern for the purposes of this study.

Table B.3 lists the biological and physical parameters used by the computer program to calculate the total activity ingested and the internal radiation doses received from the intake of radiopharmaceuticals in breast milk for newborns and one-year-olds.

B.2.2 Radiation Dose Estimates

Table B.4 lists the dose estimates for the 25 radiopharmaceuticals analyzed, for both the newborn and the one-year-old, for both best and worst case scenarios, and for all interruption schedules. Note, that in the case of iodine-131 sodium iodide the infant *thyroid doses*, instead of effective dose equivalents, were shown, due to the high doses predicted. Table B.5 shows the summary of recommendations for the radiopharmaceuticals considered in this analysis, showing the maximum administered activities assumed, the internal dose to the infant if no interruption of breast-feeding is assumed, whether or not instructions are required, the external dose from radiation during breast-feeding assuming interruption, and the recommendation on interruption of breast-feeding (which inc., adjustment for the external dose during breast-feeding).

None of the analyses for the iodine compounds included any considerations for free iodide in the product, and none of the other analyses included considerations for possible radioactive contaminants or breakthrough products. These additional components of the dose are usually very small. In addition, the assignment of numerical values to these quantities (the fraction of free iodide, percent activity of contaminants, etc.) would be arbitrary, as these values vary considerably between products, and even with time.

uptake of ingested radiopharmaceuticals from the infant gastrointestinal (GI) tract, thus it was assumed that 100 percent of the ingested activity was quickly and completely absorbed from the infant's GI tract.

Radiation doses for newborns (3.4 kg) and one-year-olds (9.8 kg), based on the mathematical phantoms of Cristy and Eckerman (CR87) have been estimated for the radiopharmaceuticals considered in this analysis and compiled in a reference on pediatric radiation dosimetry in nuclear medicine (ST95). These dose estimates generally apply to intravenous administration of these pharmaceuticals. The dose estimates are expressed as effective dose equivalents (EDE) per unit ingested activity; a summary of the values used are given in Table B.1. (Some dose estimates, based on more recent models were supplied by the Radiation Internal Dose Information Center, Oak Ridge, TN.) Typical values of activity administered to the woman per procedure were taken from various sources, to estimate the total internal dose to the infant from a typical procedure. There are certainly cases, most notably for therapeutic administrations of iodine-131 sodium iodide, in which the effective dose equivalent should not be used for decision making, and the individual organ absorbed doses should be considered.

The computer program estimated the intake and subsequent dose to newborns and one-year-olds for both the best and worst case scenarios, for no interruption (first feeding 3 hours after administration to the woman), and for the various interruption schedules described above.

An upper limit of 0.50 was placed on the total fraction of administered activity which could be excreted over all time in the breast milk. It was possible for unrealistic values (e.g., fractions greater than 1.0) to be calculated by merely permitting the computer program to sum the product of the fraction of activity per milliliter and 125 milliliter per feeding for a large number of feedings. Thus, it was thought that an upper limit of 0.50 should be placed on this value, which represents excretion through the breast milk pathway competing equally with all other excretion pathways available. This value is also compatible with the highest fraction reported for total excretion of any radiopharmaceutical, namely a fraction of 0.33 for iodine-131 sodium iodide (M089a). This is probably a conservative upper limit in most cases. In those cases in which a literature reference gave only the cumulative fraction of activity excreted in the breast milk over the coarse of the study, the fraction of injected activity excreted per milliliter of milk at different times was not available (although a clearance half-life may have been reported). A single value of cumulative excretion could not be used in this analysis, as it most likely represented the cumulative fraction excreted assuming no interruption of breast-feeding, and therefore could not be used directly to infer the cumulative fraction under different interruption schedules. To estimate the cumulative fraction under different interruption schedules, it was necessary to calculate the time-dependent behavior of the clearance. Thus, a breast milk concentration at early times was estimated which would result in a cumulative excretion equal to the value reported assuming no interruption of breast-feeding, the clearance half-life reported by the authors, and using the nursing schedule and volume assumed in this analysis. This derived early concentration was then used in the computer program with the clearance half-life chosen to estimate the cumulative fraction ingested under different interruption schedules.

B.2 RESULTS

This analyses covers 25 of the radiopharmaceuticals most commonly used in nuclear medicine procedures involving breast-feeding women.

B.2.1 Biokinetic Data for Excretion of Radiopharmacueticals in Breast Milk

The data obtained from the literature review are summarized in Table B.2. The biokinetic data for each radiopharmaceutical excreted in breast milk are given in Table B.2 as the excretion fraction, per unit volume of breast milk, the biological half-life for excretion, time of peak concentration (when data were reported as concentration rather than cumulative excretion fraction), and the

APPENDIX B

PARAMETERS AND CALCULATIONS FOR DETERMINING INSTRUCTIONS TO BREAST-FEEDING WOMEN*

B.1 CALCULATIONAL METHOD

The breast milk concentration as a function of time $C(t)$, (i.e., the activity per milliliter of breast milk) was calculated from the equation,

$$C(t) = A \alpha \exp(-(\lambda + \lambda_p)(t-3)), \quad \text{(B.1)}$$

where A = the activity administered to the woman,

α = maximum fraction of administered activity (per milliliter of breast milk),

λ = biological decay constant,

λ_p = physical decay constant,

t = time at which breast-feeding occurs.

A comprehensive search of the medical literature was performed in early 1995. From the data gathered from the literature, the highest concentration (or highest fraction) α_2 of a radiopharmaceutical in the breast milk post administration to the women and the longest biological half-life T_{b2} (not necessarily from the same study) were chosen to represent the worst case scenario, and the lowest concentration (or lowest fraction) α_1 and shortest biological half-life T_{b1} were chosen to represent the best case scenario. Breast milk concentrations reported in the literature were first corrected for radioactive decay to the time of administration (unless the article explicitly stated that such a correction had already been made). Then, this maximum concentration was assumed to occur at 3 hours post administration. It might have been more conservative to extrapolate this back from the time at which the concentration was observed to 3 hours post administration, but in many cases, only one value was reported and a biological half-life was not available. If concentrations were reported at times less than 3 hours, the highest concentration reported was used without correction for biological removal, and assumed to occur at 3 hours post administration.

A computer program was written which used Equation B.1 describing breast milk concentration as a function of time represented by each scenario to estimate the fraction of the activity administered to the woman which would be excreted in the breast milk and ingested by the infant. The program assumed that the infant would resume feeding at 3 hours post administration and would then nurse every 3 hours thereafter (i.e., 8 feedings per day), consuming 125 milliliters of milk per feeding (this represents a daily average consumption of 1,000 milliliters). Thus, the program calculated the breast milk concentration (in units of fraction of administered activity per milliliter of milk) at 3 hour intervals based on the excretion functions observed, multiplied by 125 milliliters to estimate the total fraction ingested at that feeding, and added up a total fractional absorption over all feedings (summations were carried out to 50 effective half-lives). The program also calculated cumulative ingestion for assumed interruption periods of 12 hours (0.5 day) 24 hours (1 day), 48 hours (2 days), 96 hours (4 days), 120 hours (5 days), 168 hours (7 days), 336 hours (14 days), and 672 hours (28 days). For example, if the interruption time was 24 hours, the first calculation would have been for t = 24, followed by 27 hours, 30 hours, and so on. There is no information in the literature describing

*Information in this appendix was provided by R.E. Toohey, M.G. Stabin, and J. Stubbs, Radiation Internal Dose Information Center (RIDIC), Oak Ridge Institute for Science and Education, Oak Ridge, TN.

Table A.2 Calculations of Exposure Rate Constants, Release Quantities, and Release Dose Rates (Continued)

Isotope	Half-Life (days)	Intensity (fraction/ disintegration)	Energy (MeV)	Linear Energy-Absorption Coefficient (1/m)	MeV/cm/ disintegration	Exposure Rate R/Ci-hr at 1 Meter	Exposure Rate R/mCi-hr at 1 cm	Release Quantities Based On 0.5 rem to Total Decay Q_o (mCi)	Q_o (MBq)	Q_o (GBq)	Release Dose Rate at 1 Meter for Q_o (mrem/hr)
Tl-201	3.044	0.0022	0.0306	1.80E−02	1.21E−08	1.82E−04	1.82E−03				
		0.27357	0.068895	3.45E−03	6.50E−07	9.75E−03	9.75E−02				
		0.46525	0.070819	3.40E−03	1.12E−06	1.68E−02	1.68E−01				
		0.20465	0.0803	3.20E−03	5.26E−07	7.88E−03	7.88E−02				
		0.0265	0.13534	3.20E−03	1.15E−07	1.72E−03	1.72E−02	(Occupancy Factor = 0.25)			
		0.0016	0.16588	3.30E−03	8.76E−09	1.31E−04	1.31E−03				
		0.1	0.16743	3.30E−03	5.53E−07	8.28E−03	8.28E−02				
					Exposure Rate Constant (Total):	4.47E−02	4.47E−01	4.24E+02	1.57E+04	1.57E+01	1.90E+01
Yb-169	32.01	0.002134	0.02075	6.00E−02	2.66E−08	3.98E−04	3.98E−03				
		0.52777	0.049773	5.25E−03	1.38E−06	2.07E−02	2.07E−01				
		0.93411	0.050742	5.05E−03	2.39E−06	3.59E−02	3.59E−01				
		0.38301	0.0575	4.25E−03	9.36E−07	1.40E−02	1.40E−01				
		0.43747	0.063119	3.75E−03	1.04E−06	1.55E−02	1.55E−01				
		0.026578	0.093613	3.05E−03	7.59E−08	1.14E−03	1.14E−02				
		0.17363	0.10978	3.05E−03	5.81E−07	8.72E−03	8.72E−02				
		0.018818	0.11819	3.10E−03	6.89E−08	1.03E−03	1.03E−02	(Occupancy Factor = 0.25)			
		0.11058	0.13052	3.20E−03	4.62E−07	6.92E−03	6.92E−02				
		0.21437	0.17721	3.40E−03	1.29E−06	1.94E−02	1.94E−01				
		0.3492	0.19795	3.60E−03	2.49E−06	3.73E−02	3.73E−01				
		0.001222	0.7405	3.60E−03	1.06E−08	1.59E−04	1.59E−03				
		0.017654	0.26107	3.65E−03	1.68E−07	2.52E−03	2.52E−02				
		0.10806	0.30773	3.75E−03	1.25E−06	1.87E−02	1.87E−01				
		0.001843	0.34406	3.80E−03	2.41E−08	3.61E−04	3.61E−03				
					Exposure Rate Constant (Total):	1.83E−01	1.83E+00	9.88E+00	3.66E+02	3.66E−01	1.81E+00

NOTE: See footnotes (a) and (b) of Table A.1 for the equation used to calculate the exposure rate constant and the references for the half-lives and the gamma ray and x ray intensities, energies, and linear absorption coefficients for each radionuclide. Only gamma rays and x rays with energies above 11.3 keV were used to calculate the exposure rate factor. The 11.3 keV cutoff is the one used in NCRP Report No. 41, "Specification of Gamma-Ray Brachytherapy Sources," 1974. All calculations based on bare sources, no shielding considered.

Table A.2 Calculations of Exposure Rate Constants, Release Quantities, and Release Dose Rates (Continued)

Isotope	Half-Life (days)	Intensity (fraction/ disintegration)	Energy (MeV)	Linear Energy-Absorption Coefficient (1/m)	MeV/cm/ disintegration	Exposure Rate R/Ci-hr at 1 Meter	Exposure Rate R/mCi-hr at 1 cm	Release Quantities Based On 0.5 rem to Total Decay Q_1 (mCi)	Q_1 (MBq)	Q_1 (GBq)	Release Dose Rate at 1 Meter for Q_1 (mrem/hr)
Sn-117m	13.61	0.1872	0.025	3.35E−02	1.57E−06	2.35E−02	2.35E−01				
		0.3514	0.0253	3.30E−02	2.93E−06	4.40E−02	4.40E−01	(Occupancy Factor = 0.25)			
		0.1185	0.0285	2.25E−02	7.60E−07	1.14E−02	1.14E−01				
		0.0211	0.156	3.25E−03	1.07E−07	1.60E−03	1.60E−02				
		0.864	0.1586	3.30E−03	4.52E−06	6.78E−02	6.78E−01				
				Exposure Rate Constant (Total):		1.48E−01	1.48E+00	2.86E+01	1.06E+03	1.06E+00	4.25E+00
Sr-89	50.5	0.00015	0.9091	3.65E−03	4.98E−09	7.46E−05	7.46E−04	(Occupancy Factor = 0.25)			
				Exposure Rate Constant (Total):		7.46E−05	7.46E−04	1.53E+04	5.67E+05	5.67E+02	1.14E+00
Tc-99m	0.2508333	0.021021	0.018251	7.90E−02	3.03E−07	4.54E−03	4.54E−02				
		0.040194	0.018367	7.90E−02	5.83E−07	8.74E−03	8.74E−02				
		0.012059	0.0206	5.90E−02	1.47E−07	2.20E−03	2.20E−02	(Occupancy Factor = 1.0)			
		0.8907	0.14051	3.20E−03	4.00E−06	6.00E−02	6.00E−01				
		0.000214	0.14263	3.20E−03	9.77E−10	1.46E−05	1.46E−04				
				Exposure Rate Constant (Total):		7.56E−02	7.56E−01	7.63E+02	2.82E+04	2.82E+01	5.76E+01

Table A.2 Calculations of Exposure Rate Constants, Release Quantities, and Release Dose Rates (Continued)

Isotope	Half-Life (days)	Intensity (fraction/ disintegration)	Energy (MeV)	Linear Energy-Absorption Coefficient (1/m)	MeV/cm/ disintegration	Exposure Rate R/Ci-hr at 1 Meter	Exposure Rate R/mCi-hr at 1 cm	Release Quantities Based On 0.5 rem to Total Decay Q_a (mCi)	Q_a (MBq)	Q_a (GBq)	Release Dose Rate at 1 Meter for Q_a (mrem/hr)
Se-75	119.8	0.07269	0.0117	4.25E−01	3.61E−06	5.42E−02	5.42E−01				
		0.010226	0.06605	3.65E−03	2.47E−08	3.70E−04	3.70E−03				
		0.034086	0.096733	3.00E−03	9.89E−08	1.48E−03	1.48E−02				
		0.16744	0.12112	3.10E−03	6.29E−07	9.43E−03	9.43E−02				
		0.59202	0.136	3.20E−03	2.58E−06	3.86E−02	3.86E−01	(Occupancy Factor = 0.25)			
		0.014472	0.1986	3.50E−03	1.01E−07	1.51E−03	1.51E−02				
		0.598	0.26465	3.65E−03	5.78E−06	8.66E−02	8.66E−01				
		0.25236	0.27953	3.70E−03	2.61E−06	3.91E−02	3.91E−01				
		0.013216	0.30391	3.75E−03	1.51E−07	2.26E−03	2.26E−02				
		0.11422	0.40065	3.90E−03	1.78E−06	2.68E−02	2.68E−01				
Exposure Rate Constant (Total):						2.60E−01	2.60E+00	1.85E+00	6.86E+01	6.86E−02	4.82E−01
Sm-153	1.9458333	0.17263	0.040902	7.70E−03	5.44E−07	8.15E−03	8.15E−02				
		0.31218	0.041542	7.30E−03	9.47E−07	1.42E−02	1.42E−01				
		0.12217	0.047	4.60E−03	2.64E−07	3.96E−03	3.96E−02				
		0.0517	0.069672	3.45E−03	1.24E−07	1.86E−03	1.86E−02				
		0.00194	0.075422	3.35E−03	4.90E−09	7.35E−05	7.35E−04	(Occupancy Factor = 0.25)			
		0.002	0.083366	3.20E−03	5.34E−09	8.00E−05	8.00E−04				
		0.00158	0.089484	3.00E−03	4.24E−09	6.36E−05	6.36E−04				
		0.00718	0.09743	3.00E−03	2.10E−08	3.15E−04	3.15E−03				
		0.283	0.10318	3.00E−03	8.76E−07	1.31E−02	1.31E−01				
		0.002775	0.42266	3.85E−03	4.52E−08	6.77E−04	6.77E−03				
Exposure Rate Constant (Total):						4.25E−02	4.25E−01	6.99E+02	2.59E+04	2.59E+01	2.97E+01

Table A.2 Calculations of Exposure Rate Constants, Release Quantities, and Release Dose Rates (Continued)

Isotope	Half-Life (days)	Intensity (fraction/ disintegration)	Energy (MeV)	Linear Energy-Absorption Coefficient (1/m)	MeV/cm/ disintegration	Exposure Rate R/Ci-hr at 1 Meter	Exposure Rate R/mCi-hr at 1 cm	Release Quantities Based On 0.5 rem to Total Decay Q_o (mCi)	Q_o (MBq)	Q_o (GBq)	Release Dose Rate at 1 Meter for Q_o (mrem/hr)
Re-186	3.7766666	0.016	0.058	4.20E−03	3.90E−08	5.84E−04	5.84E−03				
		0.0278	0.0593	4.00E−03	6.59E−08	9.89E−04	9.89E−03				
		0.0118	0.0672	3.60E−03	2.85E−08	4.28E−04	4.28E−03				
		0.007	0.1223	3.10E−03	2.65E−08	3.98E−04	3.98E−03				
		0.0116	0.0615	3.90E−03	2.78E−08	4.17E−04	4.17E−03	(Occupancy Factor = 0.25)			
		0.02	0.063	3.85E−03	4.85E−07	7.27E−03	7.27E−02				
		0.0086	0.0714	3.45E−03	2.12E−08	3.18E−04	3.18E−03				
		0.0952	0.1372	3.15E−03	4.11E−07	6.17E−03	6.17E−02				
		0.0006	0.7022	3.80E−03	1.60E−08	2.40E−04	2.40E−03				
				Exposure Rate Constant (Total):		1.68E−02	1.68E−01	9.10E+02	3.37E+04	3.37E+01	1.53E+01
Re-188	0.7075	0.0136	0.0615	3.90E−03	3.26E−08	4.89E−04	4.89E−03				
		0.235	0.063	3.85E−03	5.70E−07	8.55E−03	8.55E−02				
		0.0101	0.0714	3.45E−03	2.49E−08	3.73E−04	3.73E−03				
		0.1497	0.155	3.25E−03	7.54E−07	1.13E−02	1.13E−01				
		0.0105	0.478	3.90E−03	1.96E−07	2.93E−03	2.93E−02	(Occupancy Factor = 1.0)			
		0.0015	0.6331	3.80E−03	3.61E−08	5.41E−04	5.41E−03				
		0.0011	0.6725	3.80E−03	2.81E−08	4.21E−04	4.21E−03				
		0.0041	0.8295	3.70E−03	1.26E−07	1.89E−03	1.89E−02				
		0.0056	0.9313	3.70E−03	1.93E−07	2.89E−03	2.89E−02				
		0.0072	1.134	3.55E−03	2.90E−07	4.35E−03	4.35E−02				
				Exposure Rate Constant (Total):		3.37E−02	3.37E−01	6.05E+02	2.24E+04	2.24E+01	2.04E+01
Sc-47	3.351	0.68	0.15939	3.85E−03	4.17E−06	6.26E−02	6.26E−01	(Occupancy Factor = 0.25)			
				Exposure Rate Constant (Total):		6.26E−02	6.26E−01	2.76E+02	1.02E+04	1.02E+01	1.72E+01

Table A.2 Calculations of Exposure Rate Constants, Release Quantities, and Release Dose Rates (Continued)

Isotope	Half-Life (days)	Intensity (fraction/ disintegration)	Energy (MeV)	Linear Energy-Absorption Coefficient (1/m)	MeV/cm/ disintegration	Exposure Rate R/Ci-hr at 1 Meter	Exposure Rate R/mCi-hr at 1 cm	Release Quantities Based On 0.5 rem to Total Decay Q_x (mCi)	Q_x (MBq)	Q_x (GBq)	Release Dose Rate at 1 Meter for Q_x (mrem/hr)
Ir-192	74.02	0.011323	0.061487	3.90E−03	2.72E−08	4.07E−04	4.07E−03				
		0.019555	0.063001	3.85E−03	4.74E−08	7.11E−04	7.11E−03				
		0.008399	0.0714	3.45E−03	2.07E−08	3.10E−04	3.10E−03				
		0.004674	0.20131	3.45E−03	3.25E−08	4.87E−04	4.87E−03				
		0.032873	0.2058	3.50E−03	2.37E−07	3.55E−03	3.55E−02				
		0.002615	0.28326	3.70E−03	2.74E−08	4.11E−04	4.11E−03				
		0.0[illegible]264	0.37448	3.80E−03	1.03E−07	1.55E−03	1.55E−02				
		0.031628	0.48458	3.90E−03	5.98E−07	8.96E−03	8.96E−02				
		0.003989	0.48906	3.90E−03	7.61E−08	1.14E−03	1.14E−02				
		0.000797	0.42307	3.90E−03	1.32E−08	1.97E−04	1.97E−03				
		0.02635	0.065122	3.70E−03	6.35E−08	9.52E−04	9.52E−03				
		0.0[illegible]5197	0.066832	3.60E−03	1.09E−07	1.63E−03	1.63E−02	(Occupancy Factor = 0.25)			
		0.0[illegible]9675	0.0757	3.35E−03	4.99E−08	7.48E−04	7.48E−03				
		0.0[illegible]1806	0.13635	3.20E−03	7.88E−09	1.18E−04	1.18E−03				
		0.29015	0.29596	3.75E−03	3.22E−06	4.83E−02	4.83E−01				
		0.29678	0.30846	3.80E−03	3.48E−06	5.22E−02	5.22E−01				
		0.82853	0.31651	3.80E−03	9.97E−06	1.49E−01	1.49E+00				
		0.006645	0.41646	3.90E−03	1.08E−07	1.62E−03	1.62E−02				
		0.48055	0.46807	3.90E−03	8.77E−06	1.32E−01	1.32E+00				
		0.045735	0.58858	3.85E−03	1.04E−06	1.55E−02	1.55E−01				
		0.082024	0.60441	3.85E−03	1.91E−06	2.86E−02	2.86E−01				
		0.053357	0.61246	3.85E−03	1.26E−06	1.89E−02	1.89E−01				
		0.003016	0.88451	3.65E−03	9.74E−08	1.46E−03	1.46E−02				
		0.000986	0.87173	3.60E−03	3.09E−08	4.64E−04	4.64E−03				
Exposure Rate Constant (Total):						4.69E−01	4.69E+00	1.66E+00	6.16E+01	6.16E−02	7.81E−01

Table A.2 Calculations of Exposure Rate Constants, Release Quantities, and Release Dose Rates (Continued)

Isotope	Half-Life (days)	Intensity (fraction disintegration)	Energy (MeV)	Linear Energy-Absorption Coefficient (1/m)	MeV/cm/ disintegration	Exposure Rate R/Ci-hr at 1 Meter	Exposure Rate R/mCi-hr at 1 cm	Release Quantities Based On 0.5 rem to Total Decay Q_o (mCi)	Q_o (MBq)	Q_o (GBq)	Release Dose Rate at 1 Meter for Q_o (mrem/hr)
I-131	8.04	0.013468	0.029458	1.95E−02	7.74E−08	1.16E−03	1.16E−02				
		0.024987	0.029779	1.90E−02	1.41E−07	2.12E−03	2.12E−02				
		0.008883	0.0336	1.39E−02	3.88E−08	5.82E−04	5.82E−03				
		0.026182	0.080183	3.25E−03	6.82E−08	1.02E−03	1.02E−02				
		0.002648	0.17721	3.35E−03	1.57E−08	2.36E−04	2.36E−03				
		0.060521	0.2843	3.68E−03	6.33E−07	9.49E−03	9.49E−02				
		0.002507	0.32578	3.75E−03	3.06E−08	4.59E−04	4.59E−03	(Occupancy Factor = 0.25)			
		0.811640	0.36448	3.80E−03	1.12E−05	1.69E−01	1.69E+00				
		0.003605	0.50299	3.85E−03	6.98E−08	1.05E−03	1.05E−02				
		0.072605	0.63697	3.80E−03	1.76E−06	2.64E−02	2.64E−01				
		0.002195	0.6427	3.80E−03	5.36E−08	8.04E−04	8.04E−03				
		0.018025	0.72289	3.75E−03	4.89E−07	7.33E−03	7.33E−02				
		0.002304	0.32939	3.75E−03	2.85E−08	4.27E−04	4.27E−03				
						Exposure Rate Constant (Total):	2.20E−01	2.20E+00	3.27E+01	1.21E+03	1.21E+00	7.19E+00
In-111	2.83	0.23628	0.022984	4.30E−02	2.34E−06	3.50E−02	3.50E−01				
		0.44581	0.023174	4.00E−02	4.13E−06	6.20E−02	6.20E−01				
		0.14597	0.0261	2.80E−02	.07E−06	1.60E−02	1.60E−01	(Occupancy Factor = 0.25)			
		0.9024	0.17128	3.35E−03	5.18E−06	7.76E−02	7.76E−01				
		0.94	0.24539	3.60E−03	8.30E−06	1.25E−01	1.25E+00				
		0.000028	0.15081	3.25E−03	1.37E−10	2.06E−06	2.06E−05				
						Exposure Rate Constant (Total):	3.15E−01	3.15E+00	6.48E+01	2.40E+03	2.40E+00	2.04E+01

Table A.2 Calculations of Exposure Rate Constants, Release Quantities, and Release Dose Rates (Continued)

Isotope	Half-Life (days)	Intensity (fraction/ disintegration)	Energy (MeV)	Linear Energy-Absorption Coefficient (1/m)	MeV/cm/ disintegration	Exposure Rate R/Ci-hr at 1 Meter	Exposure Rate R/mCi-hr at 1 cm	Release Quantities Based On 0.5 rem to Total Decay Q_a (mCi)	Q_a (MBq)	Q_a (GBq)	Release Dose Rate at 1 Meter for Q_a (mrem/hr)
Ga-67	3.2608333	0.02856	0.091266	3.00E−03	7.82E−08	1.17E−03	1.17E−02				
		0.357	0.093311	2.95E−03	9.83E−07	1.47E−02	1.47E−01				
		0.19706	0.18458	3.40E−03	1.24E−06	1.85E−02	1.85E−01	(Occupancy Factor = 0.25)			
		0.02242	0.20895	3.50E−03	1.64E−07	2.46E−03	2.46E−02				
		0.15994	0.30022	3.75E−03	1.80E−06	2.70E−02	2.70E−01				
		0.044768	0.39353	3.96E−03	6.87E−07	1.03E−02	1.03E−01				
		0.001385	0.88769	3.65E−03	4.49E−08	6.73E−04	6.73E−03				
		0.001247	0.62941	3.85E−03	3.02E−08	4.53E−04	4.53E−03				
				Exposure Rate Constant (Total):		7.53E−02	7.53E−01	2.35E+02	8.71E+03	8.71E+00	1.77E+01
I-123	0.55	0.24631	0.027202	2.60E−02	1.74E−06	2.61E−02	2.61E−01				
		0.45954	0.027472	2.50E−02	3.16E−06	4.73E−02	4.73E−01				
		0.15952	0.031	1.73E−02	8.56E−07	1.28E−02	1.28E−01				
		0.834	0.159	3.30E−03	4.38E−06	6.56E−02	6.56E−01				
		0.001259	0.34635	3.80E−03	1.66E−08	2.48E−04	2.48E−03	(Occupancy Factor = 1.0)			
		0.004287	0.44002	3.90E−03	7.36E−08	1.10E−03	1.10E−02				
		0.003161	0.50533	3.85E−03	6.15E−08	9.22E−04	9.22E−03				
		0.013928	0.52896	3.85E−03	2.84E−07	4.25E−03	4.25E−02				
		0.00382	0.53854	3.85E−03	7.92E−08	1.19E−03	1.19E−02				
		0.004763	0.49444	3.90E−03	9.18E−08	1.38E−03	1.38E−02				
				Exposure Rate Constant (Total):		1.61E−01	1.61E−00	1.63E+02	6.04E+03	6.04E+00	2.63E+01
I-125	60.14	0.39233	0.027202	2.60E−02	2.77E−06	4.16E−02	4.16E−01				
		0.73196	0.027472	2.50E−02	5.03E−06	7.54E−02	7.54E−01	(Occupancy Factor = 0.25)			
		0.25409	0.031	1.73E−02	1.36E−06	2.04E−02	2.04E−01				
		0.0649	0.035492	1.20E−02	2.76E−07	4.14E−03	4.14E−02				
				Exposure Rate Constant (Total):		1.42E−01	1.42E+00	6.79E+00	2.51E+02	2.51E−01	9.61E−01

Table A.2 Calculations of Exposure Rate Constants, Release Quantities, and Release Dose Rates

Isotope	Half-Life (days)	Intensity (fraction/ disintegration)	Energy (MeV)	Linear Energy-Absorption Coefficient (1/m)	MeV/cm/ disintegration	Exposure Rate R/Ci-hr at 1 Meter	Exposure Rate R/mCi-hr at 1 cm	Release Quantities Based On 0.5 rem to Total Decay Q_a (mCi)	Q_a (MBq)	Q_a (GBq)	Release Dose Rate at 1 Meter for Q_a (mrem/hr)
Ag-111	7.45	0.000245	0.022984	4.30E−02	2.42E−09	3.63E−05	3.63E−04				
		0.000462	0.023174	4.00E−02	4.28E−09	6.42E−05	6.42E−04				
		0.000151	0.0261	2.80E−02	1.10E−09	1.65E−05	1.65E−04	(Occupancy Factor = 0.25)			
		0.001202	0.09675	3.00E−03	3.49E−09	5.23E−05	5.23E−04				
		0.012291	0.24539	3.60E−03	1.09E−07	1.63E−03	1.63E−02				
		0.0668	0.34213	3.80E−03	8.68E−07	1.30E−02	1.30E−01				
		0.000559	0.65472	3.80E−03	1.39E−08	2.09E−04	2.09E−03				
Exposure Rate Constant (Total):						1.50E−02	1.50E−01	5.16E+02	1.91E+04	1.91E+01	7.76E+00
Au-198	2.696	0.008053	0.968895	3.50E−03	1.94E−08	2.91E−04	2.91E−03				
		0.013695	0.070819	3.45E−03	3.35E−08	5.02E−04	5.02E−03				
		0.006024	0.0803	3.25E−03	1.57E−08	2.36E−04	2.36E−03	(Occupancy Factor = 0.25)			
		0.9551	0.4118	3.90E−03	1.53E−05	2.30E−01	2.30E+00				
		0.010602	0.67589	3.80E−03	2.72E−07	4.08E−03	4.08E−02				
		0.002292	1.0877	3.55E−03	8.85E−08	1.33E−03	1.33E−02				
Exposure Rate Constant (Total):						2.36E−01	2.36E+00	9.07E+01	3.36E+03	3.36E+00	2.14E+01
Cr-51	27.704	0.0983	0.32008	3.75E−03	1.18E−06	1.77E−02	1.77E−01	(Occupancy Factor = 0.25)			
Exposure Rate Constant (Total):						1.77E−02	1.77E−01	1.18E+02	4.36E+03	4.36E+00	2.09E+00
Cu-64	0.5292083	0.004898	1.3459	3.35E−03	2.21E−07	3.31E−03	3.31E−02	(Occupancy Factor = 1.0)			
		0.3574	0.511	3.90E−03	7.12E−06	1.07E−01	1.07E+00				
Exposure Rate Constant (Total):						1.10E−01	1.10E+00	2.48E+02	9.18E+03	9.18E+00	2.73E+01
Cu-67	2.5775	0.07	0.0913	3.00E−03	1.92E−07	2.87E−03	2.87E−02				
		0.1610	0.0933	2.95E−03	4.43E−07	6.64E−03	6.64E−02				
		0.4870	0.1846	3.40E−03	3.06E−06	4.58E−02	4.58E−01	(Occupancy Factor = 0.25)			
		0.0012	0.2089	3.50E−03	8.77E−09	1.32E−04	1.32E−03				
		0.0080	0.3002	3.75E−03	9.01E−08	1.35E−03	1.35E−02				
		0.0022	0.3935	3.90E−03	3.07E−08	4.60E−04	4.67E−03				
Exposure Rate Constant (Total):						3.33E−03	3.33E−02	6.72E+03	2.49E+05	2.49E+02	2.24E+01

[1] The exposure rate constant was calculated from the following equation (details of the calculation are shown in Table A.2):

$$\Gamma \frac{\text{mR} \cdot \text{cm}^2}{\text{mCi} \cdot \text{hr}} = (1.332 \times 10^{14} \frac{\text{dis}}{\text{mCi} \cdot \text{hr}}) (\frac{1}{4\pi\ (100\ \text{cm})^2}) \sum f_i E_i\ (\frac{\mu_{a,i}\ \text{cm}^{-1}}{\rho\ \text{gm} \cdot \text{cm}^{-3}}) (\frac{\text{gm} \cdot \text{mR}}{87.6\ \text{erg}}) (1.6 \times 10^{-6} \frac{\text{erg}}{\text{MeV}})$$

Where E_i = the energy of the *i*th gamma ray or x-ray i, MeV.

f_i = the probability of decay of gamma rays or x-rays with energy E_i per disintegration. Values for E_i and f_i were taken from: Bernard Shleien, The Health Physics and Radiological Health Handbook, Revised Edition, Scinta, Inc., 1992, pages 294-334. For Re-186, Re-188, and Sn-117m the values for E_i and f_i were taken from: Laurie M. Unger and D. K. Trubey, "Specific Gamma-Ray Dose Constants for Nuclides Important to Dosimetry and Radiological Assessment," U.S. Department of Energy, ORNL/RSIC-45/R1, 1982.

$\mu_{a,i}$ = the linear energy absorption coefficient in air of photons of energy E_i, taken from Radiological Health Handbook, U.S. Department of Health, Education, and Welfare, 1970, page 135.

ρ = the density of air at standard temperature and pressure, taken to be 0.0012929 gm/cm^3.

[†] R. Nath, A.S. Meigooni, and J.A. Meli, "Dosimetry on Transverse Axes of ^{125}I and ^{192}Ir Interstitial Brachytherapy Sources," Medical Physics, Volume 17, Number 6, November/December 1990. The exposure rate constant given is a measured value averaged for several source models and takes into account the attenuation of gamma rays within the implant capsule itself.

[††] A. Meigooni, S. Sabnis, and R. Nath, "Dosimetry of Palladium-103 Brachytherapy Sources for Permanent Implants," Endocurietherapy Hyperthermia Oncology, Volume 6, April 1990. The exposure rate constant given is an "apparent" value (i.e., with respect to an apparent source activity) and takes into account the attenuation of gamma rays within the implant capsule itself.

[†††] Not applicable (NA) because the release quantity is not based on beta emissions.

APPENDIX A

PARAMETERS AND CALCULATIONS FOR DETERMINING RELEASE QUANTITIES AND DOSE RATES FOR RADIONUCLIDES USED IN MEDICINE

Table A-1 Half-Lives and Exposure Rate Constants of Radionuclides Used in Medicine.

Radionuclide	Half-Life (days)*	Exposure Rate Constant† (R/mCi-h at 1 cm)
Ag-111	7.45	0.150
Au-198	2.696	2.36
Cr-51	27.704	0.177
Cu-64	0.5292	1.10
Cu-67	2.5775	
Ga-67	3.261	0.753
I-123	0.55	1.61
I-125	60.14	1.42
I-125 implant	60.14	1.11‡
I-131	8.040	2.20
In-111	2.83	3.15
Ir-192 implant	74.02	4.59‡
P-32	14.29	NA††
Pd-103 implant	16.97	1.48**
Re-186	3.777	0.168
Re-188	0.7075	0.337
Sc-47	3.351	0.626
Se-75	119.8	2.60
Sm-153	1.9458	0.425
Sn-117m	13.61	1.48
Sr-89	50.5	NA††
Tc-99m	0.2508	0.756
Tl-201	3.044	0.447
Y-90	0.1329	NA††
Yb-169	32.01	1.83

* Keith F. Eckerman, Anthony B. Wolbarst, and Allan C. B. Richardson, Federal Guidance Report No. 11, Limiting Values of Radionuclide Intake and Air Concentration and Dose Conversion Factors for Inhalation, Submersion, and Ingestion, Report No. EPA-520/1-88-020, Office of Radiation Programs, U. S. Environmental Protection Agency, Washington, DC, 1988.

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3. Alternative 3 relative to Alternative 2 has a net value of about $9,000,000 per year, mostly due to lower health care costs. Also,Alternative 3 has psychological benefits to patients and their families. Thus, Alternative 3 is cost effective in comparison with Alternative 2.

4. Basing the patient release criteria in 10 CFR 35.75 on the dose to individuals exposed to a patient provides a consistent, scientific basis for such decisions that treats all radionuclides on a risk-equivalent basis. The dose delivered by an initial activity of 1,110 megabecquerels (30 millicuries) or a dose rate at 1 meter of 0.05 millisievert (5 millirems) per hour varies greatly from one radionuclide to another. Thus, while the values in the current 10 CFR 35.75 may be appropriate for iodine-131, they are too high for some other radionuclides and too low for others.

5. A dose-based rule no longer restricts patient release to a specific activity, and therefore would permit the release of patients with activities that are greater than currently allowed. This is especially true when case-specific factors are evaluated to more accurately assess the dose to other individuals. For the case of thyroid cancer, in those occasional cases where multiple administrations in a year of 1,110 megabecquerels (30 millicuries) or less of iodine-131 are now administered to a patient, it may be possible to give all of the activity in a single administration. This would reduce the potential for repeated exposures to hospital staff and to those providing care to the released patient. Additionally, this would provide physicians with the flexibility to not have to fractionate doses to avoid hospitalization to meet the current requirements, which may lead to a more effective treatment.

6. Shorter hospital stays provide emotional benefits to patients and their families. Allowing earlier reunion of families can improve the patient's state of mind, which in itself may improve the outcome of the treatment and lead to the delivery of more effective health care.

6 IMPLEMENTATION

No impediments to implementation of the recommended alternative have been identified. The staff has prepared a regulatory guide (NRC96) for licensees which provides, in part, simple methods to evaluate the dose to the individual member of the public likely to receive the highest dose from the released patient. This will enable licensees to determine when a patient may be released from their control.

Table 4.14 Annual Costs and Benefits of Alternatives 1 and 3 Compared to Alternative 2 (The Status Quo)

Alternative	Collective-Dose[1]		Costs	Net Benefit $ (millions)
	Dose Averted (person-rem)	Associated Value $ (millions)	Hospitalization, Lost Time, Records and Instructions $ (millions)	
1	11,440 (savings)	23 (savings)	435 (cost)	-412 (net cost)
2	0	0	0	0
3	-2,740 (cost)	-5 (cost)	-14 (savings)	9 (net savings)

[1] A value of $2,000 per person-rem was used as the conversion factor for dose averted.

per person-rem was used as the conversion factor for dose averted (NRC95).

Because the benefits and costs for all alternatives occur in the same year, and remain the same each year for the therapeutic procedures discussed, a discounted flow of the benefits and costs of this rulemaking is not required.

4.4 Evaluation of the Alternatives With Respect to Accepted Radiation Protection Principles

Selection of the 5-millisieverts (0.5-rem) total effective dose equivalent per year criterion is consistent with: the Commission's provision in 10 CFR 20.1301(c) for authorizing a licensee to operate up to this limit; the recommendations of the International Commission on Radiological Protection (ICRP) in ICRP Publication 60, "1990 Recommendations of the International Commission on Radiological Protection"; and the recommendations of the NCRP in NCRP Report No. 116, "Limitation of Exposure to Ionizing Radiation." Each of these provide a basis for allowing individuals to receive annual doses up to 5 millisieverts (0.5 rem) under certain circumstances. Both ICRP and NCRP recommend that an individual be allowed to receive a dose up to 5 millisieverts (0.5 rem) in a given year in temporary situations where exposure to radiation is not expected to result in doses above 1 millisievert (0.1 rem) for long periods of time. The recommendations of the ICRP and NCRP are based on their finding that annual doses in excess of 1 millisievert (0.1 rem) to a small group of people, provided that they do not occur often to the same group, need not be regarded as especially hazardous. Although the risk is potentially greater under Alternative 3, it is still within the range of acceptable risk for radiation exposure accepted by the NRC (as implemented under the revised 10 CFR Part 20).

5 DECISION RATIONALE

1. All of the alternatives are acceptable according to generally accepted radiation protection principles, such as those expressed by NRC, NCRP, and ICRP (see Section 4.4 Evaluation of the Alternatives With Respect to Accepted Radiation Protection Principles).

2. Alternative 1 is considerably more expensive to the public compared to Alternative 2 (the status quo) or Alternative 3. Even neglecting the psychological costs, which have not been expressed in dollar terms, the additional cost of Alternative 1 relative to Alternative 2 is about $412,000,000 per year, mostly due to increased national health care costs. In view of this, Alternative 1 may be dismissed.

Table 4.13 Annual Attributes of Alternatives 1, 2, and 3

Alternative	Collective Dose (person-rem)	Hospital Retention (days)	Cost Estimates			
			Hospitalization cost $ (millions)	Value of lost time $ (millions)	Records & Instructions $ (millions)	Psychological cost (relative)
1	18,400	427,000	427	25.62	0	High
2	29,840	16,000	16	0.96	0	Moderate
3	32,580	0	0	0	2.3	Low

retained in a controlled environment. Indirect costs may also be incurred by individuals other than the patient who may forgo economic activities to accommodate a family member's hospital retention. Economic activities include occupational work that is lost to either the patient or his or her employer as well as non-occupational (e.g., domestic) work which must be performed by someone else at the expense of the patient.

The conversion of time lost from economic activities to equivalent dollars is most fairly achieved by means of the gross national product (GNP). The GNP is considered the most comprehensive measure of the country's economic activity and includes the market value of all goods and services that have been bought for final use during a year. From the GNP of about $5,600 billion in 1991, the gross average annual per capita income of about $22,000 is derived. The value of $22,000 per year corresponds to $60 per day. To estimate the equivalent dollar value for the number of days lost due to retention of an individual for a therapeutic procedure, one need only multiply $60 by the days of retention for the procedure presented in Table 4.12. The value of the days lost for each alternative is shown in Table 4.13.

4.3.1.3 Evaluation of Psychological Costs

Retention of patients in a hospital by design necessitates that the patient be "isolated" and that human contact, inclusive of family members, is either avoided or minimized. Such isolation may bring about numerous changes and impositions in the lives of the patient and family members that may in part be linked to, but are not reflected in, the direct and indirect economic costs identified above. The wide variety of deterioration in the quality of life brought on by illness is frequently referred to as psychological costs. For thyroid cancer or dysfunction requiring therapeutic doses of iodine-131 for example, a deterioration in the quality of life may be precipitated by the loss of bodily function, a lifetime dependence on medication, hormonal instability, uncertainty of normal life-expectancy, disruption of normal daily routines, and reduced financial security related to employment, lost earnings, and medical expenses.

While some of these elements of psychological costs are the result of the disease itself, others such as disruption of normal routines, social isolation, and enhanced financial strain are clearly elements of psychological costs that are directly related to patient retention. The conversion of psychological cost from patient retention to equivalent dollars is complex such that an evaluation is highly subjective and dependent upon the individual situation. Instead, this analysis uses a qualitative and reasonable approach to scope the range of possible responses. As shown in Table 4.13, comparison is provided on a relative scale.

4.3.2 Costs and Benefits of Alternatives

Table 4.13 summarizes the data pertaining to the annual attributes for each of the three alternatives under consideration. To determine the preferred alternative, the costs and benefits that result when Alternatives 1 and 3 are each compared with Alternative 2 (the status quo) were analyzed. The results are shown in Table 4.14. A value of $2,000

The number of releases involving breast-feeding women that require instructions under Alternative 3 is calculated in the following manner. First, the total number of administrations potentially requiring instructions for breast-feeding, approximately 4 million, was determined by summing up the number of administrations for all of the radionuclides in Table 4.2 that would require instructions based on Table B.5. For radiopharmaceuticals not identified in Table 4.2 but listed in Table B.5, the number of administrations was assumed to be negligible. Next, from Table 4.3 it was estimated that 13.5 percent of the radiopharmaceuticals are administered to females of childbearing age and that 5 percent of them, based on information in Statistical Abstracts of the United States (SA94), could be breast-feeding (assuming an average breast-feeding period of 1 year). To estimate the number of releases that require instruction, one needs only multiply 4 million by 13.5 percent, and then by 5 percent. Thus, 27,000 releases of breast-feeding women require instructions.

The number of patient releases involving breast-feeding women that require a record of instructions under Alternative 3 was calculated in the following manner. Using Table B.5, only the radiopharmaceuticals resulting in a dose to the breast-feeding infant exceeding 5 millisieverts (0.5 rem) with no interruption were identified. Of the identified radiopharmaceuticals, only those with a significant number of administrations using the data in Table 4.2 were considered. Based on this analysis, the total number of administrations potentially requiring records for issuance of breast-feeding instructions was estimated at 1.06 million (i.e., 60,000 iodine-131 administrations for thyroid cancer and ablation plus 1 million technetium-99m pertechnetate administrations). As discussed above, 13.5 percent of the radiopharmaceuticals are administered to females of childbearing age and 5 percent of them could be breast-feeding. To estimate the number of releases that require a record, one needs only multiply 1.06 million by 13.5 percent, and then by 5 percent. Thus, 7,200 releases of breast-feeding women require a record.

Costs of Providing Instructions

Alternatives 1 and 2 have no requirements for instructions, and therefore, have no related costs. However, the rule associated with Alternative 3 imposes additional costs for providing instructions, including written instructions, on the estimated 1,350 licensees. In the case in which the administered activity could cause a dose from direct radiation exceeding 0.1 rem (1 millisievert), instructions would have to be given to 62,000 patients per year at a cost of $1.4 million per year. In addition, instructions would have to be given to approximately 27,000 breast-feeding women at a cost of $0.6 million per year. In both cases, a cost of $22 per patient is estimated. The total estimated cost of instructions is $2 million per year.

Costs of Providing Recordkeeping

Alternatives 1 and 2 have no recordkeeping requirements, and therefore, have no related costs. However, the rule associated with Alternative 3 imposes additional paperwork and recordkeeping requirements on the estimated 1,350 licensees (NRC- and Agreement State licensed) that provide diagnostic and therapeutic administrations of radiopharmaceuticals. For therapeutic administrations where releases are not based on the default table of activities and dose rates in Regulatory Guide 8.39, "Release of Patients Administered Radioactive Materials" (NRC96), a record must be maintained for 3 years.

Additionally, if the released patient is a breast-feeding woman and the radiation dose to the nursing infant could result in a total effective dose equivalent exceeding 5 millisievert (0.5 rem) assuming no interruption of breast-feeding, then a record must be maintained, for 3 years, that instructions were provided. In this case, both diagnostic and therapeutic administrations of radiopharmaceuticals could require a record.

It is estimated that approximately 17,200 procedures per year would be subject to these requirements (i.e., (1) 10,000 patients treated with iodine for thyroid cancer and (2) 7,200 administrations to breast-feeding women). A cost of $17 per patient is estimated. This results in an annual estimated cost of approximately $0.3 million.

4.3.1.2 Derivation of Indirect Costs

Loss of Time

Indirect costs principally reflect the time and output lost or forfeited by the patient while

Table 4.12 Duration of Retention per Therapeutic Procedure

Therapeutic Procedure	Typical Activity Administered (MBq) (mCi)	Alternative 1 (days) hospital days per procedure	Alternative 1 (days) total hospital days	Alternative 2 (days) hospital days per procedure	Alternative 2 (days) total hospital days	Alternative 3 (days) days per procedure	Alternative 3 (days) Σ procedures (x 1000)
Thyroid Ablation I-131, 50,000 procedures/year							
	1,110 (30)	7	343,000	0	0	0	0
	2,220[1] (60)	14	14,000	1	1,000	0	0
Thyroid Cancer I-131, 10,000 procedures/year							
	5,550 (150)	1.5	70,000	1.5[2]	15,000	0	0
Permanent Implant, I-125, 2,000 procedures/year							
	1,480 (40)	0	0	0	0	0	0
Total for All Therapeutic Procedures			427,000		16,000		0

[1] Maximum activity administered. This analysis assumes that 98 percent of the patients are typically administered 1,110 megabecquerels (30 millicuries) and that 2 percent are administered the maximum activity.

[2] The analysis under Section 4.2.5.1 Collective Dose to Individuals shows 1 day of hospitalization. However, patients are typically hospitalized for 1 to 2 days. Thus, the actual observed value is shown.

because the dose to the maximally exposed individual is 1.86 millisieverts (0.186 rem). The collective dose is 5.6 millisieverts (0.56 rem).

4.2.5.2 Collective Dose to Breast-Feeding Infants

The dose to the nursing infant from breast-feeding can be controlled to less than 1 millisievert (0.1 rem) by giving the woman instructions to cease or to interrupt breast-feeding (see Section 4.2.4.4 Summary of Doses to Breast-Feeding Infants). The actual doses that would be received by most infants after interruption should be a small fraction of 1 millisievert (0.1 rem) or nothing in the case of cessation. Consequently, there is no reason to calculate the collective dose to nursing infants from breast-feeding since it does not affect the choice of alternative.

4.3 Value Impact Analysis

4.3.1 Estimates of the Potential Costs

The analysis in Section 4.2 indicates that the 1 millisievert (0.1 rem) per year dose limit imposed by Alternative 1 would result in the smallest collective dose to individuals exposed released patients. The benefit of smaller doses estimated for Alternative 1 will only be achieved if the patients to whom the radioactive materials have been administered are retained under the control of licensees for longer periods of time. The impact of retaining patients must be assessed in terms of the patient, family, and society as a whole. At a minimum, the economic cost must consider the direct cost of medical resources required to retain the patient in a hospital and the indirect cost resulting from the loss of human resources. Additional consideration should be given to the psychological impact of retention on the affected individual and family members. Hospitalization will also cause an increase in the dose to the hospital staff and other patients in the hospital. However, the increase in dose to the hospital staff is expected to be low relative to a patient going home earlier because of the precautions taken during hospitalization; e.g., patients are isolated and the hospital staff rarely enters the patient's room.

In the analysis that follows, these costs are calculated assuming that all retained patients will be hospitalized. While retention costs might be less for non-hospital locations, no attempt is made in this analysis to quantify the potential costs.

4.3.1.1 Estimates of the Direct Costs of Patient Retention

Durations of Patient Retention

Estimates of the periods of hospitalization that patients would need to remain under licensee control for each alternative were discussed in Section 4.2.5.1 Collective Dose to Individuals. Table 4.12 summarizes the duration of retention per therapeutic procedure.

Cost of Patient Retention

To estimate the annual dollar costs for these periods of retention, one needs only multiply the number of days required for each procedure by the number of procedures per year and the average cost per day of hospitalization. In 1990, the average cost per day in a community hospital was $687 (SA92). The per diem cost at the beginning of 1995 is estimated to be $800. However, as the current regulations require that patients who are hospitalized due to a therapeutic administration of radiopharmaceuticals be placed in a private room, the $800 per day estimate is adjusted to $1,000 per day. Using this figure, the potential cost of retaining patients under Alternative 1 is estimated to be $427 million. Under Alternative 2, the estimated cost is $16 million. And, under Alternative 3, there is no related cost because hospitalization is not required.

Estimates of the Numbers of Breast-Feeding Women Requiring Records and Instructions Under Alternative 3

The rule associated with Alternative 3 establishes additional requirements for recordkeeping and providing instructions. Before one can determine the costs of these requirements, it is necessary to calculate the number of patient releases involving breast-feeding women that apply to each requirement.

Table 4.11 Estimates of Collective Dose from Therapeutic Radioiodine Procedures for Alternative 3: Annual Limit of 5 millisieverts (0.5 rem)

Therapeutic Procedure	Typical Activity Administered (MBq)	(mCi)	Collective Dose/Procedure (mSv)	(rem)	Estimated Procedures per Year	Total Collective Dose (person-Sv	(rem))
Thyroid Ablation							
- iodine-131	1,110	(30)	5.2	(0.52)	49,000	255	(25,500)
	2,220[1]	(60)	10.4	(1.04)	1,000	10.4	(1,040)
Thyroid Cancer							
- iodine-131	5,550	(150)	5.6	(0.56)	10,000	56	(5,600)
Permanent Implant							
- iodine-125	1,480	(40)	2.2	(0.22)	2,000	4.4	(440)
All Therapeutic Procedures					62,000	325.8	(32,580)

[1] Maximum activity administered. This analysis assumes that 98 percent of the patients are typically administered 1,110 millisieverts (30 millicuries) and that 2 percent are administered the maximum quantity.

most exposed individual is 1 millisievert (0.1 rem). For iodine-125 implants, the dose is already less than 1 millisievert (0.1 rem) so no hospitalization is required. The collective dose per procedure is then assumed to be 3 times the dose to the most exposed individual.

Under Alternative 1, patients administered the typical and maximum quantities of iodine-131 for thyroid ablation require about 7 and 14 days of hospitalization, respectively, before release can be authorized. Whereas, thyroid cancer patients administered the typical quantity of iodine-131 require about 1.5 days of hospitalization.

In Table 4.10 (Alternative 2), the collective dose per procedure was evaluated in the following manner. For thyroid ablations using the typical activity of iodine-131, no hospitalization is required since the activity is equal to the release limit of 1,110 megabecquerels (30 millicuries). The collective dose is 3 times the individual dose (i.e., 1.73 millisieverts (0.173 rem)) or 5.2 millisieverts (0.52 rem). On the other hand, patients administered the maximum activity require about 1 day of hospitalization before release can be authorized. When released, the maximum dose from these patients will be greater than the dose from a patient administered 1,110 megabecquerels (30 millicuries) due to biological considerations. The estimated dose to the most exposed individual is 3 millisieverts (0.3 rem). The collective dose is 3 times the individual dose or 9 millisieverts (0.9 rem). The collective dose per procedure for iodine-125 implants was calculated similar to that for the typical activity administered for thyroid ablation. For thyroid cancer, an administration of 5,500 megabecquerels (150 millicuries) requires about 1 day of hospitalization to allow the retained activity to reach the release limit. Upon release, the estimated dose to the maximally exposed individual is 1 millisievert (0.1 rem). Therefore, the collective dose is 3 millisieverts (0.3 rems).

In Table 4.11 (Alternative 3), the collective dose per procedure was determined in the following manner. For thyroid ablation, patients administered the typical or maximum activity can be released immediately because the dose from each activity is less than 5 millisieverts (0.5 rem). The individual doses from the typical and maximum activities are 1.73 millisieverts (0.173 rem) and 3.47 millisieverts (0.347 rem), respectively. Thus, the collective dose is 5.2 millisieverts (0.52 rem) for the typical activity and 10.4 millisieverts (1.04 rem) for the maximum activity. The collective dose per procedure for iodine-125 implants was calculated in the same manner assuming no hospitalization. For thyroid cancer, administrations of 5,500 megabecquerels (150 millicuries) require no hospitalization

Table 4.9 Estimates of Collective Dose from Therapeutic Radioiodine Procedures for Alternative 1: Annual Limit of 1 millisievert (0.1 rem)

Therapeutic Procedure	Typical Activity Administered (MBq)	(mCi)	Collective Dose/Procedure (mSv)	(rem)	Estimated Procedures per Year	Total Collective Dose (person-Sv	(rem))
Thyroid Ablation							
- iodine-131	1,110	(30)	3.0	(0.3)	49,000	147	(14,700)
	2,220[1]	(60)	3.0	(0.3)	1,000	3	(300)
Thyroid Cancer							
- iodine-131	5,550	(150)	3.0	(0.3)	10,000	30	(3,000)
Permanent Implant							
- iodine-125	1,480	(40)	2.2	(0.22)	2,000	4.4	(440)
All Therapeutic Procedures					62,000	184.4	(18,440)

[1] Maximum activity administered. This analysis assumes that 98 percent of the patients are typically administered 1,110 millisieverts (30 millicuries) and that 2 percent are administered the maximum quantity.

Table 4.10 Estimates of Collective Dose from Therapeutic Radioiodine Procedures for Alternative 2: Limits of 1,110 megabecquerels (30 millicuries) or 0.05 millisievert (5 millirems)/hr

Therapeutic Procedure	Typical Activity Administered (MBq)	(mCi)	Collective Dose/Procedure (mSv)	(rem)	Estimated Procedures per Year	Total Collective Dose (person-Sv	(rem))
Thyroid Ablation							
- iodine-131	1,110	(30)	5.2	(0.52)	49,000	255	(25,500)
	2,220[1]	(60)	9.0	(0.9)	1,000	9	(900)
Thyroid Cancer							
- iodine-131	5,550	(150)	3.0	(0.3)	10,000	30	(3,000)
Permanent Implant							
- iodine-125	1,480	(40)	2.2	(0.22)	2,000	4.4	(440)
All Therapeutic Procedures					62,000	298.4	(29,840)

[1] Maximum activity administered. This analysis assumes that 98 percent of the patients are typically administered 1,110 millisieverts (30 millicuries) and that 2 percent are administered the maximum quantity.

appropriate. The decision to require instructions as shown in column 5 of Table B.5 is based on both the external and internal dose to the nursing infant. It can be seen from column 4 that for some radiopharmaceuticals the external dose from breast-feeding can be a significant part of the total dose. The duration of the interruption shown in column 6 is selected to reduce the maximum dose to a newborn infant to less than 1 millisievert (0.1 rem).

The actual doses that would be received by most infants for the recommended interruption periods shown should be a small fraction of 1 millisievert (0.1 rem) due to the conservatism of the analysis. The conservative factors are based on: (1) the maximum measured level of activity in breast milk, (2) the longest biological half-life, and (3) the lowest body weight (i.e., the newborn). These factors are explained in Appendix B.

4.2.5 Collective Dose

To evaluate each alternative, it is also necessary to estimate not only the dose to the maximally exposed individual, but also the collective dose to other individuals who may be exposed to patients administered radioactive materials. To calculate precisely the collective dose that would be received under any of the alternatives would require detailed information of a highly diverse group of patients relative to lifestyles, living arrangements, work environments, social activities, etc. This information does not exist and is essentially impossible to precisely determine. In place of a precise estimate we have made a rough estimate of the collective dose per therapeutic procedure which we believe is adequate for the purposes of this rulemaking.

4.2.5.1 Collective Dose to Individuals

Based on considerations of the written instructions provided patients, the demographics of the patient population (see Table 4.3), and time, distance, and shielding factors, we estimate that the collective dose per procedure is 3 times the maximal dose (i.e., the dose to the most exposed individual). This 3 times factor could occur in the following manner, based upon intuitive assumptions about a typical family and friends. In addition to the person receiving the maximal dose, who is likely to be the primary care-provider, there could be two other people who will average about half as much time near the patient. There might also be about four other people who will average about a quarter as much time near the patient as the maximally exposed individual. The sum of the collective dose to all these people is 3 times the dose to the maximally exposed individual. This situation could represent a typical family and friends. Of course some patients will spend more time near other people, but other patients will spend less. A collective dose of 3 times the dose to the maximally exposed individual is thus a reasonable average representation.

Finally, as data are not available on the distribution of the quantities of radionuclides administered for each therapeutic procedure, the estimates of collective dose for each alternative are based on the typical activities used within the ranges of activities administered and the maximum activity used for thyroid ablation.

By using the results from Table 4.8, Tables 4.9, 4.10, and 4.11 present the estimates of the collective doses for Alternatives 1, 2, and 3, respectively, for therapeutic administrations that could be affected by the choice of alternative. For the typical administration of iodine-131 for thyroid ablation, this analysis uses 1.73 millisieverts (0.173 rem) (the maximum likely dose to an individual exposed to a patient assuming no hospitalization) as the basis for estimating the collective doses. This value is the average of the four doses calculated for the thyroidal uptake fractions that characterize the majority of patients undergoing thyroid ablation. In a similar manner, the dose from the maximum quantity administered (2,220 megabecquerels (60 millicuries)), was determined to be 3.47 millisieverts (0.347 rem). For thyroid cancer, this analysis uses 1.86 millisieverts (0.186 rem) (assuming no hospitalization) as the basis for estimating the collective doses. Implants using iodine-125 are included because doses to exposed individuals approach 1 millisievert (0.1 rem). However, palladium-103 implants are not included because doses to exposed individuals are always less than 1 millisievert (0.1 rem).

In Table 4.9 (Alternative 1), the collective dose per procedure was determined in the following manner. It was assumed that all patients would remain hospitalized until the dose dropped to 1 millisievert (0.1 rem). Thus, the dose to the

maintaining the status quo to the extreme option of confining a woman for a period of time after administration of millicurie quantities of I-131 sodium iodide to ensure her milk production has stopped. Included within this range of options was the option to enhance communication between the licensee and woman regarding instructions to interrupt or discontinue breast-feeding before the woman is released from the hospital. It is estimated that approximately 400* breast-feeding women could be administered millicurie amounts of iodine-131 sodium iodide each year for diagnosis and treatment of thyroid disease.

The option of maintaining the status quo does not provide the assurance that instructions will be provided to a breast-feeding woman and could still allow for a breakdown in communciations. As indicated above, the NRC is aware of three cases of unintended exposure to a breast-feeding child during the last five years. There would be no costs associated with this option.

At the other end of the range, for the extreme option, a woman would remain in the hospital until she stopped producing milk. However, this option would result in psychological impacts to both the woman and breast-feeding infant, by requiring them to be physically separated for some period of time, which are not quantified by this analysis. This option was also considered to be impractical as it would be difficult for a medical institution to separate a woman and breast-feeding child. That is, this option does not prevent the breast-fed child from being brought into the patient nor does it address the situation of the patient releasing herself against medical advice. Also, to require cessation of breast-feeding after administration of iodine-131 sodium iodide by hospital retention, or prior to administration (to avoid hospital retention), directly impacts the practice of medicine, since it would in effect dictate when a treatment could be given. It is estimated that each woman would remain in the hospital for an average of 7 days at a cost of $1,000 per day. The estimated annual cost for the extreme option is 400 x 7 x $1,000 = $2.8 million. In addition, there would be associated costs for providing women with instructions and information as to the need for hospital retention. The circumstances of a woman choosing to ignore the warning that breast-feeding would cause significant harm to the infant and to continue to breast-feed are considered to be very rare. As stated above, NRC is not aware of any instance where this has occurred. Therefore, the extreme option was not selected because of the negative psychological impact to both the woman and infant, as well as the high annual dollar cost.

Regarding the preferred option to enhance communication, although instructions to keep doses to household members and the public as low as is reasonably achievable are currently required for radiopharmaceutical therapy in 10 CFR 35.315(a)(6), there is no requirement specific to the dose from breast-feeding. To enhance communications, amended 10 CFR 35.75(b) will require licensees to provide guidance on the interruption or discontinuation of breast-feeding and information on the rationale for following the guidance. Compliance with the regulation provides NRC with confidence that the licensee will give the instructions to breast-feeding women and it is expected that almost all women will follow instructions to interrupt or discontinue breast-feeding to protect their children from potentially harmful effects. The NRC is not aware of any instances where instructions were given to the woman but she ignored the warning and continued breast-feeding a child. Since the estimated costs per patient for providing instructions and recordkeeping are $22 and $17, respectively (see 4.3.1.1 Estimates of the Direct Costs of Patient Retention), the estimated costs for this option would be about $16,000 per year. Therefore, the option to enhance communication is selected as the preferred option. It should be noted that since the extreme option was not selected for administrations of millicurie quantities, then it would follow that for microcurie quantities it would not be cost effective.

4.2.4.4 Summary of Doses to Breast-Feeding Infants

The dose to the breast-feeding infant can be controlled by giving the woman instructions, as required by the revised 10 CFR 35.75, to discontinue or to interrupt breast-feeding as

* The number of breast-feeding women was determined as follows: 60,000 patients administered millicurie quantities of iodine-131 sodium iodide x 0.135 child bearing age x 0.05 breast-feeding = 405 patients administered millicuries of iodine who could be breast-feeding.

from exposure to a patient who has been administered a radiopharmaceutical, it is necessary to consider both the internal and external dose to the infant from breast-feeding.

4.2.4.1 Internal Dose

The potential internal dose to the breast-feeding infant was calculated for the maximum normally administered quantities of commonly used diagnostic and therapeutic radiopharmaceuticals. The results of the calculations are shown in Appendix B.

The doses can be represented as a range where the range covers the minimum and the maximum transfer of radioactive material from published data. The range is due to individual variability and measurement variability as indicated by concentrations measured in breast milk. Doses were calculated for newborn and one-year-old infants. Since the doses for newborn infants are higher, those doses were used in the analysis. The dose ranges for commonly used radiopharmaceuticals assuming no interruption of breast-feeding are shown in column 3 of Table B.5 (see Appendix B). The radionuclides in the table that are not regulated by the NRC (e.g., Ga-67) are omitted from further consideration in this analysis.

The final rule requires that instructions, including written instructions, on maintaining the doses to other individuals as low as is reasonably achievable be given to the released patient if the dose to another individual is likely to exceed 1 millisievert (0.1 rem). If the dose or the maximum value of the dose range shown in column 3 of Table B.5 exceeds 1 millisievert (0.1 rem), then instructions would be required.

4.2.4.2 External Dose

To determine a realistic estimate of the external dose to total decay to the infant during breast feeding, an occupancy factor must be selected that specifically reflects the variables involved. It can be assumed that the average infant feeds for a period lasting 30 minutes every 3 hours, resulting in an occupancy factor of 16 percent. Breast-feeding requires close contact, the analysis uses 20 centimeters as the distance between the infant and the source. Also, since only the physical half-life is considered, the analysis is conservative. The results are shown in column 4 of Table B.5 assuming no interruption in breast-feeding.

4.2.4.3 Special Considerations for Iodine-131 Sodium Iodide

There are specific issues associated with the administration of iodine-131 sodium iodide in that following both diagnostic and therapeutic administrations, the dose to a breast-feeding child could exceed 5 millisieverts (0.5 rem) if there was no interruption of breast-feeding. In particular, if the woman does not cease breast-feeding after administration of millicurie quantities of iodine-131 sodium iodide, the internal dose to the breast-feeding infant could be large enough to cause the infant's thyroid to be severely damaged, resulting in hypothyroidism. If hypothyroidism were undiagnosed in very young children, severe mental retardation may occur. However, if the patient was provided instructions to discontinue breast-feeding, as well as being advised of the consequences of not following the instructions, the NRC believes that the probability of a woman failing to cease breast-feeding after being administered iodine-131 sodium iodide is small. For example, in 1990 an administered dosage of 185 megabecquerels (5 millicuries) of iodine-131 sodium iodide to a patient resulted in her breast-fed infant receiving an unintended radiation dose of 300 grays (30,000 rads) to the infant's thyroid gland. This dose would result in ablation of the infant's thyroid. This situation was recognized in 2 days, which allowed prompt action to be taken thereby reducing potential consequences such as mental retardation. The NRC is aware of two other cases that occurred during 1991 and 1995. In each of these cases, there was a breakdown in communications, rather than lack of intent to prevent breast-feeding. This rule might therefore be expected to provide a benefit by reducing the probability of a mother breast-feeding after administration of large quantities of iodine-131.

In some cases, instructions to interrupt or discontinue breast-feeding may not be effectively communicated. To deal with this issue, the NRC considered a range of options which varied from

Table 4.8 Maximum Likely Doses to Total Decay to Exposed Individuals from Therapeutic Procedures Assuming No Hospitalization

Therapeutic Procedure (Radionuclide)	Activity Administered (MBq) (mCi)	Gamma Dose Based on Physical Half-Life[1] (mSv) (rem)	Gamma Dose Based on Effective Half-Life[1]: Extrathyroidal Component Uptake Fraction F_1	Thyroidal Component Uptake Fraction F_2	Dose (mSv) (rem)
Hyperthyroidism & Thyroid Ablation[2]					
- iodine-131	370 (10)	1.5 (0.15)	0.40	0.60	0.67 (0.067)
			0.50	0.50	0.61 (0.061)
			0.60	0.40	0.58 (0.058)
			0.70	0.30	0.45 (0.045)
	1,110[3] (30)	4.6 (0.46)	0.40	0.60	2.01 (0.201)
			0.50	0.50	1.83 (0.183)
			0.60	0.40	1.74 (0.174)
			0.70	0.30	1.35 (0.135)
	2,220 (60)	9.2 (0.92)	0.40	0.60	4.02 (0.402)
			0.50	0.50	3.66 (0.366)
			0.60	0.40	3.48 (0.348)
			0.70	0.30	2.70 (0.270)
Thyroid Cancer					
- iodine-131	1,850 (50)	7.6 (0.76)	0.95	0.05	0.62 (0.062)
	5,550[3] (150)	22.9 (2.29)	0.95	0.05	1.86 (0.186)
	7,400 (200)	30.6 (3.06)	0.95	0.05	2.48 (0.248)
Permanent Implant[4]					
- iodine-125	1,110 (30)	0.54 (0.054)	Effective Half-Life Not Applicable to Permanent Implants		
	1,480[3] (40)	0.72 (0.072)			
	1,850 (50)	0.90 (0.090)			
- palladium-103	2,775 (75)	0.29 (0.029)			
	3,700[3] (100)	0.39 (0.039)			
	4,625 (125)	0.49 (0.049)			

[1] Maximum likely dose based on an occupancy factor of 25 percent at a distance of 1 meter.

[2] Doses have been calculated for the four thyroidal uptake fractions that characterize the majority of patients treated.

[3] Typical activity administered.

[4] These dose values account for the 5 HVLs of tissue shielding by the patient and, therefore, are equal to the point source dose in air divided by 32.

Table 4.7 Maximum Likely Doses to Total Decay to Exposed Individuals from Diagnostic Procedures

Examination Type (Radiopharmaceutical)	Activity per Examination[1] (MBq)	(mCi)	Gamma Dose[2] (mSv)	(rem)
Brain				
- Tc-99m DTPA	740	(20)	0.13	(0.013)
- Tc-99m O_4	740	(20)	0.13	(0.013)
Hepatobiliary				
- Tc-99m IDA	185	(5)	0.03	(0.003)
Liver				
- Tc-99m Sulfur Colloid	185	(5)	0.03	(0.003)
Bone				
- Tc-99m Phosphate	740	(20)	0.13	(0.013)
Lung Perfusion				
- Tc-99m MAA	185	(5)	0.03	(0.003)
Thyroid				
- Tc-99m O_4	185	(5)	0.03	(0.003)
- I-131	3.7	(0.1)	0.02	(0.002)
- I-131 (maximum)	370	(10)	1.5	(0.15)
Cardiovascular				
- Tc-99m RBC	740	(20)	0.13	(0.013)
- Tc-99m Phosphate	740	(20)	0.13	(0.013)
- Tl-201 Chloride	111	(3)	0.04	(0.004)
Renal				
- Tc-99m DTPA	740	(20)	0.13	(0.013)
- I-131 Hippuran	9.3	(0.25)	0.04	(0.004)

[1] The activity is the typical quantity administered per examination (see Table 4.2). The maximum diagnostic activity of I-131 is shown because it yields gamma doses exceeding 1 millisievert (0.1 rem).

[2] Calculations assume no biological elimination, no attenuation of gamma rays in air or body of patient, and occupancy factors of 100 percent at a distance of 1 meter for Tc-99m and 25 percent at a distance of 1 meter for I-131 and Tl-201.

150 millicuries). Non-patient family members were assessed for external exposures by means of thermoluminescent dosimeters (TLDs) worn at the wrist for the full duration of exposure. Internal exposure (i.e., thyroid burden) was determined at discrete time intervals by means of a pair of 30-inch NaI crystals. Although all family members proximal to the patient had measurable thyroid burdens, dose estimates in nearly all cases indicate that internal committed effective dose equivalents were always less than 10 percent of the 5-millisievert (0.5-rem) dose limit, even when no precautions were taken, and the external dose substantially exceeded the internal dose.

The investigators also concluded that it " . . . appears certain from our study of these subjects that for spouses, there is a relation between thyroid activity and intimacy. Of the 12 husbands and wives questioned, . . . none were willing to adjust living habits with their spouses because of the radiation therapy. Most, however, are concerned for their children and are willing to listen to suggestions which minimize exposure to their children." While the authors are vague about what they mean by "adjust living habits," it appears that couples are often unwilling to abstain from brief periods of close intimate contact for prolonged periods of time. This should not be a problem because the brief times will be too short to add significant external dose and transfer of contamination is not a significant contributor to internal dose.

Thus, the studies on internal exposures suggest that internal doses from intake of contamination are likely to be much smaller than doses from external radiation and much smaller than the public dose limit. Therefore, internal exposures will not be considered in this analysis other than for the breast-feeding infant.

4.2.3 Estimate of Maximum Likely Doses to Individuals Exposed to Patients

Assessments were made of the doses that could result from exposure to a patient treated with each of the radionuclides used.

4.2.3.1 Diagnostic Procedures

The results of the dose calculations for diagnostic procedures are summarized in Table 4.7. Table 4.7 indicates that, except for some procedures using iodine-131 to detect thyroid cancer, none of the other diagnostic procedures currently being performed have the potential to deliver a 1 millisievert (0.1 rem) dose to an individual exposed to a patient. However, in the case of iodine-131, the effective half-life of the extrathroidal component is much shorter than the physical-life used to calculate doses. Therefore, the dose would be much lower than the value shown in Table 4.7. Since the doses in all cases are much below 1 millisievert (0.1 rem), diagnostic procedures will not be considered any further in this analysis.

4.2.3.2 Therapeutic Procedures

The results of the dose calculations for therapeutic procedures using the physical and effective half-lives (as applicable) are summarized in Table 4.8. All calculations assume an occupancy factor of 25 percent at a distance of 1 meter and immediate release of the patient by the licensee (i.e., no hospitalization). For hyperthyroidism (and thyroid ablation), doses based on effective half-life have been calculated using the four thyroidal uptake fractions that characterize the majority of patients with this disease. Table 4.8 indicates that the model considering biological retention and elimination provides dose estimates that are significantly less than the model that considers physical half-life only.

For the purposes of this analysis, the dose estimates for iodine-131 based on the biological model will be used because this model more closely reflects the behavior of iodine-131 in humans. For permanent implants, biological modeling does not apply. In this case, this analysis uses the dose estimates based on the physical half-life. Only the therapies involving radioiodine would be affected by any of the alternatives under consideration.

4.2.4 Assessment of Doses to Breast-Feeding Infants

If a radiopharmaceutical is administered to a woman who is breast-feeding, a fraction of the quantity administered may be deposited in the breast milk and may be transferred to the breast-feeding infant. In considering the dose to the individual likely to receive the highest dose

Breast Milk. Radionuclide excretion via the mammary gland constitutes a potential exposure pathway to the breast-fed infant. This can be a very important pathway after the administration of radioiodines. Relatively small administrations of radioiodine to a breast-feeding women can cause very large doses to the thyroid of the infant. Cessation of breast-feeding for iodine administrations avoids the potential for thyroid ablation in the infant.

Exhaled Air. Exhalation is the principal pathway for the elimination of radioactive gases such as xenon-133, which is used for lung ventilation tests. Through passive diffusion, unbound iodide in the circulating blood may also be exhaled.

Feces. Radiopharmaceuticals retained or catabolized by the liver may be secreted into the gastrointestinal lumen via the bile. Biliary secretion of a radionuclide may be followed by intestinal reabsorption.

Saliva. Salivary excretion of radionuclides is also proportional to the unbound or diffusible fraction in the plasma. However, salivary excretion is seldom an important elimination route since nearly all saliva is swallowed rather than expectorated.

Sweat. Radionuclides present in the extracellular fluid will tend to be excreted in the sweat in accordance with the fraction that is unbound in the plasma.

Urine. Radionuclide excretion in the urine is the dominant and almost universal elimination pathway.

Vomitus. The occurrence of vomiting is not related to the administration of iodine-131 or any other radiopharmaceutical (personal communication, M. Pollycove, August 1995). Furthermore, vomiting is seldom an important elimination route, since orally administered radiopharmaceuticals such as iodine-131 are rapidly absorbed, within a half hour, by the gastrointestinal system. However, a significant portion of the administered radionuclide could be excreted if vomiting occurs immediately following the administration. In this case the patient typically would not have been released, and the licensee would be able to limit exposure and clean up contamination.

4.2.2.2 Measurements of Internal Exposure

The potential for contamination by patients treated with radioiodine which may serve as a source for internal exposures to others have been assessed for various excreta pathways (BL71, MA73, NI80). Maximum excretion rates are observed shortly after an administered dose. Excretion rates decline rapidly thereafter due to renal clearance and thyroidal uptake. Almost all the excreted activity is excreted in the urine. Contamination through urinary excretion may be readily controlled by cautious but reasonable hygiene practices.

In a thorough study of two patients treated for thyroid carcinomas, Nishizawa, et al. (NI80) observed maximum excretion rates of iodine in exhalation, perspiration, and saliva of 3.2×10^{-6}/hr, 2.4×10^{-6}/hr, and 6.3×10^{-3}/hr of the administered dose, respectively. Thus, the amounts in exhalation and perspiration were very small. The amount in saliva is larger, but transfer of saliva to other people is likely to be limited.

A British study (BU70) estimated thyroid radioiodine activity in 39 subjects who, as family members, were associated with patients treated for hyperthyroidism. Administered quantities ranged from 148 to 740 megabecquerels (4 to 20 millicuries) per patient. Of the 39 patients, 28 were instructed to take precautionary measures to minimize exposure to family members. Eleven patients volunteered to disregard special precautions against contamination and minimizing spousal and family exposure. On the basis of one measurement per family, subject thyroid burdens ranged from less than 37 to 1,110 becquerels (1 to 30 nanocuries) with an average of 259 becquerels (7 nanocuries). Thus, the uptake of radioiodine by family members was only about 1 one-millionth of the administered quantity, and the dose from the uptake was less than 0.01 millisievert (1 millirem) committed effective dose equivalent. This internal dose is negligible compared to the external dose. The authors concluded that contamination is not important and "except where young children are involved, precautions to minimize contamination should be abandoned."

In a 1978 study by Jacobson, et al. (JA78), seven families were studied in which one family member had been treated with iodine-131 doses ranging from 296 to 5,500 megabecquerels (8 to

Table 4.6 Iodine-131 Biological Retention and Elimination Parameters for Hyperthyroidism, Thyroid Ablation, and Thyroid Cancer[1]

	Extrathyroidal Component		Thyroidal Component	
Disease	Uptake Fraction F_1	Biological Half-Life T_{b1} (days)	Uptake Fraction F_2	Biological Half-Life T_{b2} (days)
Hyperthyroidism and Thyroid Ablation	0.10	0.33	0.90	10
	0.20	0.33	0.80	15
	0.30	0.33	0.70	20
	0.40	0.33	0.60	20
	0.50	0.33	0.50	25
	0.60	0.33	0.40	40
	0.70	0.33	0.30	65
Thyroid Cancer	0.95	0.33	0.05	80

[1] Data taken from ICRP Publications 30 (ICRP78), 53 (ICRP87), and 56 (ICRP89), and personal communication, M. Pollycove, March 1996, based on clinical experience.

4.2.1.4 Tissue Shielding for Permanent Implants

In addition to the shielding effects of the source capsule (see 4.2.1.2 Exposure Rate Constant), a significant reduction in the dose and dose rate also occurs from the tissue surrounding the implant. For a prostate implant, tissues that serve to reduce photon flux about the patient include the soft and bone tissues of the thighs, pelvis, buttocks, abdomen, etc. The linear attenuation coefficient and corresponding soft tissue half-value layer for the 27 keV photon of iodine-125 are 0.387 cm^{-1} and 1.8 cm, and for the 21 keV photon of palladium-103, 0.770 cm^{-1} and 0.9 cm, respectively (JOH83).

To assess the impact of tissue shielding by the patient, the medical physicist of the Memorial Sloan Kettering Cancer Center was consulted (personal communication, J. St. Germain, March 1993). Based on empirical assessment involving patients with prostate implants, tissue shielding for iodine-125 is likely to exceed 5 or more half-value layers (HVLs), which would reduce the dose and dose rate by a factor of at least 32. For palladium-103 implants, in which the HVL in tissue is less than 1 centimeter, the shielding afforded by the patient's tissue is even more extensive. For other implants involving the lungs, brain, pancreas, etc., tissue shielding values of similar magnitude can be assumed for an adult male and female. However, for certain implants involving primary cancers of the neck and head, overlying tissues may provide less than 5 HVLs of attenuation. In such instances, it is standard practice to provide the patient with a small portable "shield" which effectively attenuates all emissions (personal communications, C. Jacobs, August 1993, and R. Nath, J. St. Germain and K. Suphanpharian, March 1993). A shield consists of a vinyl sheet impregnated with lead and molded to fit the anatomical surface over the implant.

For the purposes of this analysis, implants will be evaluated considering shielding by tissue equivalent to 5 half-value layers.

4.2.2 Assessment of Internal Exposure

4.2.2.1 Internal Exposure Pathways

Upon oral administration or direct injection into the circulating blood, the radiopharmaceutical undergoes the normal processes of absorption, distribution, and excretion. Removal of radionuclides from the patient's body may follow the pathways of breast milk, exhaled air, feces, saliva, sweat, urine and vomitus.

4.2.1.2 Exposure Rate Constant

The exposure rate constant Γ expresses the dose rate per hour at 1 centimeter in air for a 37-megabecquerel (1-millicurie) point source of a given radionuclide. The exposure rate constants and the physical half-lives of radionuclides used in medicine are shown in Table A.1 of Appendix A.

For permanent implants, a significant reduction in the dose and dose rate occurs from the shielding effects of the source capsule. For iodine-125 and palladium-103 implants, the dose to total decay at 1 meter was calculated using an exposure rate constant corrected for capsule shielding as shown in Table A.1 of Appendix A. The physical characteristics of other radionuclides used in permanent implants (e.g., gold-198 and ytterbium-169) are also given in Appendix A.

4.2.1.3 Biological Retention and Elimination

Effective Half-Life

A licensee may replace T_p in Equations (1) and (2) with the effective half-life T_{eff} of the radioactive material to demonstrate compliance with the dose limit in the revised 10 CFR 35.75. T_{eff} is characterized by T_p and the biological half-life T_b of the radionuclide (which accounts for the biological retention and elimination of the radionuclide from the patient's body) according to the equation

$$T_{eff} = \frac{T_p \times T_b}{T_p + T_b} \qquad (3)$$

Under the final rule a licensee could authorize release on a case-by-case basis based on the biological half-life rather than only the physical half-life of the radiopharmaceutical.

Biological Retention and Elimination of Iodine-131

For iodine-131, biological retention and elimination are characterized by the fractional amounts that reside in the thyroid (i.e., thyroidal component) and in the rest of the body (i.e., extrathyroidal component). Each component has 3 specific fractional uptake and biological half-life, both of which are dependent upon the physical condition of the patient. Table 4.6 provides the uptake fraction and biological half-life for each component with respect to patients being treated for hyperthyroidism (and thyroid ablation) and thyroid cancer. The extrathyroidal and thyroidal uptake fractions for thyroid cancer assume surgical removal of the thyroid gland prior to iodine-131 therapy.

To determine the total dose to an individual exposed to a patient administered iodine-131, considering biological retention and elimination by the patient, Equation 1 must be split into two terms that separately represent the dose contribution from the thyroidal and extrathyroidal components. The following equation was used to calculate the total dose to complete decay assuming an occupancy factor of 0.25 at 1 meter:

$$D(\infty) = \frac{34.6\Gamma Q_o T_{1eff} F_1(0.25)}{(100\,cm)^2} + \frac{34.6\Gamma Q_o T_{2eff} F_2(0.25)}{(100\,cm)^2}, \qquad (4)$$

where T_{1eff} = effective half-life of the extrathyroidal component in days (based on the biological half-life T_{b1} of the thyroidal component),

F_1 = extrathyroidal uptake fraction,

T_{2eff} = effective half-life of the thyroidal component in days (based on the on the biological half-life T_{b2} of the thyroidal component),

F_2 = thyroidal uptake fraction,

Γ = exposure rate constant for a point source, R/mCi-h at 1 cm,

Q_o = initial activity of the radionuclide in millicuries, at the time of release.

This equation is only valid if the release occurs at the time of administration.

Table 4.5 Family Doses from Patients Treated with Iodine-131 for Thyroid Carcinoma

Patient	Total Activity Administered (mCi)	Body Burden at Time of Discharge (mCi)	Measured Doses to Family Members (mrem)	Predicted Dose Based on Occupancy Factor of 25% at 1 meter (mrem)
1	210	25.2	80, 70, 30	386
2	311	26.4	50, 20, 20	404
3	209	18.4	80, 40	282

Source: HA74

when instructions to minimize time spent close to the patient are given.

The occupancy factor of 0.25 at 1 meter is also supported by empirical data. Harbert and Wells (HA74) monitored the external dose of 8 family members of 3 patients treated for thyroid carcinoma using iodine-131. All doses to family members were far below 5 millisieverts (0.5 rem) as shown in Table 4.5. The last column of Table 4.5 provides dose estimates based on the 25 percent occupancy factor in Equation 1. The actual doses are far below the calculated doses for an occupancy factor of 25 percent, indicating that the model generally provides a conservative estimate of the dose.

Harbert and Wells (HA74) also measured the external doses to 11 family members of seven hyperthyroid patients. All doses to family members were far below 5 millisieverts (0.5 rem). In each case, the measured doses were at least a factor of 10 below the doses predicted by Equation 1 using an occupancy factor of 0.25 at 1 meter.

Jacobson et al. (JA78) measured the external doses to 10 family members of 7 iodine therapy patients. In each case except one, the external dose to the family member was below that predicted by Equation 1 using an occupancy factor of 0.25 at 1 meter and well below 5 millisieverts (0.5 rem). In the case of the exception, the family went on a extended vacation spending much of the time together in an automobile. This demonstrates that if reasonable efforts to maintain distance are not made doses can be higher than predicted by Equation 1.

Buchan and Brindle (BU71) monitored the doses of 54 family members of patients who underwent iodine therapy for hyperthyroidism. This study is interesting because no instructions on minimizing dose were given. Thus, the results can be taken to represent the doses that would be received if no instructions were given or if instructions were totally disregarded. The highest measured dose to a family member was 2.7 millisieverts (0.27 rem), below the 5-millisievert (0.5-rem) limit. The effective occupancy factor at 1 meter was less than or equal to 0.25 in 45 of the 54 cases (83 percent). Thus, even in the complete absence of instructions, the occupancy factor at 1 meter was usually less than 0.25.

In conclusion, both empirical measurements and professional judgement support an occupancy factor of 0.25 at 1 meter as a generally conservative value. Using this value in Equation 1 should generally overpredict the dose even if instructions are not given or are not strictly followed. However, higher occupancy factors are certainly possible in situations where instructions are disregarded and are not considered a problem for this rulemaking. The NRC's rulemaking based on Alternative 3 provides an adequate level of protection with a significant margin of safety for those families that make a reasonable effort to follow the instructions. The NRC considers that to be sufficient.

Table 4.4 Number of Annual Therapeutic Administrations in the U.S. (significant gamma-emitting radionuclides only)

Therapeutic Procedure	Radionuclide Employed	Range of Activities Administered (MBq)	(mCi)	Estimated No. of Administrations (per year)
Thyroid Ablation and Hyperthyroidism	I-131	370 - 2,220[1]	(10 - 60)	50,000
Thyroid Cancer	I-131	1,850 - 11,100[2]	(50 - 300)	10,000
Permanent Implant	I-125	1,110 - 1,850[3]	(30 - 50)	2,000
Permanent Implant	Pd-103	2,775 - 4,625[3]	(75 - 125)	1,500
Total				63,500

[1] Based on personal communications, F. A. Mettler, March 1993 and M. Pollycove, January 1996.
[2] Based on personal communications, F. A. Mettler and K.L. Miller, March 1993.
[3] Based on information supplied by implant vendors, August 1993.

To calculate the dose to total decay $D(\infty)$, the regulatory guide uses the following equations. For radionuclides with a half-life greater than 1 day

$$D(\infty) = \frac{34.6\Gamma Q_o T_p (0.25)}{(100\,cm)^2}, \qquad (1)$$

and for radionuclides with a half-life less than 1 day

$$D(\infty) = \frac{34.6\Gamma Q_o T_p}{(100\,cm)^2}, \qquad (2)$$

where Γ = exposure rate constant for a point source, R/mCi-h at 1 cm,

Q_o = initial activity of the point source in millicuries, at the time of release,

T_p = physical half-life in days.

4.2.1.1 Occupancy Factor

Equation 1 assumes, for radionuclides with half-lives greater than 1 day, that the individual likely to receive the highest dose from exposure to the patient would receive a dose of 25 percent of the dose to total decay (0.25 in Equation 1) at a distance of 100 centimeters (1 meter). For radionuclides with half-lives less than 1 day, the factor 1.0 is used in Equation 2 because the assumption that the time that individuals will spend near the patient will be limited is not valid when most of the dose is delivered in a relatively short time.

Doses among individuals who may come in contact with a released patient are highly variable and reflect the crucial, but difficult to define, parameters of time, distance, and shielding. Based on time and distance considerations, it is reasonable to conclude that for the overwhelming majority of released patients, the maximally exposed individual is likely to be the primary care-provider, a family member, or any other individual who spends significant time close to the patient.

Based on time, distance, and shielding factors, which describe normal lifestyles of the U.S. population, it is highly unlikely that doses equal to spending 100 percent of time at a distance of 1 meter from a patient would result to any individual including a patient's spouse. As a standard medical practice, patients undergoing therapeutic treatments with radiopharmaceuticals are given firm instructions, both verbally and in writing, regarding basic principles on how to minimize doses to other individuals.

Given all considerations, a reasonable estimate of the maximal likely dose to an individual exposed to a patient is 25 percent of the dose to total decay at a distance of 1 meter (except for the short-lived radionuclides). The selection of an occupancy factor of 25 percent at 1 meter for estimating maximal likely exposure is based on the authors' professional judgment of time-distance combinations that are believed likely to occur

is nominal due to the presence of a small (less than 3 percent) average photon peak at 300 keV, that can significantly impact radiation doses to individuals in proximity to the patient.

Gold-198 implants have been used in a few instances of prostate cancer (CA88, FR88). The potential advantage of delivering a high dose within a relatively short time, however, is offset by its energetic gamma emissions, which has caused its use in recent years to fall into disfavor and be used only rarely (CA87).

A thorough search of the literature and personal communications with several prominent members of the medical and scientific community (see Acknowledgements) indicates that there is no published data available to quantify the annual number of cancer patients receiving permanent implants. However, the scientific literature and consensus opinion among the experts identified in the acknowledgments to this report does support the following:

1. permanent implants are currently considered an appropriate treatment for only a few sites of solid tumors;

2. among the cancer sites for which permanent implants are currently employed, prostate cancer represents the overwhelming majority;

3. among the 132,000 annual new cases of prostate cancer (ACS93), only a small fraction is treated with permanent implants; and,

4. for the purposes of this analysis, implants involving gold-198 (largely discontinued) and ytterbium-169 (isolated use only) may be ignored.

In the absence of documented clinical data, information was sought from the implant vendors on numbers of administrations and typical activities of radioactive material used per administration. Currently, there are only three vendor sources. Vendor supplied data suggests that approximately 2,000 implants involving iodine-125 are performed annually, at activities ranging from 1,110 to 1,850 megabecquerels (30 to 50 millicuries). For palladium-103, approximately 1,500 implants are performed annually, at activities ranging from 2,775 to 4,625 megabecquerels (75 to 125 millicuries).

4.1.2.3 Summary of Therapeutic Administrations

Table 4.4 summarizes the range of the activities of gamma-emitting radionuclides used in therapeutic administrations and the estimates of the numbers of each therapy currently performed annually.

4.2 Assessment of Doses to Individuals Exposed to Patients Administered Radioactive Materials

To identify the potential impacts associated with each of the alternatives, it is necessary to know the magnitude of doses that could be received by an individual exposed to a patient who has been administered radioactive materials. While exposure can occur via any of the elimination pathways by which radionuclides are removed from the body (e.g., exhalation, feces, saliva, sweat, urine, and possibly vomit), experience indicates that for iodine-131 and other gamma emitters, these pathways will generally be insignificant in relation to the doses that can result from exposure to the direct gamma radiation from the patient, with the exception of intake from the milk in breast-feeding infants. This section of the report assesses the external and internal doses to individuals, including a breast-feeding infant, exposed to patients who have been administered radioactive materials.

4.2.1 Methodology for Calculating External Gamma Dose

The methodology for calculating the external gamma dose from exposure to the released patient is fully described in the associated regulatory guide for the final rule (NRC96). The methodology is based on the one employed in the National Council on Radiation Protection and Measurements (NCRP) Report No. 37, "Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides" (NCRP70).

Only a very limited number of cancer patients have been treated experimentally with radiolabelled antibodies in combination with chemotherapy and external beam irradiation. Among cancers treated are hepatomas, Hodgkin's disease, and non-Hodgkin's lymphoma (LE85, NE90, OR85). In the past, radioimmunotherapy involved the use of iodine-131- and yttrium-90-labelled polyclonal antibodies raised against tumor-associated antigens in a variety of animal species. Based on avidity of tumor cells and exposure considerations of the bone marrow, single doses of 370 to 1,110 megabecquerels (10 to 30 millicuries) have been used.

The development of the hybridoma technique by Kohler and Milstein (KO75) has caused significant shift in radioimmunotherapy. The hybridoma technique allows the development of monoclonal antibodies against tumor-associated antigens. At this time, however, the use of radiolabelled monoclonal antibodies for therapeutic applications has been limited to experimental treatments. At present, these therapies are rarely used and thus have no impact in comparison with the radioiodines.

4.1.2.2 Radioactive Materials Used in Permanent Implants (Brachytherapy)

In-situ radiotherapy may involve permanent implants or brachytherapy. Brachytherapy has been around almost since the discovery of X rays. Brachytherapy can be divided into temporary implantation using high activity sources or permanent brachytherapy using the interstitial implantation of encapsulated radioactivity. In 1911, Pasteau reported the first treatment of prostate cancer by brachytherapy using radium inserted through a urethral catheter (PA11). Currently, iridium-192 (Ir-192) is the radionuclide of choice for temporary implantation. For temporary implantation, patients may be retained in the hospital for reasons that are independent of radiological considerations. Radionuclides used for temporary implants are, therefore, of no concern to this report and will not be discussed further.

Over the past 20 years, several radionuclides have been introduced to brachytherapy, allowing for the permanent implantation of radioactive "seeds." Seeds are miniature capsules that are strategically inserted within a solid tumor and over the period of their decay deliver a lethal dose of radiation to tumor cells within a short distance of the implant. The major advantage of brachytherapy over external irradiation in the treatment of solid tumors is the favorable ratio of dose delivered to tumor cells versus normal tissue. This is particularly true of prostate cancer where the surrounding normal tissue includes the bladder, rectum, and urethra. The presence of these normal tissues limits the dose of external beam radiation therapy that can be administered safely to the prostate.

The radionuclides primarily used in permanent implants are iodine-125 and palladium-103. Less frequently used radionuclides include gold-198 and ytterbium-169 (Yb-169).

The most frequently used radionuclide in permanent implants is iodine-125, which has the advantage of an extremely low energy (27 keV) photon and a physical half-life of 60 days. Besides minimizing dose to surrounding healthy tissue, the low photon energy also limits doses to hospital personnel and others when compared to temporary implants with iridium-192 or permanent implants with gold-198 (CL89, RU92). Although iodine-125 implants are most commonly used to treat cancer of the prostate (DE86, FU91, HE82, MO88, PR92, WH88), they have also been used on a very limited basis for brain tumors (AG92, OS92, SC92), carcinomas of the pancreas (MO92), non-oat cell lung carcinomas (FL92), breast cancers (RU92), and tumors of the head, neck, and eye.

Palladium-103 seeds were developed for use in brachytherapy to reduce some of the problems associated with iodine-125. Its average photon energy of 21 keV is lower than iodine-125, but, given its shorter 17 day half-life, it has a higher initial dose rate. Recently, palladium-103 seeds have been developed with the same physical parameters as iodine-125 seeds to ensure compatibility with the brachytherapy tubes and templates used for iodine implantation (ME90).

Ytterbium-169 has been hailed as a replacement for iodine-125 in brachytherapy. Compared to iodine-125 and palladium-103, it has a slightly higher initial dose rate, and its average 93 keV beta energy allows for a more favorable dose distribution and negligible tissue self-attenuation (PO90). However, its use as a permanent implant

an autonomous proliferation of marrow cells leading to an over production of red blood cells, white blood cells, and platelets. Typically, phosphorous-32 (P-32) is administered intravenously in doses of 111 to 185 megabecquerels (3 to 5 millicuries) per treatment over a period of time with average cumulative quantities of 740 megabecquerels (20 millicuries) per patient.

Bone Therapy

Since the use of radioactive strontium for the treatment of bone metastases was first described in early 1942 (PE42), bone therapy has included other radionuclides. Bone therapy may involve the treatment of primary bone tumors such as osteosarcoma (BL87) in which bone-seeking radiopharmaceuticals are in fact tumor seeking. Bone therapy may also be the treatment of painful skeletal metastases, which may be palliated by bone-seeking radionuclides. Although the literature references the palliative and tumor therapeutic use of these radionuclides (phosphorous-32: CH80, RO77; strontium-89 (Sr-89): BL88, KL87, RO87, ROE90, SI85; rhenium-186 (Re-186): KE87, MA88, SC90; samarium-153 (Sm-153): LA90, TU89), there are no databases and no studies have been performed that would allow quantitative estimates regarding the number of patients given bone therapy with radiopharmaceuticals. These other therapies are performed so seldom that they have negligible impact in comparison with the radioiodines.

Therapy with Radiolabelled Cells

For lymphoid cell malignancies, the tumor cells (i.e., lymphocytes) may retain their ability to migrate and recirculate into the lymphoreticular tissues (i.e., spleen, liver, bone marrow, and lymph nodes). The harvesting, labelling, and reinjection of lymphocytes has been demonstrated to deliver therapeutic levels of radiation doses to tumors of the lymphoreticular system (CO87). Indium-114-labelled lymphocytes have a potential therapeutic role in the management of lymphoma, and clinical studies are underway. Because use of this new therapy is not widespread, its impact may be omitted in this analysis, but it should be noted that use of a dose-based methodology provides a means to determine the quantities for which release may be authorized.

Intra-Arterial Therapy

Some primary tumors as well as metastatic lesions are highly vascularized. Direct arterial injection with insoluble radiolabelled particulates that lodge in arterioles and capillaries of the tumor is the basis of this form of therapy (EH87, ZI84). Insoluble carriers of radionuclides that have been clinically tested include iodine-131-labelled oil contrast medium, iodine-131-lipoidal or -ethiodol (PA87), yttrium-90-glass microspheres (HE88), and yttrium-90 (Y-90) resin particles (ROE90). Since these therapies are so seldom used, their impact may be ignored in this analysis.

Intracavitary Tumor Therapy

For tumors that are spread over the serosal linings of the body cavities or for ascites tumors, one approach to delivering therapeutic doses of radiation is to inject the radiopharmaceutical directly into the body cavity. For this approach, colloids, chelates, and, more recently, monoclonal antibodies labelled with gold-198 (Au-198), phosphorous-32, yttrium-90, or iodine-131 can be used.

Initially, gold-198 colloids were used, but phosphorous-32 is now preferred due to its longer half-life, more energetic beta particles, and the absence of gamma radiation. Intracavitary radionuclide therapy with phosphorous-32 in quantities of 185 to 370 megabecquerels (5 to 10 millicuries) has been applied to malignancies involving the pleural, pericardial, and peritoneal cavities (JA81, KA81, MA78).

More recently, iodine-131- or yttrium-90-labelled tumor-associated monoclonal antibodies have been used in intracavitary therapy (FI89, PE86, RI90) in doses of 740 to 2,220 megabecquerels (20 to 60 millicuries). Superiority of monoclonal antibodies over colloids is expected due to the enhanced affinity of the labelled antibody for the target cells. At present, these therapies are rarely used and thus have no impact in comparison with radioiodines.

Radioimmunotherapy

Radioimmunotherapy involves the use of radiolabelled antibodies directed against tumor-specific antigens such as the carcinoembryonic antigen (CEA) and ferritin.

hormone production of the hyperactive thyroid gland to normal levels. However, experience demonstrated that over a period of years the therapeutically induced euthyroidal condition (normal or healthy thyroid) deteriorated to one of hypothyroidism requiring thyroid hormone replacement therapy. As a result, today hyperthyroid therapy also involves the use of iodine-131 to ablate the thyroid. Approximately 50 percent of all hyperthyroid patients undergo ablation (personal communication, M. Pollycove, January 1996). Typically, activities in the range from 550 to 1,110 megabecquerels (15 to 30 millicuries) are used but about 2 percent of all patients require as much as 2,220 megabecquerels (60 millicuries), the maximum typically administered. Such doses quickly result in the total loss of thyroid function and the patient is given hormone replacement therapy from the onset (personal communications, F. A. Mettler, March 1993 and M. Pollycove, January 1996).

Thyroid Nodules

Single or multiple nodules of sufficient size may cause obvious enlargement of the thyroid. A nodule(s) refers to a replacement of the normal homogeneous cytostructure of the thyroid with a histologic pattern ranging from colloid-filled cysts and colloid adenomas to follicular adenomas. Since the incidence is 4 to 5 times as great in women as in men, and since it develops and progressively increases in size during life, it is most frequently found in females 50 to 70 years of age. It is not uncommon for nodules to remain undetected until a post-mortem examination.

Small nodules in euthyroid subjects require no therapy. If the gland is grossly enlarged and causes a cosmetic problem or tracheal compression, treatment may be indicated along with thyroid hormone replacement therapy.

A small percentage of thyroid nodules tend to produce thyroid hormones uncontrollably and in excess (i.e., the nodule is not under the regulatory control of the pituitary gland and is clinically referred to as toxic nodular goiter). The presence of these autonomously functioning thyroid nodules leads to hyperthyroidism (i.e., thyrotoxicosis).

Toxic nodular goiter, like Graves' Disease, may be treated surgically (thyroidectomy) or by therapeutic dose(s) with radioactive iodine. Estimates of the frequency of radioactive iodine treatment for this condition are included under the estimates for hyperthyroid treatment above.

Thyroid Cancer

There is no nationwide cancer registry that accurately defines the number of new cases of cancer diagnosed each year. However, the American Cancer Society (ACS) annually publishes data on cancer incidence and patient survival based on information provided by the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program.

The ACS estimates of U.S. cancer cases diagnosed for 1992, are based on age-specific incidence rates from the SEER program for 1986 to 1988 applied to the Census Bureau's population projections for 1992. The ACS's estimate of new thyroid cancers in 1992, is 12,500 (ACS93). This report assumes that 100 percent of these cases will be treated by the surgical removal of thyroid gland tissue (i.e., thyroidectomy). Following surgery, about 20 percent of these cases will not require additional thyroid cancer therapy but about 80 percent will require additional therapeutic administrations of iodine-131 to eliminate residual thyroid cancer tissue (personal communication, M. Pollycove, January 1996). Therefore, this report assumes that about 10,000 cases per year will be treated with therapeutic doses of iodine-131.

The quantities of iodine-131 used in thyroid cancer therapy depend upon the type of cancer, the status of the cancer, and the degree of uptake and retention of iodine-131 by residual cancerous thyroid tissue. As a result, current therapeutic quantities range from 1,850 to 11,100 megabecquerels (50 to 300 millicuries) (personal communications, F.A. Mettler and K.L. Miller, March 1993). The typical quantity administered is 5,500 megabecquerels (150 millicuries) (personal communication, M. Pollycove, January 1996).

Therapy for Polycythemia Vera

Since the introduction of radiophosphorus in 1936 patients with polycythemia vera have been treated successfully with this radioisotope to control rather than cure this disease. Polycythemia vera is a relatively rare disease that is characterized by

Table 4.3 Age and Sex Distribution of Patients Having Nuclear Medicine Examinations

Age	Male (%)	Female (%)	Total (%)
< 15	0.9	0.7	1.6
15 - 29	3.3	4.9	8.2
30 - 44	5.2	8.7	13.9
45 - 64	15.8	21.6	37.4
> 64	17.0	21.9	38.9

Source: ME86.

4.1.2 Therapeutic Administrations

Therapeutic use of radioactive materials involves two distinct approaches. The first involves the oral, intravenous, or intracavity administration of a radiopharmaceutical that may subsequently be distributed, concentrated, retained, and eliminated by physical, chemical, and metabolic actions occurring within the body. The second approach involves the implantation of radioactive sources (i.e., seeds) directly into a solid tumor. While both temporary and permanent implants are performed, all patients receiving temporary implants are hospitalized until the implants are removed. Thus, only permanent implants are potentially affected by this rulemaking.

4.1.2.1 Radiopharmaceuticals Used in Therapy

The in-vivo use of radiopharmaceuticals in therapy is based on the ability to differentially deliver lethal radiation doses to the selected target tissue. Most desirable are beta emitters that can deliver intense irradiation of target cells while sparing the surrounding tissues. In contrast to diagnostic procedures for which the gamma emission is essential, the emission of energetic gammas is undesirable for therapeutic purposes since it results in unwanted irradiation of surrounding healthy tissues and doses to individuals in close proximity to the patient. The more significant therapeutic applications are described below.

Hyperthyroidism

Hyperthyroidism is characterized by an increased production of thyroid hormone. Hyperthyroidism is most commonly associated with Graves' Disease. Graves' Disease is an autoimmune disease in which the body's own immune system is directed against cellular and secretary products of the thyroid gland. Hyperthyroidism can also be the result of excessive hormone production by a single "toxic" nodule, thyroid carcinomas, and medications inclusive of potassium iodide.

Hyperthyroidism is not a condition reportable to public health agencies. As a result, data on rates of occurrence and treatment must be inferred. Incidence of hyperthyroidism is reported at 3 per 10,000 adults per year, with peak incidence occurring between 30 and 50 years of age (DG79).

From the most recent data (1990) available from the U.S. Bureau of the Census, it can be assumed that about 75 percent of the U.S. population (approximately 191,500,000 persons) is 18 years of age or older. Thus, it can be estimated that about 57,500 individuals per year require medical treatment for hyperthyroidism.

Although medical treatment may in some cases involve the use of anti-thyroid drugs or surgery, it may be assumed that about 85 percent of the cases of hyperthyroidism are treated with therapeutic doses of iodine-131 (personal communication, M. Pollycove, November 1993). The resulting estimate is about 50,000 treatments per year.

In the past, therapeutic quantities of iodine-131 for treatment of hyperthyroidism tended to be of a magnitude (185 to 550 megabecquerels (5 to 15 millicuries)) that would reduce the

Table 4.2 Estimated Radiopharmaceutical Use for Diagnostic Procedures in the U.S. in 1993[1]

Examination Type (Radiopharmaceutical)	Typical Activity per Examination (MBq)	(mCi)	Number of Examinations (x 1,000)
Brain			
- Tc-99m DTPA	740	(20)	450
- Tc-99m O_4 (Pertechnetate)	740	(20)	450
Hepatobiliary			
- Tc-99m IDA	185	(5)	198
Liver			
- Tc-99m Sulfur Colloid	185	(5)	1,578
Bone			
- Tc-99m Phosphate	740	(20)	2,007
Lung Perfusion			
- Tc-99m MAA	185	(5)	871
Lung Ventilation			
- Xe-133	370	(10)	449
Thyroid			
- Tc-99m O_4 (Pertechnetate)	185	(5)	600
- I-131	3.7	(0.1)	75
- I-123	11.1	(0.3)	75
Renal			
- Tc-99m DTPA	740	(20)	157
- I-131 Hippuran	9.3	(0.25)	105
Cardiovascular			
- Tc-99m RBC	740	(20)	421
- Tc-99m Phosphate	740	(20)	211
- Tl-201 Chloride	111	(3)	421
Tumor			
- Ga-67 Citrate	111	(3)	134
Total			8,202

[1] Based on ME86; and personal communication, F. A. Mettler, March 1993, but adjusted for the 1993 U.S. population.

Table 4.1 Estimated Number of Diagnostic Radiopharmaceutical Procedures Performed in the U.S. Between 1972 and 1982

	Year								
	1972	1973	1975	1978	1980	1980	1981	1982	1982
	Source								
Examination Type	ACR	ACR	ACR	MODS	Johnson	RED 1	RED 2	RED 2	Parker
Brain	1260[1]	1510	2120	1546	870	1176	1038	812	---
Hepatobiliary	26	---	---	---	---	---	109	179	---
Liver	455	535	676	1302	1180	1399	1445	1424	---
Bone	81	125	220	1160	1270	1307	1613	1811	---
Respiratory	332	417	597	1053	830	898	1095	1191	---
Thyroid	356	460	627	699	650	506	664	677	533
Urinary	108	122	154	205	200	164	402	236	---
Tumor	10	14	22	166	130	---	125	121	---
Cardiovascular	25	33	49	160	580	558	708	950	---
Other	686	294	338	120	120	368	---	---	---
Total	3339	3510	4803	6411	5830	6374	7199	7401	7690
	(16)[2]	(17)	(22)	(29)	(26)	(28)	(31)	(32)	(33)

Source: ME85.
[1] Numbers not in parenthesis indicate number of examinations x 1,000.
[2] Numbers in parenthesis indicate number of examinations/1,000 population.

The identity, chemical form, and typical quantity administered of radionuclides used for diagnostic in-vivo procedures are cited in Table 4.2 and reflect values cited by Mettler, et al. (ME86). It can be assumed that the typical quantity per examination has not significantly changed since the time of original publication (personal communication, F.A. Mettler, March 1993).

As the results in Table 4.2 indicate, there are approximately 8.2 million diagnostic examinations employing radiopharmaceuticals performed annually in the U.S. Of these, more than 85 percent use technetium-99m (Tc-99m) as the label, about 5 percent use xenon-133 (Xe-133), about 5 percent use thallium-201 (Tl-201), about 3 percent use iodine-131 or iodine-123 (I-123), and about 2 percent use gallium-67 (Ga-67).

4.1.1.2 Age and Sex Distribution of Patients

The age and sex distribution of the U.S. population that underwent nuclear medicine examinations in 1980, as cited by Mettler, et al. (ME86), is shown in Table 4.3. For the period of observation, more than three-fourths of all nuclear medicine examinations were performed on persons over the age of 45; nearly 40 percent of these patients were 64 years and older. With the exception of the youngest age category, the percentage of females exceeded males.

produced, in which a highly pure target material is bombarded with protons, deuterons, or alpha particles. Many have relatively short half-lives. Some radiopharmaceuticals may be produced by either reactor or accelerator (e.g., palladium-103 (Pd-103) and iodine-125 (I-125)). The choice in production method is dictated by cost considerations and vendor access to a high neutron flux reactor facility. While most iodine-125 has in the past and continues to be produced by reactors, the production of palladium-103 has shifted from reactor to accelerator (personal communication, C. Jacobs, August 1993).

4.1.1 Diagnostic Administrations

4.1.1.1 Estimates of the Number of Diagnostic Procedures Performed

Estimates regarding the frequency and total number of diagnostic nuclear medicine procedures have been reported over the years in several studies reviewed and analyzed by Mettler, et al. (ME85). Among the earliest data reported was a study supported by the American College of Radiology (ACR75), which reflects data collected in 1972 by J. Lloyd Johnson Associates. Additional data for the years 1973 and 1975 were obtained in a similar fashion and also published in the American College of Radiology Manpower Survey (ACR82).

In 1975, the Bureau of Radiological Health (BRH; now the Center for Medical Devices and Radiological Health, CDRH) of the U.S. Food and Drug Administration initiated a pilot study that surveyed information reported by six hospitals to the Medically Oriented Data System (MODS). This project was later expanded to include 26 stratified hospitals that provided data for 1977 and 1978 (FDA85).

Comprehensive data on 1980 diagnostic imaging procedures were obtained by J. Lloyd Johnson Associates by mail questionnaire using a stratified random sample of general hospitals and selected office practices in the U.S. (JO83). The sample included 6,109 hospitals and was estimated to reflect about 90 percent of the total diagnostic imaging examinations. Additional studies were conducted by the BRH for the years 1980, 1981, and 1982. The hospital-based survey was called the Radiation Experience Data (RED 1 and RED 2 studies) (ME85). The RED 1 study examined the computer billing records of 81 hospitals. Data for the subsequent RED 2 study reflect information obtained by mail survey from 500 hospitals.

Data for 1982 were also provided by Parker, et al. (PA84) in which a randomized sample of 10 percent of the U.S. hospitals was surveyed. Although his survey was specifically directed to thyroid examinations, survey data also provided estimates of total examinations.

All of the studies mentioned above are summarized in Table 4.1 and represent hospital data only. However, the exclusion of non-hospital facilities should not significantly affect the accuracy of estimates since less than 1 percent of all nuclear medicine procedures are performed outside hospitals (JO83). Inspection of Table 4.1 reveals several important trends. While the total number of diagnostic procedures has shown a general increase, the number of specific procedures has in some cases dramatically increased or decreased. By 1982, there were fewer radionuclide brain imaging examinations than in 1972, undoubtedly due to replacement by computerized tomography (ME85). For the same period, liver imaging increased tenfold. The largest percent increase involves cardiovascular imaging, which increased from an estimated 25,000 procedures in 1972 to about 950,000 in 1982. Other procedures such as renal, lung, and tumor imaging have experienced only modest increases in numbers.

A search of the open literature revealed no recent comprehensive studies to assess more current U.S. use of radiopharmaceuticals. It is generally thought, however, that the frequency and usage of radiopharmaceuticals have stabilized because of the competing technologies of computerized tomography, magnetic resonance imaging, and gray-scale ultrasound (personal communication, F.A. Mettler, March 1993). For this report, the most recent RED 2 frequency distribution and the cumulative frequency of 16 diagnostic nuclear medicine procedures per one-thousand population will be used to estimate current usage. Table 4.2 provides frequency estimates of diagnostic procedures adjusted to reflect the 1993 U.S. population, which is projected at 256,466,000 by the U.S. Bureau of the Census.

2 OBJECTIVES OF THE RULEMAKING

The objective of this rulemaking is to respond to the three petitions for rulemaking by amending, as deemed appropriate, the patient release criteria in 10 CFR 35.75.

3 ALTERNATIVES

As the petitions and the public comments that were submitted to the Commission on the petitions made clear, some licensees were uncertain about whether dose limits imposed by 10 CFR 20.1301(a) or the patient release criteria established by 10 CFR 35.75 govern patient release. In the Commission's view, 10 CFR 35.75 governs patient release as explained in the Notice of Proposed Rulemaking (59 FR 30724). The public comments received on the three petitions and the Notice of Proposed Rulemaking also made it clear that the majority of commenters favored an annual dose limit of 5 millisieverts (0.5 rem). Given that 10 CFR Part 35 was deemed to be the controlling regulation, the Commission was faced with the decision regarding the regulatory approach to be pursued in 10 CFR 35.75. To evaluate the issues raised by the petitioners and those who commented on the requests made by the petitioners and the Notice of Proposed Rulemaking, the NRC determined that the following alternatives should be evaluated:

- Alternative 1: 1 millisievert (0.1 rem) total effective dose equivalent

  This alternative evaluates a dose limit of 1 millisievert (0.1 rem) to an individual exposed to a patient as the limiting factor for determining when a patient may be released from the licensee's control.

- Alternative 2: ≤ 1,110 megabecquerels (30 millicuries) or ≤ 0.05 millisievert (5 millirems)/hr at 1 meter

  In this alternative, the current patient release criteria in 10 CFR 35.75 are evaluated as the controlling requirements for determining when a patient may be released from the licensee's control.

- Alternative 3: 5 millisieverts (0.5 rem) total effective dose equivalent)

  This alternative evaluates a dose limit of 5 millisieverts (0.5 rem) to an individual exposed to a patient as the limiting factor for determining when a patient may be released from the licensee's control.

4 CONSEQUENCES

To evaluate the impacts of the three alternatives, it is necessary to determine which current procedures involving the administration of radiopharmaceuticals or permanent implants might be affected by the imposition of a 1-millisievert (0.1-rem) total effective dose equivalent dose limit for individuals exposed to released patients. For convenience, procedures involving the administration of radioactive materials to patients may be classified as: (1) diagnostic procedures involving administration of radiopharmaceuticals to obtain information about normal and pathological processes in the patient; or, (2) therapeutic procedures involving administration of radiopharmaceuticals or implantation of a radioactive source to destroy diseased tissue in the patient.

4.1 Current Uses of Radiopharmaceuticals

Radiopharmaceuticals can be defined as "drugs" that are radioactive. Although radiopharmaceuticals, diagnostic or therapeutic, may be classified as drugs, it should be noted that radiopharmaceuticals are not given for the purpose to exert any pharmacological action.

Radiopharmaceuticals are generated from two sources: nuclear reactors and accelerators. Nuclear reactors can produce radionuclides through neutron capture reactions (e.g., (n, γ), (n, p), and (n, α)), as well as by nuclear fission (n, f). Other radiopharmaceuticals are accelerator

1 STATEMENT OF THE PROBLEM

Each year in the U.S., radioactive pharmaceuticals or compounds or radioactive implants are administered to roughly 8 to 9 million patients for the diagnosis or treatment of disease. These people can expose others around them to radiation until the radioactive material has been excreted from their bodies or has decayed away.

NRC's patient release criteria in 10 CFR 35.75, "Release of patients or human research subjects containing radiopharmaceuticals or permanent implants," are as follows: "(a) A licensee may not authorize release from confinement for medical care any patient or human research subject administered a radiopharmaceutical until either: (1) The measured dose rate from the patient or the human research subject is less than 5 millirems per hour at a distance of 1 meter; or (2) The activity in the patient or the human research subject is less than 30 millicuries; (b) A licensee may not authorize release from confinement for medical care of any patient or human research subject administered a permanent implant until the measured dose rate from the patient or the human research subject is less than 5 millirems per hour at a distance of 1 meter."

On May 21, 1991, the NRC published a final rule that amended 10 CFR Part 20, "Standards for Protection Against Radiation" (56 FR 23360). The rule contained limits on the radiation dose for members of the public in 10 CFR 20.1301. However, when 10 CFR Part 20 was issued, there was no discussion in the supplemental information on whether or how the provisions of 10 CFR 20.1301 were intended to apply to the release of patients, thereby creating the need to address this issue.

Because some licensees were uncertain what effect the revised 10 CFR Part 20 would have on patient release criteria, three petitions for rulemaking were received on this issue. The first petition, submitted by Dr. Carol S. Marcus (PRM-20-20, 56 FR 26945), requested that the NRC:

(1) Raise the annual radiation dose limit in 10 CFR 20.1301(a) for individuals exposed to radiation from patients receiving radiopharmaceuticals for diagnosis or therapy from 1 millisievert (0.1 rem) to 5 millisieverts (0.5 rem).

(2) Amend 10 CFR 35.75(a)(2) to retain the 1,110-megabecquerel (30-millicurie) limit for iodine-131 (I-131), but provide an activity limit for other radionuclides consistent with the calculational methodology employed in the National Council on Radiation Protection and Measurements (NCRP) Report No. 37, "Precautions in the Management of Patients Who Have Received Therapeutic Amounts of Radionuclides" (NCRP70).

(3) Delete 10 CFR 20.1301(d) which requires licensees to comply with provisions of EPA's environmental regulations in 40 CFR Part 190 in addition to complying with the requirements of 10 CFR Part 20.

The second petition, submitted by the American College of Nuclear Medicine (ACNM) (PRM-35-10, 57 FR 8282, as revised by PRM-35-10A, 57 FR 21043), requested that the NRC:

(1) Adopt a dose limit of 5 millisieverts (0.5 rem) for individuals exposed to patients who have been administered radiopharmaceuticals.

(2) Permit licensees to authorize release from hospitalization any patient administered a radiopharmaceutical even if the activity in the patient is greater than 1,110 megabecquerels (30 millicuries) by defining "confinement" to include confinement in a private residence.

A third petition (PRM-35-11, 59 FR 37950) dealing, in part, with these same issues was submitted by the American Medical Association (AMA). The main point of the petition is that the radiation dose limits in 10 CFR 20.1301 should not apply to individuals exposed to the patient.

Since the petitions submitted by Dr. Marcus, the ACNM, and the AMA all address the patient release criteria in 10 CFR 35.75, the NRC decided to resolve these petitions in a single rulemaking.

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Tables