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Dear Sir/Madam:

I am submitting comments on Draft Regulatory Guide DG-8057. I and others have submitted many comments on this regulatory guide over the past 22 years, all in vain. The same comments are repeatedly made, but the scientifically unsupportable issues have never been fixed. I actually reviewed a very early version before this guidance first came out, in which the staff, unable to perform the appropriate mathematical calculations, made the assumption that the patients, who are well hydrated before receiving NaI-131 NaI, and who drink copious quantities of liquid immediately after radiopharmaceutical administration, do not urinate for 24 hours. When I brought this nonsense to the attention of Chairman Ivan Selin, who in addition to earning a Ph.D. in electrical engineering at an Ivy League university earned an Sc.D. in mathematics at the Sorbonne, he immediately trashed it and apologized, stating that "his people did not do their homework". I responded that his people couldn't do their homework, but he vowed to make them perform the calculations correctly. The staff stalled until he left the NRC, then produced guidance similar to the version under consideration. Chairman Shirley Ann Jackson had no ability to understand any of it, nor did NMSS management, and so this highly flawed document was published and has never been fixed. This version is even worse than the preceding ones.

What is somewhat different this time is that an appropriately critical Commission directed the NRC staff to "verify assumptions made concerning patient release guidance". The staff has failed utterly to do this and is basically mocking the Commission. Director Andrea L. Kock evidently has no competence to understand this material and cannot manage something she does not understand. She has been cuckolded by a con artist, and this situation has been going on for 22 years because no one in management or the Commission is competent to perform internal and external radiopharmaceutical dose calculations, interpret the doses using state-of-the-art radiation biology, or understands

medical practice at all. These managers and commissioners are ignorant of the literature in these fields as well. So, they are all eminently connable, because they are ignorant. Kudos to this Commission, who is trying to get an honest response. No such luck.

While I will go into specific details, the Commission should see some of the big picture. Extensive and important pharmacokinetic information and references have been omitted, because these are in complete disagreement with the fake pharmacokinetics invented by Donna-Beth Howe 22 years ago. Donna-Beth fought this patient release rulemaking with all her heart and soul for nearly seven years and has been hell bent since to make it too difficult to use. Excellent studies on actual radiation monitoring of family members of released patients have been completely omitted. These studies show that using correct calculations with no conservatism significantly overestimates the actual radiation dose family members receive. The staff does introduce references finding 10 exp -6 contamination levels, but then uses 10 exp -5 (1000% higher than the data require) in order to be "conservative". The rule sets a limit of 500 mrem to breastfeeding infants, but the staff only includes data for a 100 mrem limit (a 500% more restrictive level), even though the ACMUI unanimously voted to include the 500 mrem limits in this document, and Dr. Zanzonico of the ACMUI performed the calculations for both the 100 mrem and 500 mrem limits, and they are in the ACMUI subcommittee report. In addition, while a footnote in the NRC document states that the values for 100 mrem come from the calculations done for that report, not all of them do, and it is purposefully misleading. This was pointed out at the ACMUI meeting on the draft NRC document and the Chair of the ACMUI promised it would be fixed, but it was only partly fixed.

The real question is why we need this guidance at all as it is so uniformly scientifically unsupportable. Competent physicians don't need your guidance at all. We have our own sources of real science, not your fake science. The 800 pound gorilla in the room, carefully omitted from this draft regulatory guide, is the Radiation Absorbed Dose Assessment Resource, RADAR. This free web site contains a great deal of useful information, including information pertinent to patient discharge. It contains a tutorial about how to perform the dose calculations, complete with problems and an answer sheet. This tutorial was developed at the request of Edgar Bailey when he was the Chief of the Radiological Health Branch of the Department of Health Services of the State of California. The RADAR web site also contains an online interactive dose calculator, where physicians input patient-specific or average values for a two-compartment calculation model that then calculates the dose to others from radioactive patients using state-of-the-art methods including patient body shielding and the patient as a line source instead of a point source. **Last year the RADAR web site received 66,000 hits.** Competent professionals know where to get reliable information, and they vote with their mice.

Data on breast-feeding interruption recommendations are available from other excellent sources, and Dr. Zanzonico's calculations will one of these days appear in a respected, peer-reviewed journal. We don't need your flawed and incomplete copy of them. Information on radioactive corpses has been available since at least 1970, in NCRP

Report no. 37. The NRC has added nothing except paperwork and bureaucracy, but nothing of substance.

The NRC practice of presenting seriously flawed information for the sake of conservatism is completely inappropriate. If the NRC does anything at all, and I don't think we need it, it should present the most accurate calculations and information possible. It is the choice of the Authorized User Physician to add conservatism if he/she thinks it is wise to do so. The NRC does not seem to understand a dose of 500 mrem. It keeps talking about using ALARA to reduce this supposedly dangerous dose. The average natural background dose in the United States is 300 mrem. There are places in Colorado where natural background is 500 mrem above the 300 mrem average. Colorado has the highest natural background in the country, but instead of dropping like flies, Colorado is usually tied for the third lowest cancer death rate in the United States. The NRC permits embryos and fetuses of declared pregnant workers to receive 500 mrem, which it considers safe. After WWII, the Atom Bomb Casualty Commission began studying the Hiroshima and Nagasaki survivors, the so-called Life Span Study (LSS). The LSS had two control groups, people who were not in those cities and received no radiation from the bombs, and people in those city areas who received up to 500 mrem external radiation (the LSS has ignored radiation dose from internal emitters from "black rain"). The group with up to 500 mrem had lower cancer rates than the control group with no radiation.

It does not seem possible to get competent staff in the non-medical "Medical" Program at NRC. Twenty-two years of failure is enough. If this severely flawed regulatory guidance is "acceptable to the staff", then I think that the staff is not acceptable to us. The Commission should get rid of the people who participated in the writing of this rubbish.

I am appending a paper published in Health Physics criticizing an earlier version of this regulatory guidance, but all its observations are still pertinent because nothing has been fixed. I suggest that members of the Commission read the paper carefully. Obviously, the staff and management won't, as they have received copies of it for years but ignore it completely.

When President Trump took power, he promised to "drain the swamp". It is my opinion, and that of many other competent nuclear medicine professionals, that the non-medical "Medical" Program staff is eminently appropriate for drainage.

I doubt that the Commissioners are aware that shortly before Chairman Ivan Selin left the NRC, he offered to take language to Congress to end NRC's statutory authority over medical affairs because it was such a hopeless and useless mess. Unfortunately, Society of Nuclear Medicine (SNM) (now Society of Nuclear Medicine and Medical Imaging, SNMMI) leadership was too cowardly to pursue this, and nothing happened. Not long afterwards, the National Academy of Sciences-Institute of Medicine (NAS-IOM) completed its study of the NRC "medical" program (Radiation in Medicine-A Need for Regulatory Reform, National Academy of Sciences, 1996), and recommended that Congress remove NRC's statutory authority in medical affairs as NRC's program was

dangerous to patients as well as physicians. I strongly suggest that the Commissioners read this. NRC paid for it, so it must have copies available. Subsequently Chairman Shirley Ann Jackson sent a letter to the governor of each state, summarizing the findings of the NAS-IOM and asking if the governor was in agreement. Unfortunately, the letter Jackson sent was fraudulent, completely mischaracterizing the findings of the NAS-IOM, and I suppose Jackson figured that no governor would actually read the 300-page NAS-IOM report and realize that her letter was fraudulent. Actually, I think the letter was written by a staff person in the non-medical "Medical" Program, and Jackson merely signed it. Anyway, the governors said no, they wanted to keep the NRC medical program and the nuclear medicine organizations did not attack the fraud and nothing ever happened except that NRC decided to rewrite its medical regulations to make "improvements". The new regulations were pretty much the old regulations, but the poison pill at the end was shocking. The NRC very quietly, with no discussion and no public comment, basically made the new regulations an item of compatibility with the Agreement States and wiped out all the Agreement States medical programs, all of which were superior to NRC's. There was no coordinated fight against this underhanded attack.

Also, sometime in the 1990s, one of the non-medical "Medical Program" staff members pushed through a radical change in the membership of the ACMUI. This was not put up for public comment or discussion, either, but the ACMUI, which had been composed of multiple board-certified nuclear medicine physicians, a brachytherapist, a top medical physicist, and the nation's leading nuclear pharmacist, now had its number of board certified nuclear medicine physicians severely reduced by substituting individuals without useful nuclear medicine expertise. NRC added a representative from a patient advocacy group, an FDA representative, an Agreement State representative, a nuclear cardiologist, a hospital administrator, etc., none of whom have significant expertise in nuclear medicine and its related science. The idea was to reduce the ACMUI to a generally useless advisory committee which could then be ignored, which has happened. For example, the ACMUI recently voted to end the current rulemaking expanding Authorized User Physician status for therapy beyond nuclear medicine and radiology physicians to other physicians "to enhance patient access". However, the NRC ignored the ACMUI and this rulemaking continues.

The goal of NRC's Medical Program has to be the provision of high quality nuclear medicine procedures and the safe use of radioactive material. That is the goal of every other country's program. Why is it that the Commission is unaware of how every other first world country and many third world and developing countries, such as India, have achieved this goal? Their solution is simple. In all these other countries, you cannot practice any or all of nuclear medicine unless you are board certified in nuclear medicine. By restricting the practice to highly qualified individuals you optimize the probability of high quality medicine and the safe use of radioactive material. The NRC could do the same with some grandfathering provisions. Throw away all of Part 35 and substitute that to practice any or all of nuclear medicine the physician has to be board certified in nuclear medicine, and keep the requirement that to practice any or all of radiation oncology using radioactive material the physician must be board certified in radiation oncology. We don't need licensing at all. The origin of

licensing is that after WWII all the reactors were owned by the Atomic Energy Commission (AEC), and the thought was that they couldn't just give away government-owned radionuclides. So, they "licensed" their use. However, today none of our radionuclides come from AEC (now Department of Energy) reactors, and licensing has taken on a malevolent life of its own. Control freak regulation by licensing does no good for anyone, except for the control freak. Licensing has no worthwhile function and should be ended. Unbudget all of your Medical Program staff and inspectors. Without all the reams of useless record-keeping and paperwork there is nothing for inspectors to inspect, and we need no inspections at all. In the unlikely event of any real radiation safety issue, the NRC could retain some board certified nuclear medicine physicians and radiation oncologists as consultants. However, these issues are very unusual; I can think of three that occurred during the last 30 years (Indiana, PA, Tripler Army Base, and the Rb-82 generator), but NRC not only did not help these situations, but made them worse.

Specific Comments

P.6 bullet 7: This is an utterly preposterous section. For radionuclides with a half-life that is less than or equal to one day, it is actually easier, not more difficult, to justify an occupancy factor of 0.25 and perhaps less, because the patient is in the nuclear medicine clinic and their contacts can be controlled. In addition, it is virtually impossible for reasons of pharmacokinetics, biochemistry, and dosimetry that a therapy radiopharmaceutical with a half-life of one hour or less and moderate to strong gamma radiation accompanying most or all disintegrations will ever be developed. The NRC staff does not appear to understand enough nuclear medicine to realize this.

P.8 Section 1.1: This whole section is ridiculous. In the first place, keeping calculations for NRC inspection makes no sense because the NRC staff does not understand how to do these calculations and can't check anything. Second, it is likely these days that many or most calculations are done using the RADAR interactive dose calculator. So go check RADAR, but quit bothering the physicians with this asinine paperwork.

P.11 Table 2: I don't think that Ag-111, Au-198, I-125, Re-186, Re-188, Sc-47, Se-75, Sn-117m, or Yb-169 have been used in decades. On the other hand, F-18, N-13, O-15, Ga-68, Lu-177, I-124 and Ra-223 are missing from the table. Doesn't the NRC know what radionuclides are being used in nuclear medicine?

P.12 Paragraph 1: The regulatory limit is 500 mrem, not 100 mrem. The NRC is fraudulently stating that the dose to a nursing infant must be under 100 mrem. The NRC ought to know its own regulatory limit.

P.12and 13, Table 3: The ACMUI subcommittee report submitted newly calculated breastfeeding interruption limits. It also included a reference to older limits being used at Memorial Sloan Kettering Cancer Center. That reference is not to be substituted for the newer calculations submitted by the subcommittee (basically Pat Zanzonico's subcommittee calculations). In addition, some values in DG-8057 do not correspond to the subcommittee's calculations. For example, I-123 MIBG should not be 24 hours. It

should be "no interruption". Ga-67 and Zr-89 do not state to what they are attached. Lu-177 is not used as a diagnostic agent. As a therapeutic agent, the interruption should be for 27 days, not complete cessation. For Zr-89 whatever, it should read 21 days, not 28 days. Ga-68 octreotide should read Ga-68 all radiopharmaceuticals, and it should read no interruption, not 4 hours. I-124 NaI should read 28 days, not complete cessation. Note that all these NRC errors err on the conservative side, even though the calculations themselves are very conservative. But they are blamed on the subcommittee report, not the NRC staff.

The most egregious problem is that the NRC has failed to include the 500 mrem calculations, all of which are in the subcommittee report. The ACMUI voted unanimously to include the 500 mrem calculations, but the NRC staff ignored them.

P. 13 Footnote b, at the end, the NRC states, "For Tc-99m radiopharmaceuticals, rather than a radiopharmaceutical-specific interruption period, a single 24-hour interruption period is recommended. Although this time interval may be longer than necessary for some Tc-99m labeled radiopharmaceuticals, it is compliant with the 0.1-rad dose limit and simplifies the guidance, thereby avoiding confusion and reducing the likelihood of error." First, the limit is 0.5 rad, not 0.1 rad. Second, suggesting that physicians are too dumb to read a number for a specific radiopharmaceutical off a table and are prone to making errors doing so is insulting and ridiculous. Although NRC staff can't copy numbers correctly into a table, physicians are a lot smarter. The 0.5-rad limit for each Tc-99m radiopharmaceutical should be included so no one is unnecessarily conservative.

P.14 Paragraph 3: The NRC cautions against the volatility of I-131 NaI. This was only an issue in past years when the NRC made a rule forbidding adding any chemical to an FDA-approved radiopharmaceutical. All American manufacturers of I-131 NaI, as solution or capsules, were made extremely basic and EDTA was added to chelate metal ions that might contribute to volatility. This decreased the volatility from 10-15% (roughly) to 10 exp -6 for the solution and 10 exp -5 for the capsules (measured in several radiopharmacies). FDA did approve a NaI-131 from France that was not stabilized against volatility. The FDA assumed the radiopharmacy would take care of it. In fact, the radiopharmacies *were* taking care of it until NRC passed this foolish rule. Volatile I-131 NaI was all over the place until the rule was rescinded after much effort (it took about five years of hard work). At present, and for many years, all preparations of I-131 NaI are stabilized against volatility, and therefore volatility is no longer a problem.

P.15 Item e: Competent nuclear medicine physicians know enough to not give I-131 NaI to dying patients. It doesn't do any good and leaves us with a radioactive corpse. Once in a great while a patient given I-131 NaI dies of something other than thyroid cancer (for example, a heart attack), but this is extremely unusual. Competent nuclear medicine physicians need to then measure the exposure rate from the corpse at a meter with an ion chamber, and then do the calculations and decide about burial or cremation, and whether the body needs to be stored in the morgue before either procedure. It's not difficult. Usually at least several days have gone by from I-131 NaI administration to death, and most of the I-131 has been excreted.

P. 16 (1): Children and pregnant women may receive up to 500 mrem just like other adults, and in almost all cases may remain at home. If the child is very young and requires a great deal of care, then another caregiver needs to be present. But they can be in the same household.

P.16 (2): If the patient is making food for others, explain that I-131 comes out in sweat and give the patient multiple pairs of disposable gloves that can be reused after rinsing. It might not be practical to try to stop the patient from cooking for others.

P.16 (3): No data have ever been shown to require separate bathrooms. I-131 as iodide is soluble in water, so using the sink, the shower, or the toilet should not preclude others from using the same facility. A few loose atoms here and there are not important.

P.16 (4): No data have ever been shown that requires separate washing, in a sink or a dishwasher. Do *not* encourage the patient to use disposables, because these end up in garbage dumps that may be monitored for radioactivity and although the levels of radioactivity are not dangerous, the people who run garbage dumps don't understand that and there can be problems.

P.16 (6): No data have ever been shown that requires separate washing of clothing.

While numerous nuclear medicine documents throughout the years have promoted separate washing of eating utensils and clothing, and the use of separate bathrooms, and the NRC may reference these, none have ever shown data supporting such advice.

P.16 last paragraph: It is not necessary to dwell on measures to limit contamination of objects and surfaces. This contamination level has been measured and is very low and not a problem.

P.17 Paragraph 2: In the event a patient becomes pregnant around the time of I-131 NaI administration, 5 rem is too low a dose for reporting. A dose like this may occur with a dose of I-131 NaI for hyperthyroidism. But this is too low a dose to have an effect on the embryo (Schwulst SJ and Son M: Diagnostic imaging in pregnant patients with suspected appendicitis. JAMA 322(5):455-456, 2019). All the NRC accomplishes is making the patient fearful. A dose of 50 rem would be a scientifically more reasonable reporting limit, if we need one at all. What can NRC do about it?

P.17 Patient Instructions: a, b, and d are not necessary, and in c remove disposable kitchen utensils. In i, omit preparing food, but state that if preparing food it's a good idea to wear disposable gloves.

P.18 k: Children and pregnant women do not require different instructions than other adults at this low radiation dose.

P.18 Paragraph 2: Licensees do not usually meet family members of patients to be treated, and only occasionally meet caregivers. Talking to family members and caregivers about the possible death of a patient does not make sense. Dying patients belong in the hospital and should not receive I-131 NaI.

P.18 2.3.4: No paperwork documenting patient acknowledgement of instructions is necessary. The contents of 2.3.4 is not a regulatory requirement, and this extensive paperwork is an excessive burden with no value.

P.18 2.4: The Authorized User (AU) Physician should be handling this, rather than the RSO (who is often another physician). Autopsies are very rarely done on these patients.

P.19 2.5: I am not aware of any long-lived contaminant in any therapeutic radiopharmaceutical that is present in high enough concentration to be an actual hazard. If NRC has no actual examples, this paragraph should be removed.

P.20 3.1: NRC states that the record should include the patient's identifier. At the end of section 3.1 NRC states that the records should not contain the patient's name or any other information that could identify the patient. These are mutually exclusive requirements. The patient's hospital number could be used to identify the patient. Just exactly what does the NRC want us to use? Please give specific examples. In addition, the word "RADAR" should be enough for a and c.

P.20 3.2: Needed corrections to Table 3 were mentioned previously.

Appendix A, P.A-1: As noted previously, these radionuclides are very dated.

Appendix B, P.B-1, B-1.1: As mentioned previously, it makes no sense to use an occupancy factor of 1.0 instead of 0.25 just because the radionuclide has a half-life under an hour. In addition, the continuation of this paragraph on the next page states that an occupancy factor of 0.25 may be used with the *physical half-life*. This is fraudulent. An occupancy factor of 0.25 may be used with the *effective half-life*.

Appendix B, P.B-2 Paragraph 2: This is utter nonsense. The AU decides on the occupancy factor, not the NRC.

Appendix B, P.B-2, B-1.2: This is concocted NRC garbage and an effort to thwart the use of the occupancy factor with irrelevant variables. It has no basis in science and has not been used for 22 years and should be rejected in its entirety. Remove this entire section, with the fraudulent example as well. Scientifically correct examples are on RADAR.

Appendix B, Page B-3 B-2: The equations for effective half-life are correct. However, the entire section following on p. B-4 is fraudulent. Absorption from the stomach is very rapid, and urinary hold-up is not an issue because patients start off well hydrated and drink copious amounts of water after dose administration and urinate very quickly and frequently. This has been pointed out to the NRC for 22 years, to no avail. The fake

pharmacokinetic claim of the NRC continues to pollute this document, with NRC refusing to accept published pharmacokinetic data, such as found in ICRP No. 53 and its references. Example 2 is worthless and should be thrown out. More extensive scientifically correct examples, including answers, are in RADAR.

Appendix B, Page B-5, Table B-1: The NRC calculates an effective half-life of 5.2 days for the thyroid fraction of a hyperthyroid patient with an 80% uptake. The NRC states that it used data from a paper by Stabin MG, et al. However, in looking at the data in that paper, the biological half-life of the thyroidal fraction in a patient with 80% thyroidal uptake did not average 15 days, as NRC states, but averaged 10 days, and the effective half-life is not 5.2 days, as NRC states, but 4.4 days. Example 3 is worthless and should be omitted.

Appendix B, P.B-6, B-3: This section is fraudulent because the literature shows an assumed fractional intake of 1x10 exp-6 and NRC uses 1x10 exp-5, 1000% too large.

Conclusion

The gross inaccuracies of this draft regulatory guide expose an individual at NRC trying very hard to make 10 CFR Part 35.75 extremely difficult to use by concocting fraudulent material. The fact that other staff members who worked on this document and NMSS management who approved this document did not point out the fraud and insist upon changes illustrates the general degree of incompetence of both staff and management.

This entire draft regulatory guide should be discarded, the existing guide should be discarded, and the NRC should not try to write an accurate one, because it cannot do so despite having tried to for 22 years. Competent AU physicians do not need NRC's worthless "guidance". Incompetent AU physicians should not have been licensed by the NRC at all.

Thank you for your attention and consideration.

Sincerely,

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Paper

LICENSEE OVER-RELIANCE ON CONSERVATISMS IN NRC GUIDANCE REGARDING THE RELEASE OF PATIENTS TREATED WITH ^{131}I

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Abstract—**Medical licensees are required to comply with U.S. Nuclear Regulatory Commission (NRC) regulations pertaining to the release of patients administered radioactive material. However, use of the associated NRC guidance expressed in NUREG-1556, Volume 9, is completely optional and has been shown to be overly conservative. Rigid adherence to the guidance recommendations has placed an undue burden on nuclear medicine therapy patients and their families, as well as licensees responsible for ensuring compliance with NRC requirements. More realistic guidance has been published by other responsible professional societies and will be presented in this work. These more realistic calculations allow for higher releasable activity levels than the widely adopted NUREG levels, particularly for thyroid cancer patients. The guidance-suggested releasable activity limit is similar to our calculational result for hyperthyroid patients, 2.1 GBq (57 mCi) compared to 2.3 GBq (62 mCi), but is significantly lower for thyroid cancer patients, 6.6 GBq (179 mCi) vs. 16.9 GBq (457 mCi) using the regulatory definition of the total effective dose equivalent (TEDE). Higher limits are both possible and reasonable, if the permissible extra-regulatory definition of the TEDE is used in which the effective dose equivalent (EDE), rather than the deep-dose equivalent (DDE), is determined. We maintain that professionals evaluating compliance with the NRC requirements for patient release, pursuant to 10 CFR 35.75, should use the procedures presented here and not rely automatically on the NUREG.**

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Key words: nuclear medicine; dosimetry; safety standards; medical radiation

INTRODUCTION

U.S. NUCLEAR Regulatory Commission (NRC) regulations for the release of patients administered radioactive material, pursuant to 10 CFR 35.75, authorize patient release according to a dose-based limit, i.e., the dose to other individuals exposed to the patient (U.S. NRC 1997). The dose-based limit, which replaced the activity- or dose-rate-based release limit, <1,110 MBq (30 mCi) or <0.05 mSv h^{-1} (5 mrem h^{-1}) at 1 m in 1997, better expresses the NRC's primary concern for the public's health and safety and makes good scientific sense. A licensee may release patients, regardless of administered activity, if it can be demonstrated that the total effective dose equivalent (TEDE) to another individual from exposure to a released patient is not likely to exceed 5 mSv (0.5 rem).

Individuals exposed to released radionuclide therapy patients can potentially receive radiation doses by two distinct sources: external exposure and internal intake. The TEDE concept makes it possible to combine these dose components in assessing the overall risk to the health of an individual. The TEDE, pursuant to 10 CFR 20.1003, is equal to the sum of the deep-dose equivalent (DDE), due to external exposure, and the committed effective dose equivalent (CEDE), due to internal intake. Thus, TEDE = DDE + CEDE.

U.S. NRC regulations, pursuant to 10 CFR 20.1101, require that applicants and licensees develop, document, and implement operating policies and procedures as part of an overall radiation protection program that will ensure compliance and the security and safe use of licensed materials. These radiation protection policies and procedures for their implementation are neither detailed in the regulations nor required to be submitted as part of the license application (Siegel 2004). Some practitioners have developed their own radiation protection programs, but most have relied on model procedures published by the NRC in guidance documents. There is no question that licensees must comply with NRC regulations, but doing so by adopting regulatory guidance is not necessary. The NRC will accept alternative approaches, but a large number of licensees know that use and adoption of NRC-proposed guidance will clearly provide an acceptable approach to the NRC and many licensees are not able to devote the time or resources

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necessary to establish their own alternative implementing procedures and policies. Although guidance documents do not contain regulatory requirements, if licensees commit to following these procedures they will become conditions of their licenses.

We do not take issue here with the NRC regulations related to patient release. We do, however, note that the associated NRC guidance for licensee compliance with 10 CFR 35.75 as promulgated in NUREG-1556, Vol. 9, Rev.1, Appendix U, *Model Procedure for Release of Patients or Human Research Subjects Administered Radioactive Materials*, has been shown to be overly conservative and places a high burden on nuclear medicine therapy patients and their families, as well as on licensees who adopt the guidance. A series of published studies and guidelines issued by other responsible professional societies has provided guidance in compliance with the applicable NRC requirements at a clearly lower burden to all parties involved. Substitution of these approaches for those in the NUREG will provide a clear benefit to patients and their families, and will make the job of licensees easier as well. We will confine our arguments to the release of patients who have received oral $Na^{131}I$ for the treatment of thyroid cancer or hyperthyroidism, but note that the rationale of the arguments applies also to other radionuclide therapy agents.

The purpose of this work is to critically evaluate the compliance-implementing procedures as proposed in the NUREG and to suggest alternative compliance methods. We examine the guidance methods to assess the external dose component, the internal dose component, and thus the TEDE, and by so doing, demonstrate that the guidance procedures are overly conservative and introduce an unnecessary regulatory burden not codified in NRC requirements. We propose alternative procedures to enable licensee compliance with 10 CFR 35.75, and we recommend that all licensees use these procedures instead of automatic reliance on the NRC guidance documents.

PATIENT RELEASE BASED ON NRC GUIDANCE

The external dose component (DDE)

NUREG-1556, Vol. 9, Rev.1, Appendix U (U.S. NRC 2005) provides model procedures for calculating the external dose to others from exposure to released patients. According to the NUREG, compliance with the NRC regulatory dose limit requirement can be demonstrated by licensees by either: (1) using provided default tables for activity or dose rate at 1 m for a variety of radionuclides; or (2) performing a patient-specific dose calculation.

Use of the "default" values. The "default" patient release values are based on integration of external dose to a maximally exposed individual to total decay after release of patients receiving radioactive material. Two very conservative assumptions are involved in modeling this dose in NUREG-1556, Vol. 9: 1) that the activity in the patient can be represented as an unshielded point source; and 2) that removal of activity from the patient is only due to physical decay of the radionuclide involved. This approach fails to consider the distributed nature of most radiopharmaceutical agents and does not account for the often significant biological elimination that diminishes activity levels in the patient (and thus dose rates outside the patient) over time. This method is highly over-conservative for ^{131}I sodium iodide. Therapy patients receiving ^{131}I do not retain 100% of the radioactivity for the physical half-life of the radionuclide (8 d); rather, a significant portion of the administered activity is not taken up by the thyroid gland and is rapidly excreted. For ^{131}I, the 5 mSv dose limit is predicted in the NUREG to be achieved with an administered activity of 1,221 MBq (33 mCi), or a dose rate of 0.07 mSv h^{-1} (7 mrem h^{-1}) at 1 m, for both thyroid cancer and hyperthyroid patients, representing a value of 4.10×10^{-3} mSv MBq^{-1} (15.2 mrem mCi^{-1}) (this dose per unit administered activity is an order of magnitude higher than if a patient-specific dose calculation is performed; compare to values given below based on eqn 1). In essence, use of NRC "default values" for $Na^{131}I$ represents a return to the historical "30-mCi rule" and is quite regressive, especially since there is no credible origin or scientific basis for this rule (Siegel 2000). Further, empirical data recently obtained by measurement of the dose received by family members of thyroid cancer patients receiving ^{131}I (Grigsby et al. 2000) support and confirm that the use of a 1,221 MBq activity limit for all patients is overly conservative.

Clearly, use of only simple knowledge of administered activity, without consideration of such things as radionuclide clearance from the body and the patient's lifestyle, require issuance of patient instructions to maintain doses to others that are as low as is reasonably achievable (ALARA) that would have to be in place for an extremely long time. Rational analysis suggests that the use of overly simplistic "point-source-radioactive-decay-only" models will significantly overestimate doses to others from $Na^{131}I$ (and many other radiopharmaceuticals), and this has been confirmed by actual measurements (Grigsby et al. 2000). Thus, there is no question that patient-specific dose calculations that would permit the release of patients from radioactive isolation with more than 1,221 MBq must be performed for ^{131}I therapy patients to provide a more complete and appropriate

estimation of dose (and patient release instructions) to individuals likely to be exposed to the patient.

Use of the patient-specific dose calculation. The "patient-specific" dose equation provided in the NUREG that can be used to estimate the likely external exposure to total decay, i.e., DDE at infinite time or $DDE(\infty)$ in mSv (mrem), to an individual from a released radionuclide therapy patient receiving oral $Na^{131}I$ for thyroid cancer and hyperthyroidism is:

$$DDE(\infty) = [34.6\Gamma Q_0]/(100\text{ cm})^2\{E_1T_p(0.8)[1 - e^{-0.693(T_{NV})/T_p}] + e^{-0.693(T_{NV})/T_p}E_2F_1T_{1eff} + e^{-0.693(T_{NV})/T_p}E_2F_2T_{2eff}\}, \quad (1)$$

where:

- 34.6 = conversion factor of 24 h d^{-1} times total integration of decay (1.44);
- Γ = exposure rate constant for an unshielded point source, for ^{131}I = 0.595 mSv cm^2 MBq^{-1} h^{-1} (2,200 mR cm^2 mCi^{-1} h^{-1});
- Q_0 = administered activity in MBq (mCi);
- E_1 = occupancy factor for first 8-h non-void period = 0.75;
- T_p = physical half-life in days = 8.04 for ^{131}I;
- 0.8 = an assumed factor indicating that 80% of the administered activity is removed from the body only by the physical half-life of ^{131}I during the non-void period;
- T_{NV} = non-void period in days = 0.33 (8 h);
- E_2 = occupancy factor from 8 h to total decay = 0.25;
- F_1 = extrathyroidal uptake fraction = 0.20 in hyperthyroid patients = 0.95 in thyroid cancer patients;
- T_{1eff} = effective half-life of extrathyroidal component = 0.32 d in hyperthyroid patients = 0.32 d in thyroid cancer patients;
- F_2 = thyroidal uptake fraction = 0.80 in hyperthyroid patients = 0.05 in thyroid cancer patients; and
- T_{2eff} = effective half-life of thyroidal component = 5.2 d in hyperthyroid patients = 7.3 d in thyroid cancer patients.

Eqn (1) represents the dose to an individual likely to receive the highest dose from exposure to released ^{131}I patients as it is taken to be the dose to total decay. The equation contains 3 components: (1) a non-void period for the first 8 h after administration; (2) an extrathyroidal component from 8 h to total decay; and (3) a thyroidal component from 8 h to total decay. Eqn (1) can be solved for the external dose component per unit administered activity, Q_0.

In the case of thyroid cancer patients:

- $DDE(\infty)/Q_0$ (mSv MBq^{-1}) = 2.06×10^{-3} {0.135 + 0.0739 + 0.0887} = 6.12×10^{-4} mSv MBq^{-1}; and
- $DDE(\infty)/Q_0$ (mrem mCi^{-1}) = 7.61 {0.135 + 0.0739 + 0.0887} = 2.27 mrem mCi^{-1},

where the percentages of the total dose due to the non-void, extrathyroidal, and thyroidal components are 45%, 25%, and 30%, respectively.

In the case of hyperthyroid patients:

- $DDE(\infty)/Q_0$ (mSv MBq^{-1}) = 2.06×10^{-3} {0.135 + 0.0739 + 0.0887} = 2.39×10^{-3} mSv MBq^{-1}; and
- $DDE(\infty)/Q_0$ (mrem mCi^{-1}) = 7.61 {0.135 + 0.0156 + 1.01} = 8.84 mrem mCi^{-1},

where the percentages of the total dose due to the non-void, extrathyroidal, and thyroidal components are 12%, 1%, and 87%, respectively.

These 2 equations can be solved for the maximum allowable administered activities for authorizing patient release based on the 5 mSv regulatory dose limit. Eqn (1) can also be solved for the maximum allowable dose rates at 1 m, given by $\Gamma Q_0/(100\text{ cm})^2$. These values are shown in Table 1.

These activity limits, as well as those in later sections, can be applied to all patient releases. According to the NUREG, the parameter values in eqn (1) are "acceptable" values (e.g., the occupancy factors and the representative uptake fractions and effective half-lives) to be used in class-specific dose calculations for patients with thyroid cancer and hyperthyroidism. Thus, individual dose calculations need not be performed on a case-by-case basis for these patients, unless a specific patient's situation warrants the use of parameter values different from those used in eqn (1). For example, the licensee may select more realistic uptake fraction and effective half-life values from the scientific literature or choose to measure the biokinetics in individual patients, measure the dose rate and/or use an occupancy factor <0.25, if appropriate. In these cases, as stated in the NUREG, a patient-specific calculation would be required

Table 1. Maximum activities and dose rates at 1 m for authorizing patient release for thyroid cancer and hyperthyroid patients (based on eqn 1).

	Activity in GBq (mCi)	Dose rate in mSv h^{-1} (mrem h^{-1})
Thyroid cancer	8.2 (221)	0.49 (49)
Hyperthyroidism	2.1 (57)	0.12 (12)

in place of the use of the class-specific values given in Table 1.

This class-specific approach is highly conservative and unnecessarily restrictive. Several assumptions were made by the NRC in assigning values to the parameters used in eqn (1). The two biggest contributors to the conservatism are: 1) use of the exposure rate constant, which is an unshielded point source value; and 2) use of an 8-h non-void period and associated 0.75 occupancy factor. Since a patient is not adequately represented as an unshielded point source (particularly with respect to their extrathyroidal activity distribution), an exposure rate constant accounting for radionuclide distribution and patient attenuation must be used since without such considerations unrealistic and unnecessarily conservative results will be obtained, perhaps as high as a factor of 2 (Sparks et al. 1998; Siegel et al. 2002a).

During the first 8 h after administration, 80% of the ^{131}I administered is assumed to be removed from the body at a rate determined only by its physical half-life to account for the time of the ^{131}I to be absorbed from the stomach to the blood and the holdup of iodine in the urine while in the bladder. The remaining 20% of the administered activity must be associated with some unknown physiological mechanism as it is unaccounted for during this initial 8-h non-void period. It is important to note that there are no scientific data to support the notion of a "non-void" period of any significant length. Patients are hydrated before the administration of $Na^{131}I$ and are strongly urged to drink plenty of fluids for several days afterwards. Patients often void before even leaving the Nuclear Medicine service, and frequently thereafter. $Na^{131}I$ is absorbed within 10–15 min after an oral administration (Loevinger et al. 1988) and upon reaching the blood is immediately filtered out by the kidneys; with large fluid intakes, the patient may typically void hourly.

A recent international controlled study of iodine biokinetics in radioiodine therapy of thyroid cancer (Hänscheid et al. 2006) indicated that the whole body retention of radioiodine was generally described by a biexponential activity-time curve, with no significant activity excretion time delay, based on whole-body probe and gamma camera scanning measurements. The total body residence times obtained (mean value of 24.1 h in hypothyroid patients) were in good agreement with the value of 23.2 h, a value that would be calculated based on the NRC guidance representative values for a 2-component total body retention curve involving extrathyroidal and thyroidal components. In addition, this latter total body residence time of 23.2 h with an associated activity excretion of 48% at 8 h, corresponding to generally hypothyroid patients, is in excellent agreement with that reported in MIRD Dose Estimate Report No. 5 (Berman et al. 1975) for the case of a maximum thyroid uptake of 5% in euthyroid patients. It should be noted that mean whole-body residence times have been observed to be longer for hypothyroid (24.1 h) than euthyroid (17.3 h) patients (Hänscheid et al. 2006). Thus, established models and recent data indicate that approximately 50% of the administered activity is excreted from the body during the NRC's presumed non-void period in the case of a thyroid cancer patient.

The inclusion of the non-void component in eqn (1) has a profound effect on the estimated dose an individual is likely to receive, particularly from released thyroid cancer patients. As demonstrated above, 45% of the total dose is attributable to the non-void component for these patients (Siegel 1999); thus, its inclusion represents an additional factor of 2 conservatism as the 8.2 GBq activity limit in Table 1 is likely to result in a dose of only 2.75 mSv, equal to 3.35×10^{-4} mSv MBq^{-1} (1.24 mrem mCi^{-1}). In support of this claim, a regulatory analysis on the revised 10 CFR 35.75 completed in 1996 (Schneider and McGuire 1996) made no mention of an initial non-void period and estimated, for example, that based on use of only a two-component model consisting of thyroidal and extrathyroidal biokinetics, the maximum likely dose to total decay to individuals exposed to a thyroid cancer patient would be 2.48 mSv from a 7.4 GBq activity administration, equal to 3.35×10^{-4} mSv MBq^{-1} (1.24 mrem mCi^{-1}). For hyperthyroid patients, inclusion of the non-void component has minimal effect (as demonstrated above, the percent of the total calculated dose attributable to this initial non-void period is 12%) and is really not necessary as it is mathematically redundant; approximately 14% of the administered activity is excreted from the body at 8 h based on the NUREG representative uptake fractions and effective half-lives.

Direct measurements are the best way to obtain the dose any individual is likely to receive based on the reality of daily life. Dosimeter measurements obtained in 65 household members of 30 patients who received outpatient ^{131}I therapy for thyroid carcinoma indicated that the measured radiation dose was on average a factor of 10 lower than the radiation dose predicted based on eqn (1) (Grigsby et al. 2000). These empirical data are further evidence demonstrating the overly conservative nature of the dose calculation as implemented through use of eqn (1).

The internal dose component (CEDE)

NRC guidance in NUREG-1556, Vol. 9, Rev.1, Appendix U uses the following equation for the likely internal dose component (i.e., CEDE) for individuals who may come in contact with a released patient who received oral $Na^{131}I$:

- CEDE (Sv) = Q_0 (MBq) × 10^{-5} × 1.43 × 10^{-2} Sv MBq^{-1}; and
- CEDE (rem) = Q_0 (mCi) × 10^{-5} × 53 rem mCi^{-1}, (2)

where 10^{-5} is the NRC assumed fractional intake and 1.43 × 10^{-2} Sv MBq^{-1} (53 rem mCi^{-1}) is the dose conversion factor to convert an intake of ^{131}I in MBq (mCi) to a CEDE in Sv (rem). It is obvious from this equation that the predicted internal dose component per unit activity will always be a constant value of 1.43 × 10^{-4} mSv MBq^{-1} (0.53 mrem mCi^{-1}). Thus, unlike the guidance for the external dose component, which permits variability and thus patient-specificity, only a fixed or case-specific internal dose component is considered for both thyroid cancer and hyperthyroid patients.

A common "rule of thumb" is to assume that no more than 1 millionth of the activity being handled will become an intake to an individual working with the material. This heuristic was developed for cases of worker intakes during normal workplace operations, worker intakes from accidental exposures, and public intakes from accidental airborne releases from a facility (Brodsky 1980), but it does not specifically apply for cases of intake by an individual exposed to a patient. Admittedly, there are limited data for thyroid uptakes in family members exposed to Na^{131}I patients. Two studies performed in the 1970's (Buchan and Brindle 1970; Jacobson et al. 1978) on the intakes of individuals exposed to patients administered ^{131}I indicated that intakes were generally on the order of 1 millionth of the activity administered to the patient and that internal doses were far below external doses. Based on these two studies, NUREG-1492 (Schneider and McGuire 1996), the regulatory analysis for 10 CFR 35.75, concluded that internal doses are likely to be much smaller than external doses and much smaller than the public dose limit, and therefore did not consider internal exposures in their analyses. In addition, the National Council on Radiation Protection and Measurements (NCRP) 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."

As given in eqn (2), NRC guidance recommends use of 10^{-5} for the assumed fractional intake. According to NRC, this value was chosen in order to account for the most highly exposed individual and to add a degree of conservatism to the calculation. However, no such "highly exposed" individual has ever been found, and no documentation substantiates that this "factor of 10" conservative approach is advisable, necessary, or accurate.

The total effective dose equivalent (TEDE)

Summing the values of $DDE(\infty)$ per unit administered activity, based on the patient-specific dose calculation given by eqn (1) and the CEDE per unit administered activity values based on eqn (2), the TEDE per unit administered activity is given as follows.

In the case of thyroid cancer patients:

- TEDE/Q_0 (mSv MBq^{-1}) = 6.12 × 10^{-4} mSv MBq^{-1} + 1.43 × 10^{-4} mSv MBq^{-1}; and
- TEDE/Q_0 (mrem mCi^{-1}) = 2.27 mrem mCi^{-1} + 0.53 mrem mCi^{-1}.

In the case of hyperthyroid patients:

- TEDE/Q_0 (mSv MBq^{-1}) = 2.39 × 10^{-3} mSv MBq^{-1} + 1.43 × 10^{-4} mSv MBq^{-1}; and
- TEDE/Q_0 (mrem mCi^{-1}) = 8.84 mrem mCi^{-1} + 0.53 mrem mCi^{-1}.

Using this approach, the internal dose component will always be 23% (1.43/6.12) and 6% (1.43/23.9) of the external dose component for thyroid cancer and hyperthyroid patients, respectively, irrespective of the administered activity.

NRC guidance states that when the internal dose component is less than 10% of the external component, it does not need to be considered (U.S. NRC 2005). Thus, internal contamination will never have to be considered for hyperthyroid patients whereas the summation of internal and external dose components will always be required for thyroid cancer patients if a patient-specific dose calculation is performed. In the case of the NUREG default-value approach, the TEDE is assumed to be equal to the external dose "because the dose from intake by other individuals is expected to be small." The values in Table 1 are therefore valid for the release of hyperthyroid patients, e.g., the maximum releasable activity is 2.1 GBq. However, the Table 1 values cannot be used for thyroid cancer patients, e.g., the maximum releasable activity of 8.2 GBq is not applicable. The dose calculation approach will always result in a maximum releasable activity for thyroid cancer patients of 6.6 GBq (179 mCi) (the constraint that the CEDE is always 23% of the $DDE(\infty)$, which forces a DDE of approximately 4.05 mSv and an associated CEDE of 0.95 mSv to be in compliance with the 5 mSv TEDE limit). Although not applicable, if the same logic is followed, but this time with the constraint that the CEDE always be 6% of the

DDE(∞), the maximum releasable activity for hyperthyroid patients would be 2.0 GBq (53 mCi).

The advice requiring inclusion/exclusion of the internal dose component in the NUREG for the TEDE calculation has no basis in regulatory requirements; in fact, it adds an "extra-regulatory" burden on licensees. It is also incorrect as it may violate NRC regulations. For example, Example 4 in the NUREG uses the "default" value external dose of 5 mSv for a 1,221 MBq ^{131}I administration and determines a CEDE of 0.17 mSv. Since the internal dose is only 3% of the external dose, it is stated that the CEDE determinations are never necessary in the TEDE calculation if the default-value approach is taken; however, the TEDE will exceed the regulatory limit of 5 mSv (5 mSv + 0.17 mSv = 5.17 mSv) and the licensee would be in violation of NRC regulations.

The maximum activity release values given in this section are based on the assumption that the "patient-specific" dose calculation approach (use of eqns 1 and 2) used for determination of the TEDE is accurate. As described above, the NUREG approach is, at the very least, unjustifiably conservative, potentially by a factor as high as 4 in the case of thyroid cancer patients. The conservatism is due mainly to the assumption of an essentially non-existent non-void period, the use of an exposure rate constant representing an unshielded point source for the extrathyroidal activity biodistribution, and the use of an intake value of 10^{-5}. The more appropriate maximum fractional intake value of 10^{-6} should be used since this level is seldom, if ever, exceeded by the reported data. This "seldom exceeded" criterion was used in the NUREG in Footnote 1 of Table U.6 for selection of the thyroid uptake fraction in the hyperthyroidism case. The impact of these assumptions in the case of hyperthyroid patient release is much less significant since we have shown that the majority of the calculated total dose to others (i.e., 87%) is due to the thyroidal component.

When data are not available, use of conservative calculations may be reasonable, as they can identify or rule out a potential problem and may be used to add a margin of safety to procedures that do not have well-defined outcomes. However, when data are available, as they are in the case of patients treated with Na^{131}I for thyroid cancer and hyperthyroidism, the overuse of conservatism does not serve the goal of radiation protection practice, which is to provide optimization of radiation doses (economic, social, and other factors considered) within a system of dose limitation. Massive conservatism violates the principle of optimization and places an undue burden on those enforcing dose limits and on those subject to the limitations; in this case, radionuclide therapy patients and their families. Importantly, the regulations, pursuant to 10 CFR 35.75(a), do not require any calculational conservatism, let alone that promulgated in the NUREG; licensees must only demonstrate that the TEDE to any other individual from exposure to a released patient is not likely to exceed 5 mSv. Maintaining this calculated dose to others ALARA is the purpose of the required instructions, pursuant to 10 CFR 35.75(b). In point of fact, a patient receiving 1,221 MBq of ^{131}I for hyperthyroidism can potentially expose individuals to a larger radiation dose than a patient receiving 7.4 GBq of ^{131}I for thyroid cancer if appropriate instructions are not provided, due to the much longer retention of a significant fraction of ^{131}I in the body in the former case.

Therefore, we recommend that licensees perform more realistic calculations (e.g., use of an appropriate shielding factor for the exposure rate constant, no non-void period, use of a fractional intake value of 10^{-6}) and not simply automatically adhere to the approaches provided in the NUREG in order to permit realistic release limits and patient instructions that still are clearly in compliance with NRC regulations.

PATIENT RELEASE BASED ON SNM/ACNP GUIDANCE

One alternative approach to that given in NRC guidance that can be used for patient release has been proposed in a Society of Nuclear Medicine and American College of Nuclear Physicians (SNM/ACNP) guidebook (Siegel 2004). Using eqn (1), but substituting an exposure rate constant equal to 0.459 mSv cm^2 MBq^{-1} h^{-1} (1,700 mR cm^2 mCi^{-1} h^{-1}) (Carey et al. 1995), a non-void period of 1 h, and an occupancy factor of 0.25 during this period, the maximum allowable activities and dose rates for authorizing patient release are given in Table 2.

In our opinion, licensees can quite justifiably use the values in Table 2 as their basis for patient release. The maximum activity and dose rate values are higher in Table 2 than in Table 1 due to the use of less conservative and more realistic parameter values. It should be noted that this method assumes that the TEDE is equal to the external dose. This is because the internal dose was

Table 2. Maximum activities and dose rates at 1 m for authorizing patient release for thyroid cancer and hyperthyroid patients (based on SNM/ACNP guidebook).

	Activity in GBq (mCi)	Dose rate in mSv h^{-1} (mrem h^{-1})
Thyroid cancer	18.2 (493)	0.84 (84)
Hyperthyroidism	3.0 (80)	0.14 (14)

considered to be negligible due to the use of an intake factor of 10^{-6}. This is certainly a preferred approach to that given in the NUREG as it results in more realistic activity and dose rate release limits.

PATIENT RELEASE BASED ON METHODOLOGY DESCRIBED IN THIS WORK

We recommend that the patient-specific dose calculation be performed as follows:

$$\text{TEDE} = DDE(\infty) + \text{CEDE},$$

where:

$$DDE(\infty) = [34.6\ \Gamma Q_0]/(100\ \text{cm})^2 \times 0.25\{F_1 T_{1\text{eff}} \times 0.6 + F_2 T_{2\text{eff}}\} \quad (1a)$$

and

$$\text{CEDE} = Q_0\ (\text{MBq}) \times 10^{-6} \times 1.43 \times 10^{-2}\ \text{Sv MBq}^{-1}. \quad (2a)$$

Eqn (1a) includes only 2 components representing the thyroidal and nonthyroidal biokinetic components (the non-void period has been eliminated), the factor 0.6 represents a more accurate correction to the exposure rate constant given in eqn (1) (Siegel et al. 2002a) for the extrathyroidal component (the exposure rate constant is appropriately applicable only to activity confined to the thyroid gland), and F and T_{eff} are the same as those used in eqn (1) for thyroid cancer and hyperthyroid patients. Note that eqn (2a) recommends use of an intake factor equal to 10^{-6}.

Upon rearrangement and summation of eqns (1a) and (2a), the TEDE per unit administered activity is as follows.

In the case of thyroid cancer patients:

- $\text{TEDE}/Q_0\ (\text{mSv MBq}^{-1}) = 2.82 \times 10^{-4}\ \text{mSv MBq}^{-1} + 1.43 \times 10^{-5}\ \text{mSv MBq}^{-1}$; and
- $\text{TEDE}/Q_0\ (\text{mrem mCi}^{-1}) = 1.04\ \text{mrem mCi}^{-1} + 0.053\ \text{mrem mCi}^{-1}$.

In the case of hyperthyroid patients:

- $\text{TEDE}/Q_0\ (\text{mSv MBq}^{-1}) = 2.16 \times 10^{-3}\ \text{mSv MBq}^{-1} + 1.43 \times 10^{-5}\ \text{mSv MBq}^{-1}$; and
- $\text{TEDE}/Q_0\ (\text{mrem mCi}^{-1}) = 7.99\ \text{mrem mCi}^{-1} + 0.053\ \text{mrem mCi}^{-1}$.

In both cases the internal dose component does not have to be taken into account, as it will always be less than 10% of the external dose component. The maximum activities for authorizing patient release are 17.7 GBq (481 mCi) and 2.3 GBq (63 mCi) for thyroid cancer and hyperthyroid patients, respectively, based on the DDE. A better approach would be to neglect the "10% of the external dose" NUREG guidance as discussed above and include the internal dose component in the calculation. The maximum activities for authorizing patient release are then 16.9 GBq (457 mCi) and 2.3 GBq (62 mCi) for thyroid cancer and hyperthyroid patients, respectively, based on the TEDE.

These activity limits are still conservative as they are based on the use of the DDE for the TEDE, which does not account for attenuation and scatter within the exposed individual (pursuant to 10 CFR 20.1003, the DDE is the dose equivalent at a tissue depth of 1 cm), and therefore only approximates the likely surface entrance dose to the exposed individual (Sparks et al. 1998). In situations where doses are calculated rather than measured, we recommend that licensees use the EDE in place of the DDE in the TEDE determination, and according to an NRC Regulatory Issue Summary (U.S. NRC 2003) no prior NRC approval is required. The EDE has been reported to be a factor of 0.6, on average, less than the DDE for ^{131}I (Sparks et al. 1998). Using this permissible extra-regulatory definition of the TEDE (i.e., TEDE = EDE + CEDE), the maximum activities for authorizing patient release are 27.2 GBq (739 mCi) and 3.8 GBq (103 mCi) for thyroid cancer and hyperthyroid patients, respectively. The administered dosages for these patients will virtually always be less than these activity limits, indicating that all patients are immediately releasable based on patient-specific calculations according to NRC regulations.

NRC regulations pursuant to 10 CFR 35.75(b) also require that released individuals be provided with instructions on actions recommended to maintain doses to others ALARA. Pursuant to 10 CFR Part 20.1003, ALARA means making every reasonable effort to maintain exposures to radiation as far below the dose limits as is practical. NRC has stated that "dose" in this context means the TEDE. Internal and external doses are not minimized separately, and ALARA efforts should be directed at minimizing their sum, the TEDE. Since the internal dose is such a small fraction of the external dose, the TEDE can be most effectively minimized by efforts to minimize the external dose component through adequate patient instructions. A three step approach is necessary (Siegel et al. 2002a):

1. An evaluation of individual's living and working conditions must be performed to ascertain whether or not the patient can be safely released;
2. An appropriate patient-specific dose calculation should be performed to ensure that no individual will likely be exposed to a dose in excess of 5 mSv; and
3. Written, not just oral, instructions that are simple and clear must be provided so that the patient can limit the radiation dose to others to as low as reasonably

achievable. The Authorized User (AU) physician must be satisfied that patient compliance with these instructions is highly likely.

Each of these three steps is equally important. Just because patients are releasable based on the patient-specific dose calculation does not mean that these patients should necessarily be released. For example, it is important to know if infants, young children, or pregnant women reside in the released patient's home (or are likely to come in contact with the patient) in order to conclude that the patient should be released and/or in order to provide meaningful instructions to minimize exposure to these individuals, which in the professional opinion of the AU physician will be comprehended by the patient and likely complied with. Any licensee releasing patients without giving due consideration to the three steps above should be considered to be not in compliance with 10 CFR 35.75 [licensees must also maintain a record of the basis for authorizing patient release pursuant to 10 CFR 35.75(c)]. Clearly, regulations will not prevent all unintended exposures. The underlying premise of NRC regulations is that AU physicians will understand radiation safety principles and practices and will make appropriate decisions. Licensees have certain responsibilities and need to implement policies and procedures to ensure adequate and effective radiation safety practices.

The NUREG is of limited value in providing appropriate and adequate patient instructions. As a good example, the suggested durations of the instructions provided for the occupancy factor selection in Section B.1.2 do not differentiate between thyroid cancer and hyperthyroid patients. As demonstrated by our analyses of eqn (1), 30% of the total dose is attributable to the time period from 8 h post-administration to total decay in the case of thyroid cancer patients, while 87% of the total dose is delivered over this same time period for hyperthyroid patients. It seems appropriate, therefore, that the times necessary for the relevant instructions to remain in effect should differ for these two groups of patients. Finally, it is important to note that radioactive articles in the household trash of patients are sometimes appearing at solid waste landfills that have installed radiation monitors to prevent the entry of any detectable radioactivity. Even though the radioactivity levels potentially contained in any household waste of patients released in accordance with 10 CFR 35.75 pose an insignificant hazard to the public health and safety or to the environment, professionals can take steps to avoid issues with landfill owners and operators and even individual states (Siegel and Sparks 2002). It is probably wise to instruct patients to avoid or minimize use of items that cannot be disposed of via plumbing (toilet, sink, dishwasher, washing machine), such as plastic utensils and paper plates (Siegel 2004).

SUMMARY OF MAXIMUM RELEASABLE ACTIVITIES

Table 3 summarizes the maximum releasable activities for both hyperthyroid and thyroid cancer patients presented in this work.

All values in Table 3 were determined based on an occupancy factor of 0.25 for the extrathyroidal and thyroidal components. If a licensee determines that a lower occupancy factor (e.g., 0.125) is justified for a particular patient, then even higher activities would be calculated.

THE LICENSEE'S ROLE IN PATIENT RELEASE

More realistic calculations allow for even higher releasable activity levels, particularly for thyroid cancer patients. The guidance approach involving patient-specific dose calculations results in a releasable activity limit similar to our calculational approach for hyperthyroid patients (2.1 GBq vs. 2.3 GBq), but the activity limit

Table 3. Summary of maximum releasable activities.

Method (TEDE definition)	Activity in GBq (mCi)	
	Hyperthyroidism	Thyroid cancer
1. NUREG		
a. Default value (TEDE = DDE)	1.2 (33)	1.2 (33)
b. Calculation (TEDE = DDE)	2.1 (57)	8.2 (221) (NA)[a]
c. Calculation (TEDE = DDE + CEDE)	2.0 (53) (NA)	6.6 (179)
2. SNM/ACNP		
Calculation (TEDE = DDE)	3.0 (80)	18.2 (493)
3. This work		
a. Calculation (TEDE = DDE)	2.3 (63)	17.7 (481)
b. Calculation (TEDE = DDE + CEDE)	2.3 (62)	16.9 (457)
c. Calculation (TEDE = EDE + CEDE)	3.8 (103)	27.2 (739)

[a] NA = not applicable.

for thyroid cancer patients is significantly lower (6.6 GBq vs. 16.9 GBq) using the regulatory definition of the TEDE. The similarity in the hyperthyroid case is due to the fact that the majority of the estimated dose to others is due to the thyroidal component and the overly conservative assumptions made in guidance have minimal effect. If a licensee chooses to replace the DDE with the EDE, then the release limits are even higher (27.2 GBq and 3.8 GBq for thyroid cancer and hyperthyroid patients, respectively) and now significantly different even for hyperthyroid patients. Thus, it is reasonable to ask the question, "Why have licensees broadly adopted the NUREG guidance for patient release?"

Given that regulatory requirements for patient release have historically been unrealistically conservative and that the current NUREG guidance procedures are still overly conservative, particularly with regard to thyroid cancer patients, it is difficult to justify providing such information to nuclear medicine physicians to determine patient release limits. Perhaps many licensees have adopted these procedures because most of their clinical treatments involving $Na^{131}I$ can be managed under the guidance release limits of either: 1) 1,221 MBq based on the default-value approach; or 2) 2.1 GBq and 6.6 GBq using the patient-specific calculational dose approach for hyperthyroid and thyroid cancer patient treatments, respectively. Rarely, they might argue, is there a need for hyperthyroid treatments involving >1,221 MBq or thyroid cancer treatments with >6.6 GBq and, therefore, the higher activity release limits in our recommended approaches may not be required. The important point is that, quite distinct from medical judgments by physicians in deciding what activity prescription is best suited for their patients, the activity release limits we have determined here from a radiation safety perspective pose little or no adverse impact on the public health and safety. Many institutions are providing thyroid cancer treatments based on a dosimetric approach, rather than an empiric fixed activity, generally involving an activity prescription >7.4 GBq, and these institutions need not be subjected to an unnecessary "tie-down" license condition preventing them from releasing their patients with activities greater than 6.6 GBq.

If more realistic activity limits, as presented and discussed in this work, were given to physicians by their Radiation Safety Officers (RSOs), higher activity administrations might be more routine. For example, treating autonomous hyperfunctioning nodules with empiric fixed dosages of ^{131}I that have been determined solely on the basis of the quantity of activity that would not require hospitalization (currently believed by many to be 1,221 MBq) is a common practice. However, for large nodular thyroid glands, administered dosages, if calculated based on volume and fractional uptake of iodine, could exceed this activity limit (Iagaru and McDougall 2007). It is important to note that RSOs are not required to blindly accept and adopt optional NRC guidance, but they are required to release radioactive patients in a manner that complies with 10 CFR 35.75 and, therefore, must be proficient in determining the likely dose to others from exposure to such released patients. We have shown that less conservative activity levels can achieve these goals. RSOs generally are not able to devote the time or resources necessary to perform complex modeling calculations to verify the adequacy of NUREG recommendations. Thus, it is common practice for licensees to simply adopt NRC guidance documents without critical assessment of their strengths and weaknesses. Uniform adoption of a single standard across the profession also facilitates the work of NRC inspectors. We have demonstrated, however, that a more scientifically sound but still easily implementable approach, i.e., one not requiring patient-specific biokinetic studies and dose calculations, can achieve the same goals as use of the NUREG, and lessen the burden on licensees, patients, and others.

CONCLUSION

Licensees must comply with NRC regulations but are under no obligation to adopt NRC guidance. Presently, there appears to be a considerable degree of confusion as to what is required by the regulations and what is optional, i.e., guidance. Rigid adherence to the guidance recommendations has placed an undue burden on nuclear medicine therapy patients and their families, as well as licensees responsible for ensuring compliance with NRC requirements. We have shown that guidance-suggested releasable activity limits are similar to those we have calculated for hyperthyroid patients, 2.1 GBq (57 mCi) vs. 2.3 GBq (62 mCi), but are much lower for thyroid cancer patients, 6.6 GBq (179 mCi) vs. 16.9 GBq (457 mCi) using the regulatory definition of the TEDE. Higher limits are both possible and reasonable, if the permissible extra-regulatory definition of the TEDE is used in which the EDE, rather than the DDE, is determined. We maintain that professionals evaluating compliance with 10 CFR 35.75 should use the approaches presented here to comply with NRC requirements. These approaches are easily implementable by licensees, as they do not require patient-specific biokinetic studies and dose calculations.

A repeat of the quiescence with which NRC's "30-mCi rule" was accepted by those in the radiation safety community is not justified. As chronicled by Siegel (2000), this activity limit, lacking scientific justification or evidence demonstrating it would actually

present a hazard to the public health and safety, was responsible for inappropriately low treatment activities, unnecessary patient hospitalizations and increased health care costs for over 50 y.

Use of the 1,221 MBq activity (or 0.07 mSv h^{-1} at 1 m dose rate) patient release limit based on the NRC guidance "default" approach should never be employed by any licensee permitted to release patients pursuant to 10 CFR 35.75. These values indicate lower limits for which NRC does not believe it necessary to perform patient specific calculations to demonstrate that others potentially exposed to a released patient will not likely receive a radiation dose that exceeds 5 mSv. However, the assumptions made by the NRC in arriving at these guidance values are inaccurate and unjustifiably conservative. Even if a licensee were to follow the patient-specific dose calculational approach provided for in NRC's NUREG guidance document, thyroid cancer and hyperthyroid patients receiving greater than 6.6 GBq and 2.1 GBq, respectively, would always have to be hospitalized. There is also no scientific basis or justification for these so-called "forced activity level" confinements. The NUREG patient release methodology also introduces a regulatory burden not as yet codified in NRC requirements. Indeed, patients, particularly thyroid cancer patients, can be released in accordance with NRC regulations with much higher activities, as demonstrated in this work, without adversely impacting on the public health and safety.

Patients and their families share the largest burden when overly restrictive release criteria are enforced. Alternative guidance for patient release by stakeholder professional organizations is available for use (Siegel 2004). Licensees may adopt and implement the approach presented here, or they could develop their own appropriate approach given that a wealth of scientific literature now exists (Siegel et al. 2002b; Mathieu et al. 1999; Barrington et al. 1999; Zanzonico et al. 2000; Venencia et al. 2002; Siegel et al. 2002a). Possible consequences of overly rigid adherence to the NUREG procedures include the under-treatment of patients, issuance of overly restrictive release instructions, and unnecessary confinement of patients to hospital beds. The significant and unjustified additional cost to patients and their loved ones, the requirement for hospitals to prepare and decontaminate unneeded rooms so that staff can receive unnecessary radiation exposures, and the adoption of substandard patient release policies associated with licensee adherence to NRC patient-release guidance should be critically re-evaluated given the guidance presented in this work. These procedures are in compliance with NRC requirements and their use can lessen the burden on licensees.

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JAMA Insights

Diagnostic Imaging in Pregnant Patients With Suspected Appendicitis

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Diagnosing the source of acute abdominal pain during pregnancy is challenging. While obstetric causes are the most common source, acute appendicitis is the most common nonobstetric surgical emergency. Yet, diagnosing acute appendicitis can be particularly challenging during pregnancy because of the overlap in symptoms between appendicitis and normal pregnancy, the higher likelihood for nonclassic symptoms with appendicitis during pregnancy, anatomic changes related to the gravid uterus, and the physiologic leukocytosis of pregnancy. These diagnostic challenges can lead to the development of complications from a delay in diagnosis and treatment or misdiagnosis resulting in a negative appendectomy. Both scenarios have been associated with increased risks for maternal and perinatal morbidity. In the largest study to date, which included 94 789 patients, appendectomy for perforated appendicitis was associated with a 6% rate of fetal loss and 11% rate of early delivery; for negative appendectomy, the rate of fetal loss was 4% and the rate of early delivery was 10%.[1] Compared with simple appendicitis, perforated appendicitis (odds ratio, 2.69) and negative appendectomy (odds ratio, 1.99) are the major factors associated with fetal loss. These data highlight an opportunity to improve strategies to allow for more timely and accurate diagnosis of appendicitis to reduce the risks of perforation or unnecessary operation in pregnant patients and improve perinatal outcomes.

Both the American College of Obstetrics and Gynecology (ACOG) and the American College of Radiology (ACR) offer guidance for various imaging techniques during pregnancy.[2,3] Because obstetric causes are the most common source of abdominal pain in pregnant women, ultrasonography should be the initial imaging test (**Figure**).[3] However, ultrasonography has poor specificity for ruling out the possibility of acute appendicitis during pregnancy, with a normal appendix visualized in less than 2% of pregnant patients without appendicitis.[4] While computed tomography (CT) is the most accurate imaging modality for evaluating nonpregnant patients with suspected appendicitis, a theoretical risk to the fetus from ionizing radiation has led the ACR to recommend magnetic resonance (MR) imaging rather than CT.[2] However, the ability to obtain and interpret MR imaging varies widely, with onsite MR imaging available at only 66% of US emergency departments.[5] To complicate matters further, compared with radiologist experts in MR imaging, interpretation by nonexpert radiologists has suboptimal sensitivity (89% vs 97%) and specificity (83% vs 93%) for diagnosing acute appendicitis.[2]

When diagnostic uncertainty remains and MR imaging or a radiologist expert in MR imaging is not readily available, CT should be utilized without delay. There is a broad body of knowledge regarding the potential effects of radiation exposure on the developing fetus. Based on data from atomic bomb survivors, the lowest clinically documented dose to produce birth defects is 610 mGy. Although fetal risks for anomalies, growth restriction, or abortion vary depending on the gestational age, there are no reported cases with radiation exposure of less than 50 mGy, a level well above the range of exposure for diagnostic procedures. The ACOG Diagnostic Imaging During Pregnancy Guidelines[3] indicate that "with few exceptions," radiation exposure through radiography, CT scan, or nuclear medicine imaging techniques is a dose much lower than the exposure associated with fetal harm and "should not be withheld from the

Figure. Imaging Algorithm for Abdominal Pain in Pregnancy

Abdominal or Vaginal Ultrasonography

- Fetal radiation exposure: none
- Harmful radiation effects: none

Primary diagnosis	Incidence, %	Sensitivity, %[a]	Specificity, %[a]
Appendicitis	0.07-0.125	31.8-83.9	56.7-96.7
Miscarriage	10-20	78-99	96-100
Fibroid degeneration	1-2.5	92-99	80-100
Ectopic pregnancy	1-2	87-100	94-100
Placental conditions	0.4-1	24-100	71-96
Cholecystitis	0.01-0.07	96-98	86-95
Adnexal torsion	0.02-0.07	21-100	91-99

Inconclusive or nondiagnostic ultrasonography findings and **MR imaging available**

Inconclusive or nondiagnostic ultrasonography findings and **MR imaging not available**

Magnetic Resonance (MR) Imaging

- Fetal radiation exposure: none
- Harmful radiation effects: none

Primary diagnosis	Incidence, %	Sensitivity, %[a]	Specificity, %[a]
Appendicitis	0.07-0.125	91-99 (expert) 84-93 (nonexpert)	87-97 77-88
Bowel obstruction	0.03-0.07	92-100	93-100
Pancreatitis	0.03-0.07	58-96	69-98
Inflammatory bowel disease	0.001-0.003	87-100	85-93
Choledocholithiasis	0.00008-0.001	90-100	90-100

Inconclusive MR image findings

Computed Tomography (CT) Scan

- Fetal radiation exposure: 10-25 mGy (as low as 2.5 mGy with pregnancy protocol CT scan)
- Harmful radiation effects: None if total fetal exposure is <50 mGy

Primary diagnosis	Incidence, %	Sensitivity, %[a]	Specificity, %[a]
Appendicitis	0.07-0.125	90-100	98-100
Bowel obstruction	0.03-0.07	93-100	95-100
Pancreatitis	0.03-0.07	52-93	63-96
Inflammatory bowel disease	0.001-0.003	94-100	95

[a] Sensitivities and specificities sourced from ACR Appropriateness Criteria and source material.[2]

pregnant patient." The risk of subsequent carcinogenesis as a result of in utero exposure to ionizing radiation is less clear and fetal exposure from a CT scan of the abdomen and pelvis may increase the risk of leukemia by a factor of 1.5 over the background rate of approximately 1 in 3000.[3] While a typical abdominal/pelvic CT scan delivers 10 to 25 mGy of radiation, the fetal radiation exposure in these studies may be as low as 4.8 mGy.[6] Additionally, the use of a "pregnancy protocol" CT scan can further reduce fetal radiation exposure to approximately 2.5 mGy by increasing scan pitch, decreasing the milliampere-seconds value, and use of z-axis modulation.[7]

For women with suspected acute appendicitis during pregnancy, perforated appendicitis and negative appendectomy are the greatest determinates of fetal loss and preterm delivery.[1] Delay in diagnosis and misdiagnosis are primary contributors to each. Improved obstetric outcomes in these patients requires more timely and accurate diagnosis. Following reassurance from ultrasonography findings that there is not an obstetric source for the acute abdominal pain, timely subsequent imaging should occur. MR imaging should be utilized in institutions that have immediate access to both MR imaging and radiologists who are experts in MR imaging. However, in settings that do not have ready access to MR imaging or MR imaging expert radiologists, CT should be utilized without delay because it is the quickest and most definitive imaging modality to diagnose acute appendicitis and should not be withheld from a pregnant patient (Figure).

While there has been considerable interest in the use of antibiotics instead of surgery in cases of simple appendicitis, the largest clinical trial to date demonstrated a nearly 40% recurrence rate at 5 years and specifically excluded pregnant patients as well as patients with perforation or abscess.[8] In the absence of clinical trial findings, appendectomy is the preferred approach for pregnant patients with appendicitis.

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