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General Comment

See attached file(s)

Attachments

NRC RG 8.39 analysis

Comment Submission – Docket ID NRC-2023-0086

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Comment 1 - Table Format and Typos

1. In RG 8.39 (Rev. 0), the calculated values in Tables 2 and 3, in general, are rounded to two significant figures. Values less than 10 millicuries or 10 millirem per hour are rounded to one significant figure. In the proposed RG 8.39 (Rev.2 - 2023), the values in the corresponding tables are not rounded. The resulting tables reflect an unnecessary level of precision and evoke several questions, including, for Table 2, "Basic Measurement Thresholds for Radionuclides", the ability of our survey meters to read with such precision. Apparently, this issue has been pointed out before given the, semi apologetic, item a. (bottom of Table 2, page 14), as follows: "a. Values listed in the table are calculated and shown for completeness. Values do not consider detection capabilities". The Tables 1 and 2 should be redone with an appropriate amount of rounding.

2. Table 2. Basic Measurement Thresholds for Radionuclides - Page 14 – "e. Dose rate thresholds do not apply to these radionuclides …" is included at the bottom of the table, but no radionuclide in column 1 is labeled with an e.

3. Table 3. Breastfeeding Activity Thresholds Assuming No Breastfeeding Interruption (Page 21), for I-125, at the bottom of the table it is noted, "10 percent of the activity is administered as I-123 (to consider nuclide contamination)". Is this in reference to the fact that one method of producing I-123 results in I-125 as a radionuclidic contaminant? Should the "administered as I-123" be "administered as I-125"?

Two FDA approved manufacturers of I-123 NaI capsules in the United States, Cardinal Health and Curium note in their package inserts (Cardinal Health (4/18) and Curium (12/18)) that the I-123 NaI capsules contain "not less than 97.0 percent I-123, not to exceed **2.9 % I-125**, and not more than 0.1 percent all others (I-121 or Te-121) "**at calibration"** and not less than 87.2 % I-123, **not more than 12.4 percent I-125**, and not more than 0.4 percent all others **at expiration** (30 hours from calibration)". Is the entry "10 percent of the activity is administered as I-123

(to consider nuclide contamination)" a reference to the potential I-125 radionuclidic impurity found in the I-123 NaI capsules? If so, this entry is very confusing and, in addition, why in Column 2 is the "Pharmaceutical" listed as "NaI (CA)" in when the I-125 contaminant is found in I-123 NaI capsules that are used for evaluating thyroid function as well thyroid CA.

3. Page B-6 – last paragraph "dose rate ratio" not "dose rate ration"

Comment 2 – Assume unity for the occupancy factor when patient-specific information is not known

It has always been "two-tiered" approach except that the first tier originally used an occupancy factor of 0.25 as a starting point. Although using an occupancy factor of 1 allows for Table 1 to be extremely conservative, it unnecessarily complicates the release and record keeping for a significant number of therapy patients. The 0.25 is well established and well documented.

The NRC has discussed an occupancy factor of 0.25 in the past, for example:

1. NUREG-1492 Regulatory Analysis on Criteria for the release of Patients Administered Radioactive Materials - Final Report (1997)

S. Schneider, S. A, McGuire

"Base 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 United States 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. The selection of an occupancy factor of 25 percent at 1 meter for estimating maximal likely exposure is based on the authors' professional

judgement of time-distance combinations that are believed likely to occur when instructions to minimize time spent close to the patient are given."

Also from the NRC

"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 over predict 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."

An occupancy factor of 0.25 combined with the following instructions (NUREG 1556, Vol. 9),

1. Maintain a prudent distance from others for at least the first 2 days
2. Sleep alone for at least the first night
3. Do not travel by airplane or by public transportation for at least the first day
4. Do not travel on a prolonged automobile trip with others for at least the first 2 days
5. Have sole use of a bathroom for at least the first 2 days
6. Drink plenty of fluids for at least the first 2 days.

have been the basis for patient release for years and typically significantly overestimate the dose to members of the public. Of course, one must adjust the instructions to increase isolation days if a member of the public must spend more time caring for the patient and of course one increases the isolation days for pregnant women and children (especially held children). And, of course, patients or caregivers who do not follow instructions are at risk of higher exposures. Licensees must choose outpatients wisely and attempt to improve compliance with patient instructions but why overly complicate guidance that has worked well.

Comment 3 - Δ_{pr} - the dose rate constant for a point source at 1 m in mSv/GBq h

The exposure rate constant is a much more practical than the total dose rate constant Δ_p. In addition, if Δ_p is to becomes part of an NRC Regulatory Guide, it should be vetted in a peer reviewed scientific journal.

The Proposed Revision 2 of RG 8.39 (2023) introduces the total dose rate constant, Δ_{pr}. The Δ_{pr} formulation assumes isotropic emission from a point source within the patient and dose delivery to a point in tissue at a distance of 1 m. The source is embedded in an infinitely small sphere of tissue so that bremsstrahlung can be generated. This dose-rate constant is the sum of the primary photon emissions and external bremsstrahlung photons from the electron emissions from positron and negatron decay emissions and from internal conversion and Auger electrons. The low energy cutoff is 10 keV. They use decay schemes from ICRP 107 (2009) and mass-energy absorption coefficients (Hubbell and Seltzer (NIST 1996)).

The authors calculate the bremsstrahlung component. However, they note that compared to primary photon emissions, bremsstrahlung contributions tend to be insignificant unless the radionuclide is a pure beta emitter or when gamma ray and X-ray emissions are very weak. Because the source and receptor are modeled as separate points of tissue in a vacuum, the bremsstrahlung generated by high activity beta emitters in the patient's body is not included in Δ_{pr}. It is interesting that internal bremsstrahlung was not considered as a part of the bremsstrahlung kernel in the calculation of Δ_{pr}. In the definition of the exposure rate constant, the ICRU Report 19 (1971) included internal bremsstrahlung.

RG 8.39 (Rev. 0) was on the right track. Release activities were calculated by using, as a starting point, the method discussed 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". The equation for calculating the accumulated exposure in roentgens included Γ, the specific gamma ray constant for a point source, R/mCi-hr at 1 cm. The NCRP equation was modified to calculate the activities at which patients may be released. The exposure rate constant (R/mCi-h at 1 cm) is used and it is assumed that 1 roentgen is equal to 1 rem. NCRP Report 155 also supports the use of exposure. In the section on Patient Release Criteria, they state "measurements of the amount of photon radiation emitted from patients are generally made with instruments that are calibrated to indicate exposure (X) in roentgens" and that instruments can also be calibrated to indicate air kerma (K_a). They note that the absorbed dose (gray) to tissue can be obtained by multiplying the air kerma by the mean tissue-to-air mass-energy-absorption coefficient for the applicable photon-energy range.

Smith and Stabin (Health Phys. 102:271-291; 2012) used the exposure rate constant in R cm^2 / mCi h at 1 meter. They also use the decay schemes from ICRP

107 (2009) and mass-energy absorption coefficients (Hubbell and Seltzer (NIST 1996)). They include gamma rays, x-rays, and annihilation photons with energies of at least 15 keV. Bremsstrahlung is not included. This seems like a more practical reference for RG 8.39. Exposure rate constants are expressed in Roentgen and in millicurie. Our survey meters are calibrated in Roentgen (e.g., mR/h) and our radiopharmaceutical dosages are measured in mCi. In addition, a point source in air rather than a point source in an infinitely small sphere of tissue seems appropriate given that our are exposure rate measurements are made in air. For conversion to tissue dose, 1 R = 1 rad = 1 rem has been a useful and safe simplification for many years.

Comment 4 – Not Simplified

In SECY-18-0015 – 2018 the NRC staff recommended that the guidance in RG 8.39, as well as the equations and parameters contained/referenced in the guide, should be updated, simplified, and made more clear and explicit.

The guidance in RG 8.39 was updated but it was not simplified, and made more clear and more explicit*. The calculations in Appendix B look more like a laboratory exercise for graduate students rather than a practical guide for patient release. The "Calculational methodologies" using modifying factors for biokinetics, occupancy, geometry, and attenuation based on patient-specific information are not for the faint of heart.

Attenuation modifying factors look interesting but should be tested using actual measurements from patients. There are several articles in referred scientific journals that have patient exposure rate data. And, in addition to articles addressing the exposure rates from I-131 patients, there are several articles for Lu-177 that address attenuation based on patient weight and BMI. A comparison with using the proposed attenuation factors would be very useful. The ACMUI was correct in stating, "The Patient-Specific Modifying Factors and Methods presented in Appendix B, and Example Calculations illustrated in Appendix C, are overly complex and require an unrealistic level of knowledge of extended patient behavior following release."

In addition, for I-131 NaI treatment for thyroid CA, the NRC, in an earlier version of 10CFR35 allowed patient release when the patient retained activity was down to 30 mCi or 5 mR/h at 1 meter. The 5 mR/h at 1 meter reflected patient geometry and attenuation and reflected an effective exposure rate constant of 1.7 mR per hour at 1 meter for the average patient. This value is supported by years of thyroid

CA patient release data. Rather than calculations using "geometric" and "attenuation" modifying factors from mathematical plots, the revision should reference actual published exposure data from patients and suggest effective exposure rate constants for therapeutic radionuclides.

* Expressing all details in a clear and more obvious way, leaving no doubt to the meaning.

Comment 5 – Compliance with Patient Discharge Instructions

The NRC staff identified that the dominant factor in determining both internal and external doses to members of the public is based on the behavior of the patient after release. Thus, assuring compliance with discharge instructions is key to reducing the dose to members of the public. However, discharge instructions need to be as short, clear, and easy to follow. Long complicated instructions can lead to issues with patients struggling to understand the instructions or potentially never engaging with information. It is probably a bit late for this current revision, but formats in addition to oral and written (paper) instructions should be explored (text messages and portals). Assuring patient compliance in the medical arena seems to have evolved beyond just oral and written instructions.

Comment 5 – Hold Time

Release of patients after a hold time based on patient-specific "biological removal" is not a practical option. Although an interesting academic exercise, it is not a practical option. Collecting patient urine using a diagnostic dosage of the treatment radiopharmaceutical is time consuming. For performing patient specific dosimetry it may be worth the effort but for calculating a "hold time" it is a wasteful use of limited resources. At best it would provide an only a rough estimate of a "hold time" and patient release-based measured dose rates would still be required. RG 8.39 (Rev. 0) allowed for delayed release based on a radioactive decay equation. For short-lived radionuclides one did not need to use it and for long-lived radionuclides it was not useful. In a well-run radiopharmaceutical therapy program, a measurement with a survey meter at 1 m would still be taken.

Comment 6 – Release of Patients Based on the Measured Dose Rate

RG 8.39 (Ver. 0) - Page 4, allows that patients to be released based upon measured the dose rate at 1 meter "from the surface of the patient". RG 8.39 (Ver. 2 (2013)) - Page 16, changes this to the dose rate "at the highest measured exposure point"

taken at 1 meter from the patient. This is similar to how we measure the exposure rate at the surface of a radioactive package. However, the package is easier to flip around. Most patient measurements are taken at 1 meter from the front surface of the patient (standing or sitting) or from the side of the patient (if in bed). Although the exposure rate may vary across the surface of the patient, a measurement taken at the level of the umbilicus usually gives a reasonable measurement. Come back in a 30 minutes and it may have changed given biodistribution. From the surface of the patient" seems more appropriate.

Survey meter selection and measurement protocols are important for accurately determining the exposure rate at 1 meter. A section on survey meter selection and accepted patient exposure rate measurement protocols would be a useful addition to the guide given that the use of threshold exposure rates is one of the two major modes of patient release.

Comment 7– Class of Patient

The proposed Regulatory Guide 8.39 Revision 2 (2023) contains no tables for a class-of-patient. This is unfortunate. Table B-1. Uptake Fractions and Effective Half-lives for Iodine-131 Treatments was very helpful. Unfortunately, in Rev. 2 (2023), one has to hunt for any mention of class-of-patient. It is hinted at on Page 30 as follows: "In some situations, a calculation may be case specific for a class of patients who all have the same patient-specific factors and on Page B-9 "Licensees may also assume the patients exhibits slow biological clearance according to the manufacturer of peer reviewed scientific journal article information unless the patient's medical condition or voiding habits affect biological clearance and excretion rates". If Table B-1 is no longer considered correct, update it, but please put it back in. In addition, the change of the Occupancy factor from 0.25 to 1 was a de facto elimination of the concept class-of-patient from the basic equation.