Advisory Committee on Medical Uses of Isotopes (ACMUI)
***Sub-Committee on Draft Final Rule,* 10 CFR Parts 30, 32 and 35**

Draft Comments on

NUCLEAR REGULATORY COMMISSION (NRC)

10 CFR Parts 30, 32 and 35

RIN: 3150-AI63 [NRC-2008-0175]

Medical Use of Byproduct Material
- Medical Event Definitions, Training and Experience, and Clarifying Amendments

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Date of Submission: December 23, 2015

Executive Summary

This document provides comments by a Sub-Committee of the ACMUI on the public version of 10 CFR Parts 30, 32 and 35, RIN: 3150-AI63 [NRC-2008-0175] - Medical Use of Byproduct Material - Medical Event Definitions, Training and Experience, and Clarifying Amendments, hereafter identified as the "Proposed Rule." (The Sub-Committee identifies its comments with respect to the relevant page and line numbers in a version of the foregoing document in which it has inserted line numbers.) This ACMUI Sub-Committee had previously reviewed the Draft Proposed Rule and submitted a report dated March 28, 2013 (revised April 5, 2013) with its comments on that Draft. The NRC formally responded to the ACMUI comments in a document entitled, "The US Nuclear Regulatory Commission Staff Responses to the Advisory Committee on the Medical Uses of Isotopes Comments on the Draft Part 35 Proposed Rule" (Enclosure 5 of SECY-13-0084). The Draft Final Rule incorporates revisions made in response to that Sub-Committee Report as well as comments submitted by professional societies and other stakeholders.

Our recommendations on the major elements of the current Draft Final Rule are as follows.

- The Sub-Committee endorses that component of the current proposed rule re-defining medical events in permanent implant brachytherapy in terms of activity (i.e., source strength) rather than radiation dose. [General Comments. Section 1.a.-d.]

- The Sub-Committee endorses, with reservations, designating the current proposed rule re-defining medical events in permanent implant brachytherapy as Compatibility Category C, with activity-based medical event metrics defined as an essential program element. [General Comments 1.e.]

- The Sub-Committee recommends changing the language for a "wrong-location" medical event in permanent implant brachytherapy *from* the current proposed language,

> "Sealed source(s) implanted directly into a location where the radiation from the source(s) will not contribute dose to the treatment site, as defined in the written directive," *to*
>
> "Sealed source(s) implanted directly into a location discontiguous from the treatment site, as defined in the written directive."

[General Comments Section 1.f.]

- The Sub-Committee recommends revising the passage in lines 4182-4186 on page 167 in the Draft Final Rule as follows, thereby eliminating the dose-based criteria for a "leaking-source" medical event

> "3) An administration that includes the wrong radionuclide; the wrong individual or human research subject; a leaking sealed source; or a sealed source or sources implanted into a location discontiguous from the treatment site, as defined in the written directive."

[General Comments 1.g.]

- The Sub-Committee endorses the elimination of the preceptor-statement requirement for Board-certified individuals for an individual seeking regulatory authorization as an authorized user, authorized medical physicist, Radiation Safety Officer, or authorized nuclear pharmacist. [General Comments 2.a.]

- With respect to the amended requirements for preceptor attestation for an individual seeking regulatory authorization as an authorized user, authorized medical physicist, Radiation Safety Officer, or authorized nuclear pharmacist through the alternate pathway, the Sub-Committee endorses changing the language for the preceptor attestation *from*

> the individual "…has achieved a level of competency to function independently…" for the authorization *to*
>
> the individual can "…independently fulfill the radiation safety-related duties…" associated with the authorization being requested.

[General Comments 2.b.]

- The Sub-Committee recommends that the date of recognition by the NRC of a certifying board should *not* impact individuals seeking to be named as an authorized user, authorized medical physicist, Radiation Safety Officer, or authorized nuclear pharmacist through the certification pathway. [General Comments 3.a.-c.]

- The Sub-Committee recommends that the NRC adopt the parent-breakthrough limits for radioisotope generators specified in the relevant FDA-approved package inserts. [General Comments [4.a.-b.]

- The Sub-Committee does *not* endorse the new requirement in the Draft Final Rule that

licensees report to the NRC as well as to the manufacturer/vendor generator elutions with out-of-tolerance parent-breakthrough but, instead, recommends a single reporting requirement to the manufacturer/vendor. [General Comments 4.c.]

- The Sub-Committee endorses allowing Associate Radiation Safety Officers (ARSO) to be named on a medical license. [General Comments 5.a.-b.]

- The Sub-Committee recommends that the designation of a board-certified an authorized user, authorized medical physicist, or authorized nuclear pharmacist as the RSO or as an ARSO requires their board certification to include the designation, "RSO Eligible". [General Comments 6.a.]

- The Sub-Committee does *not* endorse establishing a separate category of Authorized Users for parenteral administration of alpha-emitting radiopharmaceuticals but, instead, recommends deleting § 35.390(b)(1)(ii)(G)(4) in the current Draft Final Rule and revising the pertinent passage in § 35.390(b)(1)(ii)(G)(3) as follows,

  > "Parenteral administration of any radioactive drug for which a written directive is required."

  [General Comments Section 7.a.]

- The Sub-Committee endorses the elimination of the requirement to submit copies of NRC Form 313, Application for Material License, or a letter containing information required by NRC Form 313 when applying for a license, an amendment, or renewal.

- The Sub-Committee recommends changing the "medical-events" language in lines 5531-5532 (page 232) of the Draft Final Rule *from*,

  > "A licensee shall report as a medical event, any administration requiring a written directive, except for an event that results from patient intervention…," *back to the language in the current Draft Final Rule,*
  >
  > "A licensee shall report any event, except for an event that results from patient intervention…"

Relevant background material and commentary as well as the NRC's responses to the ACMUI's *previously submitted comments on the Draft Proposed Rule* (where applicable) are provided in the General Comments and the Specific Comments below. Suggested editorial revisions are provided in an Addendum.

General Comments

1. Medical event (ME) definitions for permanent implant brachytherapy

a. The text in § 35.41(b)(6) in the Draft Final Rule was modified to remove § 35.41(b)(6)(ii) and (iii) which would have required the licensee to determine absorbed dose to the maximally exposed 5 contiguous cubic centimeters of normal tissue located both outside and within the treatment site. The NRC acknowledges that while some treatment

planning systems can identify contiguous volumes, others may not. In response to this concern and others raised by various commenters, the NRC removed § 35.41(b)(6)(ii) and (iii).

The NRC retained the requirement to determine the total source strength administered outside of the treatment site compared to the total source strength documented in the post-implantation written directive.

NRC Staff's response to the comment as previously submitted: The staff agrees with the ACMUI recommendation to allow licensees the use of total source strength as a substitute for total dose for determining MEs for permanent implant brachytherapy until the Part 35 rulemaking is complete. In this regard, in a Staff Requirements Memo dated, May 21, 2013, the Commission has approved the staff's proposed interim enforcement policy as described in SECY-13-0044, "Interim Enforcement Policy for Permanent Implant Brachytherapy Medical Event Reporting." On July 9, 2013, the NRC issued the interim enforcement policy for permanent implant brachytherapy ME reporting. *End of NRC Staff's response*

b. Inclusion of additional language is recommended to clarify explicitly what is meant by the "treatment field." As noted by the NRC in Lines 1170-1171 on page 47, "The authorized user may define the treatment site to include *all* tissues into which sources will be purposely implanted." This may include tissues (i.e., normal tissues) outside the clinical tumor volume.

c. Changing the number-of-seeds component of the ME definition to be compared to the post-implant written directive (WD) is appreciated, since it clarifies that the AU is allowed to change the implant plan based on his/her medical judgment during the implant procedure.

d. There was originally some concern that the proposed ME definition for permanent implant brachytherapy, which included dose-based criteria, might discourage practitioners from utilizing this therapy. The ACMUI and its Rulemaking Sub-Committee had therefore recommended that NRC solicit information on whether the previously proposed ME definition for permanent implant brachytherapy would discourage licensees from using this therapy option or will otherwise adversely impact clinical practice. The NRC has solicited such information on the Draft Final Rule and has amended the Rule, in the form of the Draft Final Rule, accordingly.

NRC Staff's response to the comment as previously submitted: Although the ACMUI's specific recommendation to solicit information on this subject was not incorporated into the *Federal Register* notice (FRN), we believe we addressed the intent of the ACMUI comment in our general solicitation of information related to the economic impact of the proposed rule. Additionally, the staff has prepared a regulatory analysis which will be available for public comment when the proposed rule is published. *End of NRC Staff's response*

e. There is also concern that the draft rule designating MEs in permanent implant brachytherapy as Compatibility Category C would allow Agreement States to retain the dose-based criteria for definition of a ME. The ACMUI and its Rulemaking Sub-Committee had therefore originally recommended that the draft rule re-defining medical events in permanent implant brachytherapy be designated as Compatibility Category B.

The reasons for conversion from dose-based to activity-based criteria are: (1) the failure of dose-based criteria to sensitively and specifically capture clinically significant misadministrations in permanent implant brachytherapy and (2) the practical difficulties in implementing and regulating dose-based criteria. Retaining the dose-based criteria would still result in *clinically insignificant* occurrences being identified as MEs and thereby perpetuate the confusion associated with such criteria. It was based on these compelling considerations that the ACMUI and its Rulemaking Sub-Committee had recommended that the activity-based rule re-defining medical events in permanent implant brachytherapy be designated as Compatibility Category B. The NRC's argument for retaining Compatibility Category C defining MEs in permanent implant brachytherapy - that MEs do not have significant "transboundary" health and safety implications (i.e., direct and significant effects in multiple jurisdictions) - is persuasive, however. Specifically, the NRC designates regulatory program elements as Compatibility Category B only if they have significant direct transboundary implications, not simply for the purpose of ensuring uniformity across the country with respect to a program element. It must be noted, however, that a single "national" definition of an ME serves to minimize the risk of such an event through the standardization of all processes involved in the procedure - from administrative to logistical to treatment planning to the actual performance of the procedure by the AU. Embedding safe and consistent procedures into the workflow of an AU and her/his department and team is perhaps the most important consideration in minimizing MEs, and it is not uncommon for AUs to practice in multiple jurisdictions, which are not uncommon. Compatibility C is therefore suboptimal and actually increases the risk of an ME. Nevertheless, based on its recognition of the regulatory distinction between Compatibility Category B and C designations, the ACMUI now agrees with Compatibility Category C designation for the current activity-based definition of MEs in permanent implant brachytherapy - contingent on this definition of an ME being considered an *"essential element"* of the regulation of MEs in permanent implant brachytherapy and thereby requiring an Agreement State to use the activity-based definition.

Importantly, the ACMUI and its Rulemaking Sub-Committee strongly advise that Agreement States *not* also adopt dose-based criteria for MEs. If such problematic multiplicity of criteria (i.e., activity- and dose-based criteria) in different jurisdictions (i.e., Agreement States and NRC-regulated states) were to occur, the ACMUI's recommendation to designate MEs in permanent implant brachytherapy as Compatibility Category C, rather than Compatibility Category B, would have to be reconsidered.

NRC Staff's response to the comment as previously submitted: The issue of the Compatibility Category for MEs is discussed in detail in the draft FRN. Currently, MEs are designated as Compatibility Category C. The Standing Committee on Compatibility (SCC) reviewed the proposed rule and strongly supported retaining Compatibility Category C designation for § 35.3045, the section that contains the criteria for determining if a ME has occurred. As noted in the discussion in the proposed draft FRN, with a Compatibility Category C designation, Agreement States would have the flexibility to require both the dose-based criteria and source strength-based criteria as long as the Agreement States' reports to NRC related to MEs are based on the requirements in § 35.3045.

The SCC stated that many Agreement States have additional state requirements and laws to gather information on MEs. A Compatibility Category B requirement would prohibit the Agreement States from gathering additional information, such as diagnostic

reports, shorter reporting times, or lower dose limits for reporting. After reviewing the issue, the SCC determined that identical reporting requirements were not necessary for the national program on a transboundary basis. The SCC concluded that a change to a Compatibility B would not acknowledge the inherent state function to protect public health and safety of its citizens which forms the basis of the Section 274b amendment to the Atomic Energy Act of 1959.

Although the staff is proposing to retain the proposed Compatibility for MEs at Compatibility Category C, the NRC is seeking specific comments on the Compatibility Category in the draft FRN. *End of NRC Staff's response*

f. There is concern regarding the meaning and implementation of the "Wrong-location" criterion for an ME. The current proposed criterion for a "Wrong-location" ME is, "Sealed source(s) implanted directly into a location where the radiation from the source(s) will not contribute dose to the treatment site, as defined in the written directive." Given the exponential attenuation of gamma- and x-rays in stopping media such as tissue, a seed anyway in the body actually would deliver some non-zero (though insignificant) dose to a tumor elsewhere in the body. More importantly, an AU may purposely implant seeds in muscle or other normal tissue adjacent to (i.e., outside of) what might be considered the nominal treatment site to achieve the desired dose distribution to the clinical tumor volume (CTV); this conceivably could be misinterpreted by regulators as a ME based on the foregoing "Wrong-location" criterion. The Sub-Committee therefore proposes the following language for the "Wrong-location" ME criterion, "Sealed source(s) implanted directly into a location discontiguous from the treatment site, as defined in the written directive." The term, "discontiguous," is defined as "disconnected or without contact." Note that it is the seed location, not the seed itself, which is discontiguous for an ME based on the suggested "Wrong-location" ME criterion. For example, if a seed were implanted into muscle or other non-CTV tissues *adjacent* to the CTV (in order to deliver a satisfactory dose distribution), the *location* of that seed would *not* be discontiguous and, appropriately, an ME would not result. Further, inserting the term, "directly," eliminates the possibility that migration of seeds, edema-related mispositioning of seeds, and patient-related processes would precipitate an ME. Finally, by appending the phrase, "as defined in the written directive," the treatment site could be broadened beyond the CTV and even including adjacent normal tissues, if deemed appropriate by the AU.

g. For consistency with the new activity-based criteria for an ME in permanent implant brachytherapy, the passage in lines 4182-4186 on page 167 should be revised as follows, "3) An administration that includes the wrong radionuclide; the wrong individual or human research subject; a leaking sealed source; or a sealed source or sources implanted into a location discontiguous from the treatment site, as defined in the written directive." Note that for the leaking-sealed source ME criterion it is recommended that the tissue or organ radiation dose threshold (i.e., 0.5 Sv (50 rem)) be eliminated. This is not only consistent with the transition from dose-based to activity-based criteria for an ME in permanent implant brachytherapy but also eliminates the practical difficulty of estimating organ or tissue dose from a leaking source or sources.

2. Training and experience (T&E) requirements for authorized users (AUs), medical physicists, Radiation Safety Officers (RSOs), and nuclear pharmacists.

a. The Sub-Committee reiterates its enthusiastic support for eliminating the preceptor statement requirement for Board-certified individuals.

b. With respect to the amended requirements for preceptor attestation for an individual seeking regulatory authorization as an RSO, AMP, ANP, or AU via the alternate pathway, the Sub-Committee endorses the attestation language in the proposed rule stating that the individual can "…independently fulfill the radiation safety-related duties…" associated with the authorization being requested. This replaces the language in the current rule requiring the preceptor to attest that the individual "…has achieved a level of competency to function independently…" for the authorization. The proposed language thus eliminates burdening preceptors with making a subjective judgment as to the professional competency of an individual. The latter language requires, more reasonably, the preceptor to simply attest that an individual satisfactorily completed the residency and other requirements of a training program (an objective determination) but does not require the preceptor to make a judgment as to the actual competency of the individual (a subjective determination).

3. Extending grandfathering to certain certified individuals (Ritenour petition)

a. The ACMUI recommended in September 2012 that all individuals who were able to meet the requirements of the previous Subpart J for an authorized user, authorized radiation safety office, authorized medical physicist, or authorized nuclear pharmacist before that subpart was eliminated as of October 24, 2005 should be grandfathered, thus relieving them of meeting the current training and experience requirements. The Draft Final Rule contains the provision, "…for the modalities that they practiced as of October 24, 2005 and that their previously-acceptable qualifications for authorized status should continue to be adequate and acceptable from a health and safety standpoint such as to allow them to continue to practice using the same modalities."

b. Some of the terminology NRC has historically used and now uses in discussing the draft final rule continues to be confusing. The NRC Staff did not accept all of the ACMUI recommendations made in preparation of the Proposed Rule, explaining their reasons in Enclosure 5 of SECY-13-0084. The ACMUI had suggested for clarification that the meaning of the terms, "type of use", "modality", and "category," be explicitly defined in Section 35.2 (Definitions), so that the regulatory meaning of these three terms is clearly understood.

NRC Staff's response to the comment as previously submitted: The term "type of use" is already defined in Part 35.2: Type of use means use of byproduct material under §§ 35.100, 35.200, 35.300, 35.400, 35.500, 35.600, or 35.1000. The terms "category" and "modality" were reviewed and determined to be defined by common use (i.e., what is found in a dictionary): "Category" - any of several fundamental and distinct classes to which entities or concepts belong; "Modality" - the classification of logical propositions according to their asserting or denying the possibility, impossibility, contingency, or necessity of their content; or a usually physical therapeutic agency. *End of NRC Staff's response*

c. What remains unclear with respect to the Ritenour petition is the impact of the date of recognition of a certifying board by the NRC. The ACMUI and its Rulemaking Sub-Committee recommend that the date of recognition by the NRC of a certifying board should *not* impact individuals seeking to be named as an authorized user, authorized radiation safety office, authorized medical physicist, or authorized nuclear pharmacist through the certification pathway. At this point in time, individuals who received board certification prior to October 24, 2005 and were not named on a license for a given type

of use will continue to have difficulty knowing how to obtain approval for a new type of use. The Sub-Committee suggests that guidance be included in the revise NUREG 1556 Vol 9 to describe how these individuals can apply for a new type of use without having to repeat the entire training-and-experience pathway. The NRC has already included this kind of guidance in its licensing guidance for Leksel Gamma Knife Perfexion.

NRC Staff's response to the comment as previously submitted: The date of the individual's board certification is relevant. Boards that were recognized by the NRC or Agreement State on or prior to October 24, 2005 (listed in the now removed Subpart J), met different T&E requirements than boards whose processes have been recognized by the NRC or Agreement States after October 24, 2005.

Further, the staff determined that the ACMUI recommendation that all individuals who were able to meet the requirements of the previous Subpart J should be grandfathered would go beyond the intent of the resolution of the Ritenour petition, which requested recognition of individuals who were certified by boards listed under former Subpart J to perform AMP and RSO duties on or prior to October 24, 2005, but were not named on a license. The NRC, in resolving the Ritenour petition, determined that other medical professionals may have also been adversely affected when Subpart J expired. The intent of the resolution was to include all these individuals and grandfather them for the modalities they practiced on or prior to October 24, 2005. Grandfathering individuals who met the Subpart J requirements but were not board certified would also negate the new T&E requirements that became effective on October 25, 2005. *End of NRC Staff's response*

4. Measuring molybdenum contamination for each elution and reporting of failed breakthrough tests

a. Only two generator systems are specified in the current and proposed rules, molybdenum-89 (Mo-99)/technetium-99m (Tc-99m) and strontium-82 (Sr-82)/rubidium-82 (Rb-82) generators.

The current Food and Drug Administration (FDA) labeling requirement (i.e., the package insert) for a Mo-99/Tc-99m generator states that each eluate should be tested for Mo-99 content to verify it does not exceed the stipulated limit of 0.15 μCi of Mo-99 per mCi of Tc-99m at the time of patient administration. The originally proposed paragraph (b) of § 35.204 with its requirement to comply with § 35.204(a) essentially makes the NRC regulation equivalent to the FDA labeling requirements. The draft final NRC regulation, specifically, the passage that includes the language, "…at the time of elution…," is unnecessary and confusing. Therefore, the ACMUI and its Rulemaking Sub-Committee recommend that the NRC adopt the FDA-approved package insert for parent-breakthrough limits for radioisotope generators.

Pursuant to its recently revised labeling requirement for strontium-89 (Sr-89)/rubidium-82 (Rb-82) generators, the FDA's regulation is now more restrictive than the NRC's rule in terms of breakthrough limits. The new FDA limits are one-half of those of the NRC and an action level limit has been introduced. The NRC, however, is not revising its rule to be consistent with all of the FDA-approved package inserts. The NRC limits are consistent with those for the Tc-99m generator, but not those for the Rb-82 generator. As discussed at the ACMUI meeting on April 18, 2012, the NRC encourages licensees to follow good medical practice but would not cite a licensee if the licensee did not follow

the applicable FDA regulatory requirements. This position, however, seems to be inconsistent with the Memorandum of Understanding between the NRC and the FDA.

The NRC staff expressed concerns with ACMUI's previous recommendation that the NRC adopt language for radionuclidic purity limits for radioisotope generators consistent with the FDA-approved package insert.

NRC Staff's response to the comment as previously submitted: The ACMUI recommendation that the NRC adopt the FDA-approved package insert for breakthrough limits for radioisotope generators was not accepted because revising the regulations to require licensees to follow the FDA-accepted package inserts with regard to testing eluates would reverse the NRC's December 2, 1994 rulemaking (59 FR 61781) that removed the requirements to follow the FDA package inserts for preparation of radiopharmaceuticals from NRCs regulations.

Finally, the staff has determined the NRC's current breakthrough limits for both Tc-99m and Rb-82 radioisotope generators are safe. *End of NRC Staff's response*

b. For generator breakthrough testing, conformity between the corresponding FDA regulations and NRC rules is highly recommended, and the ACMUI is recommending conformity specifically with the one section of the respective package insert that deals with breakthrough testing of the generator's parent radionuclide. This would be especially beneficial as new generators (e.g., the germanium-68 (Ge-68)/gallium-68 (Ga-68) generator) become FDA-approved products. The NRC would be able to inspect, immediately, for compliance with the applicable FDA breakthrough testing requirements and thus would not have to await revision of its rules for testing newly introduced generators. Our Rulemaking Sub-Committee unanimously recommends that the NRC adopt the parent-breakthrough limits for radioisotope generators as described in the relevant FDA-approved package inserts.

The NRC's December 2, 1994 rulemaking (59 FR 61781) cited above dealt with the preparation of radiopharmaceuticals and would allow, for example, radiopharmacists to add a quantity of Tc-99m pertechnetate to a kit that exceeded the amount that was listed in the kit's FDA package insert. As stated in the summary of the rulemaking:

> "This final rule is intended to provide greater flexibility by allowing properly qualified nuclear pharmacists and authorized users who are physicians greater discretion to prepare radioactive drugs containing byproduct material for medical use."

This rulemaking did not alter the NRC's regulatory authority to regulate radiation safety associated with the use of radiopharmaceuticals. The NRC addressed this issue in the same rulemaking as follows.

> This final rule is not duplicating regulation by other federal or state agencies. In fact, this rule is designed to avoid duplication of the regulations of other federal agencies (e.g., see response to comments on Sec. 35.6). In the area of medical use of byproduct material, the NRC and FDA signed a Memorandum of Understanding (58 FR

47300; September 8, 1993) to coordinate existing NRC and FDA regulatory programs.

In general terms, the FDA regulates the manufacture and distribution of radioactive drugs and medical devices for safety and efficacy, while the **NRC regulates radiation safety associated with the actual use of these products** (emphasis added)**.**

The ACMUI's recommendation for conformity between the corresponding FDA regulations and NRC rules regarding breakthrough testing of the generator's parent radionuclide is consistent, we feel, with the NRC's position in that regulating the radionuclidic purity of generator elutions is essential to protecting patients from prohibitively high radiation doses. This issue, therefore, is one of the radiation safety of radiopharmaceuticals, rather than regulation of radiopharmaceutical preparation.

It was during the recall of the strontium-82 (Sr-82)/rubidium-82 (Rb-82) generator when the FDA extensively re-examined every aspect of that generator. Subsequently, the FDA revised the radionuclidic purity limits to ½ of their previous levels. The NRC staff subsequently stated that staff determined that the older, higher levels were safe but provided no data to support this position. Although the NRC staff noted that the new FDA limits are at (but not below) the lower limit of the assay capabilities of dose calibrators, this does not negate the effectiveness of the newly issued FDA limits.

NRC Staff's response to the comment as previously submitted: Currently there are no other generator systems that are available for general medical use. Any new generator system that becomes available would need to be evaluated by the NRC before developing any requirements and would be authorized under § 35.1000. Additionally, expanding the regulations from the specific requirements for Mo-99/Tc-99m and Sr-82/Rb-82 generators to apply to generators generally is beyond the scope of this rulemaking. *End of NRC Staff's response*

c. The proposed NRC reporting requirement for out-of-tolerance generator elutions was debated at length by the ACMUI at the time it reviewed the Draft Proposed Rule. Specifically, the NRC proposes to add two new reporting requirements related to breakthrough of Mo-99 and Sr-82 and Sr-85 contamination. One reporting requirement in § 35.3204(a) would require licensees to report three times, twice to the NRC and once to the manufacturers or distributors of medical generators, any measurement that exceeds the limits specified in § 35.204(a). This reporting requirement is the one which currently appears in the Draft Final Rule. The second, alternative requirement would require manufacturers/distributors to report to the NRC when they receive such a notification from a licensee. To lessen the reporting burden on licensees, the ACMUI considered reducing the reporting requirement for licensees to a single requirement, namely, reporting to the manufacturer/distributor. If licensees were required to report out-of-tolerance elution results to the manufacturers/distributor, then a requirement for the manufacturer/distributor to report such results to the NRC or their Agreement State should be imposed. Reports sent directly from licensees to the NRC could conceivably take 38 different pathways (corresponding to the NRC and the 37 Agreement States) before finally reaching the NRC. Once the reports arrive at the NRC, it would then be tasked with collating the information. The vendor is best situated to collate all relevant information and to prepare an accurate and timely summary reports for the NRC. Our Sub-Committee reiterates that it does *not* support the new requirement in the Draft Final

Rule that licensees report to the NRC as well as the manufacturer/distributor generator elutions with out-of-tolerance parent-breakthrough.

In practice, compliant licensees already appropriately report out-of-tolerance parent-breakthrough results. That is, if a licensee has a generator that produces an unusable elution (i.e., one with out-of-tolerance parent-breakthrough results), this elution is not used in patients. Without a usable elution, the licensee is highly motivated to contact the manufacturer immediately to report the unusable elution and to request a replacement generator and/or otherwise solicit assistance. Further, although NRC staff had expressed concern regarding the content of out-of-tolerance parent-breakthrough reports (i.e., inclusion of the appropriate information in these reports), the requisite content of the reports can be easily standardized in regulation or guidance. NRC staff was also concerned about gathering patient-exposure information. However, even if such data were solicited, it is unlikely to generate anything beyond anecdotal information. Otherwise, to accrue relevant information, a compliant licensee would have to first determine their elution is unusable, contact the manufacturer/vendor, and then take the implausible step of actually administering the out-of-tolerance elution to patients. It should be noted that the past incident involving patients who were administered out-of-tolerance strontium-82 (Sr-82)/rubidium-82 (Rb-82) generator elutions occurred among licensees who were not compliant in performing the breakthrough tests in the first place. It should also be noted that in past events with Mo-99 generator elutions where the radiopharmacists determined that the elutions were unusable, they were fully compliant and did not use these out-of-tolerance elutions in patients.

NRC staff described multiple possible causes for failed breakthrough tests, but did not provide any substantive information to support these hypothetical causes and thereby justify the number of reports proposed. In the past, there have been rare and anecdotal potential failed breakthrough tests due to human error and/or faulty equipment. However, these are typically corrected by the licensee's internal procedures; such procedures include critical review of the elution and radioassay techniques, re-checking of dose-calibrator quality-control results, and careful examination of the Mo-99 assay shield for possible damage.

Failed breakthrough tests on a larger scale are due to manufacturing, rather than end-user, issues, and the manufacturer/distributor is best positioned to collate all relevant information (such as the generator size, the day generator was manufactured, the age of generator when it was eluted, the geographic areas affected etc) and also to submit an accurate, informative, and timely report to the NRC. The Sub-Committee thus recommends such manufacturer/distributor-generated reports as being the most effective mechanism for the NRC to collect the relevant information on out-of-tolerance parent-breakthrough results.

NRC Staff's response to the comment as previously submitted: The staff agrees with the ACMUI that the FDA authority in relationship to foreign manufacturers or distributors of generators was incorrect and has revised the FRN for the proposed rule.

However, the staff determined that licensees should report to both the NRC and the manufacturer or distributor when a generator fails a breakthrough test because the information that would be reported by medical use licensees to the NRC is different than the information that would be reported to the manufacturers or distributors. For

example, reports from a medical use licensee to the NRC would have information on patient exposures, probable cause and assessment of failure in the licensee's equipment, and procedures or training that contributed to the excessive readings if an error occurred in the licensee's breakthrough determination. The licensee would only report information related to the generator failure to the manufacturer or distributor. Also, the corrective actions reported to the NRC by the licensee and the manufacturer or distributor would be different for each. The licensees' corrective actions would focus on procedures while the manufacturers or distributors' corrective actions would focus on manufacturing processes. Breakthrough tests exceeding the regulatory standard could be due to many different issues including from problems with the generator elution procedures, as a result of transportation, or problems with the manufacturer's production of the generator. The two separate reporting requirements would provide the NRC with the necessary information to determine the scope of the issue and the appropriate actions applicable to each entity.

Although both NRC/Agreement States and FDA have regulatory authority over the radioactive drug manufacturers, their regulatory responsibilities are different. The NRC regulates both the end user and the radioactive drug manufacturer whereas FDA regulates only the product and drug manufacturer. The NRC/FDA MOU was initiated to provide a mechanism for sharing information that is of mutual regulatory interest to both agencies. The NRC believes that it is important for medical use licensees and commercial nuclear pharmacies that elute generators (i.e., the end users) as well as manufacturers or distributors to report breakthrough failures to NRC as quickly as possible. If the generator breakthrough values exceed the regulatory limits, the problem could be with the procedures of the generator elution site, a result of transportation, or with the manufacturer's production of the generator. The NRC believes that 24-hour notification will assist in quickly differentiating generator elution licensee problems from those of the manufacturer. Requiring end user reporting also provides the NRC with a confirmation of whether patients were administered radiopharmaceuticals with excessive breakthrough. The generator manufacturer/distributor report to the NRC of breakthrough within 24 hours would assist the NRC and the Agreement States in identifying the scope of the problem and the regulatory efforts needed to address it. *End of NRC Staff's response*

5. Allowing Associate Radiation Safety Officers (ARSO) to be named on a medical license

a. With the addition of the term, "ARSO," § 35.15 (Exemptions regarding Type A specific licenses of broad scope) should also be updated. The ACMUI and its Rulemaking Sub-Committee unanimously recommend that the addition of ARSOs and Temporary RSOs also be included in these exemptions in the same manner as AUs, ANPs, and AMPs are allowed to be named on medical licenses.

NRC Staff's response to the comment as previously submitted: Unlike ANPs, AMPs, and AUs, who are not specifically listed on the broad scope medical use license, RSOs are listed on a broad scope medical use license, and the NRC specifically reviews the T&E of each individual before he/she is listed as an RSO on every medical use license including a broad scope medical license. This review is important because the RSO is responsible for implementing the radiation safety program for the licensee. An ARSO will have similar duties working under the RSO, and like the RSO, would be listed specifically on the license. Because of this, the staff has determined that the NRC needs

to review the T&E of each individual before he/she is listed as an ARSO. The NRC does not exempt the medical broad scope licensee in § 35.15 from notifying NRC when it appoints a temporary RSO because the NRC needs to know when an RSO leaves any medical use licensee and the licensee has to name a temporary RSO.

For these reasons, the provisions in § 35.15 for a temporary RSO is unchanged from the current regulations that allow a licensee to permit a qualified individual to serve as the RSO for up to 60 days each year. Additionally, changes to the temporary RSO provision are beyond the scope of this rulemaking. *End of NRC Staff's response*

b. When an individual who does not have board certification is named as an RSO, ARSO, or any of the other authorized individuals, does any of their additional future training for an additional type of use (ie "modality" or "category") require a preceptor signature? If so, examples of how this should be done (eg for an RSO) should be provided in the revised NUREG 1556 Vol 9 guidance.

NRC Staff's response to the comment as previously submitted: Under the proposed rule, RSOs, ARSOs, or other authorized individuals who are not board certified would need to obtain a written attestation. The associated guidance will clarify that all individuals coming through the alternate pathway will need a preceptor statement for the additional training. *End of NRC Staff's response*

6. "RSO- Eligible" designation on board certificates

a. The Draft Final Rule discusses designation of an AU, AMP, or ANP as the RSO or ARSO on medical licenses. The Sub-Committee suggests that the NRC include in this discussion a declaration that for a board-certified AU, AMP, or ANP to be named as the RSO or an ARSO the board certification of the AU, AMP, or ANP must include the designation, "RSO Eligible".

7. § 35.390(b)(1)(ii)(G)(4) (Based on the NRC's determination that there are fundamental radiation safety differences between alpha- and beta/gamma-emitting radionuclide)

a. Our Sub-Committee continues to *disagree* with maintaining a separate category for parenteral administration of alpha-emitting radiopharmaceuticals in the Draft Final Rule. As stated in the ACMUI Report on Licensing for Radium-223 (^{223}Ra), $^{223}RaCl_2$ and, by extension, other alpha-emitting radiopharmaceuticals do not differ significantly in terms of clinical use and management, radiation safety, and logistics from currently approved radiopharmaceuticals. Therefore, physicians already authorized to use therapeutic radiopharmaceuticals under § 35.390 or § 35.396 have the requisite education, training, and experience to safely and effectively use alpha-emitting radiopharmaceuticals As such, licensing of authorized users of $^{223}RaCl_2$ under § 35.390 (Category (G)(3) or (G)(4)), or § 35.396(d)(2), was therefore recommended.

The NRC's response in justifying the need to keep a separate category for parenteral administration of alpha-emitting radiopharmaceuticals [§ 35.390(b)(1)(ii)(G)(4)] stated that "…there are fundamental differences between the clinical use and the radiation safety of the radioactive drugs used primarily for their alpha emission versus beta emission." The Sub-Committee, as noted, *disagrees* with this assertion and believes the NRC staff has not provided a sufficient basis to state there are such "fundamental differences". Addendum 2 presents a tabulation of the physical properties of current or

under-development therapeutic radionuclides. Note that each of the alpha-emitting radionuclides emit gamma radiation and two also emit beta radiation, so these radionuclides do not require different radiation-detection equipment. AUs training for clinical use includes not only what radionuclide properties must be considered, but also the pharmaceutical properties. The only fundamental difference in the list of.§ 35.390(b)(1)(ii)(G) "categories" is the route of administration being parenteral. The Sub-Committee strongly recommends that.§ 35.390(b)(1)(ii)(G)(4) should be deleted and the pertinent passage in § 35.390(b)(1)(ii)(G)(3) revised as follows, "Parenteral administration of any radioactive drug for which a written directive is required."

NRC Staff's response to the comment as previously submitted: The staff has determined that there are fundamental differences between the clinical use and the radiation safety of the two groups identified in proposed § 35.390(b)(1)(G)(3) or (4). The radiation detection equipment used to monitor and detect photons, electrons, and beta particles can be very different from that used to monitor and detect alpha particles, and calibration procedures for measuring activities of beta emitters and alpha emitters are more complicated than for photon emitters. Further, the relationship between activity and radiation dose delivered to the patient for alpha emitters is not the same as that for low-energy photons, beta particles and electron emitters.

The staff recognizes that medical use licensees have radiation safety T&E, medical use experience, and ready access to low-energy photon and beta-emitting radionuclides. However, radioactive drugs primarily used for their alpha radiation characteristics are new to most medical use licensees (the first alpha-emitting radiopharmaceutical was approved by Food and Drug Administration (FDA) in May 2013). The staff determined that there are important radiation safety considerations associated with alpha-emitting radiopharmaceuticals. They include patient radiation safety (e.g., administrative controls to prevent an ME), steps to ensure the proper dosage is delivered (e.g., quality control procedures on instruments used to determine the activity of dosages, calculating, measuring, and safely preparing dosages), and radiation safety (e.g., ordering, receiving, performing radiation surveys, containing spills safely and proper decontamination procedures). Therefore, the staff has determined that an AU should have experience with alpha-emitting radiopharmaceuticals in addition to the experience the AU may have with the low-energy photon- and beta-emitting radionuclides.

The staff has determined that this requirement would not be a burden on licensees. The proposed requirements will ensure that AU's have the proper radiation safety training in the use of alpha emitters. Licensees only need to document the physician's T&E using the broad categories listed in § 35.390(b)(1)(G) and need not document each individual radionuclide used in a category. *End of NRC Staff's response*

Specific Comments

Pg 5	Lines 110-113	Regarding the statement, "This cost will be spread over the 7,418 impacted licensees for an average implementation cost of approximately $1,100 per licensee," does the number refer to NRC licensees , Agreement-State licensees or both?
Pg 5	Lines 113-114	Does this sentence refer to net or gross revenues?

Pg 5	Lines 117-118	This sentence should be revised as follows, "The benefits of this final rule are associated with reducing unnecessary radiation exposure to patients, modifying requirements for T&E, and affording more latitude to licensees."
Pg 10	Lines 245-246	The phrase, "…, as RSOs who have relevant timely work experience (even if they have not been formally named as an RSO), is confusing, as it makes the meaning of this sentence unclear in that the prior portion of this sentence and the Ritenour petition itself refers to all board-certified medical physicists, not only RSOs.
Pg 13	Lines 313-314	This sentence should be revised as follows, "The final rule clarifies the current regulations and provides greater flexibility to licensees without compromising patient, worker, or public health and safety and without unnecessarily restricting patients' access to medical procedures."
Pg 14	Line 335	The phrase , "…no suitable clinically used dose metric…," should be changed to, "…no clinically meaningful and practical dose metric…"
Pg 16	Lines 384-396	The statement in lines 305-396, "The ME criteria in the final rule do not include absorbed doses to normal tissues located outside of the treatment site or located within the treatment site," is confusing in that it apparently contradicts what was stated in the preceding paragraph. That paragraph states in lines 387-390, "…this ACMUI-recommended ME reporting criterion for normal tissue structures located within the treatment site was retained in SECY-12-0053 because the ACMUI and the staff determined there should be some form of ME reporting criterion for overdosing of normal tissue structures located within the treatment site." If the latter statement (i.e., in the preceding paragraph) was included in order to recount the evolution of the current ME criteria in the final rule, the distinction between the previously recommended and the current ME criteria must be made clearer and more explicit.
Pg 19	Line 455	The phrase, "…will not contribute dose to the treatment site…," should be changed to, "…will not contribute a therapeutically significant dose to the treatment site…" Although not perhaps true of iodine-125 (which emits only very low-energy and relatively non-penetrating gamma radiations), most radionuclides emit gamma- radiations sufficiently penetrating to deliver, from any location in the body, some non-zero dose to any other location of the body; this is the rationale for including the qualifier, "therapeutically significant."

Pg 19	Line 460	The phrase, "…a location far from the treatment site," should be changed to, "…a location discontiguous from the intended treatment site."
Pg 19	Line 464-465	The phrase, "…will not contribute dose to the treatment site…," should be changed to, "…will not contribute a therapeutically significant dose to the treatment site…"
Pg 22	Line 528	The phrase, "…for individuals with whom the preceptor is not personally familiar," should be appended to the end of this sentence.
Pg 22	Lines 533-534	Here and elsewhere in the rule, the term, "board certified," should be changed to, "board-certified."
Pg 22	Line 542	The parenthetical phrase, "…(such as the attending staff or faculty of the attestor's clinical service)…," should be inserted between the comma and the word, "irrespective."
Pg 24	Line 594	The phrase, "…however a generator can be eluted several times…," should be changed to, "however, a generator can be eluted multiple times…"
Pg 71	Lines 1772-1773	The statement, "The NRC agrees that the proposed language could be clearer," is unnecessary and actually somewhat confusing, as the preceding statement declares that the clarifying change has been made.
Pg 75	Lines 1871-1874	Regarding the statement, "The NRC is retaining the separate dosage category used primarily for alpha emitters because there are fundamental differences between the clinical use and the radiation safety of the radioactive drugs used primarily for their alpha emission versus beta emission," the ACMUI and its Sub-Committee strongly disagree with this and similar assertions by the NRC. The ACMUI and its Sub-Committee feel that that there are *no* fundamental differences in the clinical use and radiation safety of radioactive drugs used between those used primarily for their alpha emission versus beta emission, and, as noted, the NRC has provided no basis for its assertion to the contrary.
Pg 82	Line 2045-2047	The meaning of the statement, "The proposed rule change was made in part to ensure that the ophthalmology physicist (or authorized medical physicist) performs a minimum number of tasks at the ophthalmology office," is unclear. It should be deleted.
Pg 133	Lines 3320-3323	The Sub-Committee does *not* support the proposed change in wording from "commits" to "satisfies" the label requirements in § 32.72 Manufacture, preparation, or transfer for commercial

		distribution of radioactive drugs containing byproduct material for medical use under 10 CFR part 35. This change appears to be an inappropriate regulatory action in that it has no substantiated basis for remediating any harm being caused. This change will increase costs for commercial radiopharmacies and for drug manufacturers in order to comply with this new, but unnecessary, standard beyond what they are meeting now - with no perceptible improvement in patient safety.
Pg 135	Lines 3354-3356	This passage should be revised as follows, “For license amendments or renewals, this paragraph is amended to remove the requirement to submit a copy in addition to the original of NRC Form 313 or a letter containing information required by NRC Form 313. This change will relieve the burden on the licensee by requiring less paperwork to be submitted.”
Pg 163	Lines 4071-4073	Our Sub-Committee endorses the extension of the full inspection and servicing interval between each full inspection for gamma stereotactic radiosurgery units from 5 to 7 years.

Addendum 1
Editorial Revisions

Pg 3	Line 64	The semi-colon between the words, “amended” and “and,” should be changed to a comma.
Pg 4	Lines 89-90	The phrase, “…for failed Mo-99/Tc-99m and strontium-82 (Sr-82)/Rb-82 generators,” should be changed to, “…out-of-tolerance parent breakthrough results for Mo-99/Tc-99m and strontium-82 (Sr-82)/rubidium-82 (Rb-82) generators.”
Pg 5	Line 103	The comma between the terms, “2005” and “be,” should be deleted.
Pg 8	Line 178	The comma between the closing parenthesis and the word, “for,” should be deleted.
Pg 9	Line 205	The comma between the words, “rule” and “see,” should be changed to a semi- colon.
Pg 14	Lines 329-330	The phrase , “…, as well as with substantial input from various stakeholders, and the public comments received on the proposed rule,” should be changed to, “… and on substantial input from the public and various other stakeholders on the proposed rule.”
Pg 15	Line 360	A comma should be inserted between the words, “report” and “was.”
Pg 15	Line 361	The comma between the terms, “2011” and “teleconference,” should be deleted.
Pg 15	Line 364	The term, “source-strength based,” should be changed to, ““source strength-based.”
Pg 16	Line 386	The comma between the words, “reporting” and “that,” should be deleted.
Pg 19	Line 455	The phrase, “This wrong treatment site medical event criterion…,” should be changed to, “This wrong treatment-site ME criterion…”
Pg 19	Line 466	The phrase, “…, however it is defined as a medical event…,” should be changed to, “…; however, it is defined as such…”
Pg 19	Line 467	The term, “treatment site,” should be changed to, “treatment-site.”

Pg 19	Line 472	The phrase, "…in tissue immediately adjacent to the misplaced seed," should be appended to the end of this sentence.
Pg 24	Line 600	The word, "may," should be changed to, "will."
Pg 24	Line 610	Here and in line 622, the word, "numerous," should be changed to, "multiple," as the former term seems excessive.
Pg 25	Line 622	The term, "contamination issues," should be changed to, "parent-breakthrough issues."
Pg 25	Line 624	The phrase, "…unexpected levels…," should be changed to, "…unexpectedly high levels…"
Pg 26	Line 635	The word, "can," should be changed to, "will."
Pg 29	Line 709	The term, "120 day," should be changed to, "120-day."
Pg 29	Line 711	The comma at the end of this line should be deleted.
Pg 29	Line 714	The comma between the terms, "2015" and "to," should be deleted.
Pg 29	Line 722	The semi-colon between the terms, "2011" and "and," should be deleted.
Pg 30	Line 727	The comma between the terms, "SECY-10-0062" and "to," should be deleted.
Pg 31	Line 751	The word, "the," between the words, "of" and "Congress," should be deleted.
Pg 31	Line 764	The comma between the words, "outside" and "or," should be deleted.
Pg 32	Line 779	The comma between the words, "individuals" and "and," should be deleted.
Pg 33	Line 813	The comma between the words, "modalities" and "or," should be deleted.
Pg 33	Line 820	The term, "180 day," should be changed to, "180-day."
Pg 34	Line 826	The comma between the words, "petition" and "should," should be deleted.
Pg 34	Line 829	The word, "determined," should be changed to, "decided."
Pg 34	Lines 839 and 840	The word, "products," should be changed to, "radiopharmaceuticals."

Pg 34	Line 840	The term, “lower risk,” should be changed to, “lower-risk.”
Pg 35	Line 867	The word, “meets,” should be changed to, “meet.”
Pg 43	Line 1066	A comma should be inserted between the words, “Therefore” and “for.”
Pg 44	Line 1099	The word, “judgment,” is misspelled.
Pg 44	Line 1102	A comma should be inserted between the word, “language,” and the quotation mark.
Pg 45	Lines 1117 and 1118	The terms, “before implantation” and “after implantation,” when used as compound adjectives, should be changed to, “before-implantation” and “after-implantation,” respectively.
Pg 46	Line 1139	The term, “two part,” should be changed to, “two-part.”
Pg 46	Lines 1143	The term, “post treatment,” should be changed to, “post-treatment.”
Pg 54	Line 1340	The term, “medical use,” should be changed to, “medical-use.”
Pg 66	Line 1666	The term, “board certified,” when used as a compound adjective, should be changed to, “board-certified.”
Pg 71	Line 1765	The word, “was,” should be changed to, “were.”
Pg 79	Line 1964	The comma between the words, “characteristic” and “can,” should be removed.
Pg 82	Lines 2055-2056	The sources to which the phrase, “…the full calibration measurements and decay corrections…,” refers should be identified explicitly.
Pg 84	Line 2112	The comma between the words, “supervision” and “or,” should be removed.
Pg 87	Line 2164	The term, “photon emitting,” should be changed to, “photon-emitting.”
Pg 89	Line 2232	The comma between the words, “basis” and “each,” should be removed.
Pg 93	Line 2312	The term, “medical event,” when used as a compound adjective, should be changed to, “medical-event.”
Pg 93	Line 2314	The term, “absorbed dose based,” should be changed to, “absorbed dose-based.”

Pg 96	Line 2393	The term, “post Dosimetry CT scan,” should be changed to, “post-dosimetry CT scan.”
Pg 97	Line 2411	The term, “normal tissue,” when used as a compound adjective, should be changed to, “normal-tissue.”
Pg 97	Line 2415-2416	The term, “treatment planning software,” when used as a compound adjective, should be changed to, “treatment-planning software.”
Pg 103	Line 2566	The comma between the words, “migrated” and “‘would,” should be removed.
Pg 109	Line 2708	The word, “is,” should be changed to, “are.”
Pg 110	Line 2746	The comma between the words, “policy” and “that,” should be removed.
Pg 115	Line 2873	The term, “high-quality implant,” should be changed to, “high-quality implant.”
Pg 116	Line 2875	The term, “prostate implant program,” should be changed to, “prostate-implant program.”
Pg 117	Lines 2903-2905	The statement, “The NRC is not aware of cases where medically significant events have occurred and 20 percent or less of the source strength was implanted outside the treatment site,” is somewhat confusing as well as unnecessary; it should be removed.
Pg 117	Line 2915	The word, “judgment,” is misspelled.
Pg 119	Line 2953	The comma between the words, “requirements” and “and,” should be removed.
Pg 120	Line 2993	A comma should be inserted between the words, “Therefore” and “Agreement.”
Pg 121	Line 3027	The term, “medical event reporting criteria,” should be changed to, “medical-event reporting criteria.”
Pg 122	Line 3031	The comma between the words, “program” and “because,” should be removed.
Pg 125	Line 3127	The word, “assure,” should be changed to, “ensure."
Pg 128	Line 3190	The phrase, “…then the rule language be changed…,” should be changed to, “…then the rule language should be changed…”

Pg 128	Line 3198	The word, “the,” between the words, “are” and “more,” should be removed.
Pg 129	Line 3206	The comma between the words, “procedures” and “such,” should be removed.
Pg 129	Line 3217	The comma between the words, “criteria” and “because,” should be removed.
Pg 148	Line 3697	The word, “several,” should be changed to, “multiple.”
Pg 171	Line 4254	Can the parenthetical placeholder now be replaced with the actual pertinent material?
Pg 181	Line 4326	Can the parenthetical placeholder now be replaced with the actual pertinent material?
Pg 181	Lines 4328-4335	The Draft Final Rule could be shortened, and improved, by eliminating redundancies and consolidating related sections, eliminating identical or nearly identical passages appearing multiple times throughout the document.
Pg 182	Lines 4344-4356	Confirm that the US Pharmacopeia does not include a recommendation to perform an assay of parent breakthrough on every generator elution. If it does, that would like constitute an applicable “voluntary consensus standard.”
Pg 183	Line 4382	This line, in Section XV. Environmental Assessment and Final Finding of No Significant Environmental Impact, is simply, “Place holder for the final Environmental Assessment.” What is the status of this assessment? Can this section now be appropriately updated?
Pg183 (5th line from bottom)		Can the placeholder, “xxxx,” now be replaced with the appropriate number in the number?
Pg183 (4th line from bottom)		Can the placeholder, “____,” now be replaced with the appropriate number of hours?
Pg184 (3rd line from top)		Can the placeholder, “xxxx,” now be replaced with the appropriate number in the number?
Pg 184	Line 4392	This line, in Section XVII. Regulatory Analysis, is simply, “Place holder for the final Environmental Assessment.” What is the status of this analysis? Can this section now be appropriately updated?
Pg 184	Line 4404	The word, “from,” should be deleted.
Pg 186	Line 4344	The comma between the words, “that” and “the,” should be deleted.

Pg 192	Lines 4524-4534	Here and elsewhere in the document, what is the meaning of the asterisks (in lines that are otherwise blank)?
Pg 193	Lines 4556	The term, “medical use,” when used as a compound adjective, should be changed to, “medical-use.”
Pg 196	Line 4628	The phrase, “…reduces radiation safety…,” is rather ambiguous criterion. Could more explicit and precise language be used instead?
Pg 196	Line 4644	The term, “Device specific training,” should be changed to, “Device-specific training.”
Pg 197	Line 4651	The comma between the terms, “2007” and “or,” should be removed. The comma between the terms, “2009” and “or,” should be removed.
Pg 198	Line 4695	Does the term, “60 days per year,” refer to actual calendar days or business days?
Pg 204	Line 4833	The comma between the terms, “section” and “and,” should be removed.
Pg 206	Line 4890	Is the section number, 15, correct?
Pg 207	Line 4907	Is the section number, 16, correct?
Pg 211	Line 5000	Is the section number, 17, correct?
Pg 212	Lines 5029-5030	Is the section number, 18, correct?
Pg 213	Line 5057	Is the section number, 19, correct?
Pg 213	Lines 5069-5070	Is the section number, 20, correct?
Pg 215	Line 5103	Is the section number, 21, correct?
Pg 215	Lines 5110-5111	Is the section number, 22, correct?
Pg 217	Line 5165	Is the section number, 23, correct?
Pg 218	Line 5195	Is the section number, 24, correct?
Pg 220	Line 5225	Is the section number, 25, correct?
Pg 222	Line 5288	Is the section number, 26, correct?
Pg 223	Line 5300	Is the section number, 27, correct?

Pg 224	Lines 5328-5329	Is the section number, 28, correct?
Pg 225	Line 5360	Is the section number, 29, correct?
Pg 225	Line 5371	Is the section number, 30, correct?
Pg 226	Line 5391	Is the section number, 31, correct?
Pg 227	Line 5421	Is the section number, 32, correct?
Pg 227	Line 5434	Is the section number, 33, correct?
Pg 229	Line 5454	Is the section number, 34, correct?
Pg 229	Lines 5465-5566	Is the section number, 35, correct?
Pg 231	Line 5501	Is the section number, 36, correct?
Pg 231	Line 5512	Is the section number, 37, correct?
Pg 231	Line 5520	Is the section number, 38, correct?
Pg 232	Line 5528	Is the section number, 39, correct?
Pg 234	Line 5590	Is the section number, 40, correct?

Addendum 2
Physical Properties of Radionuclides
Currently in Use or Under Development for Therapeutic Radiopharmaceuticals

		Major Radiation Emissions[+]		
Radionuclide	**Half-Life**	**Radiations**	**Yield (Bq-sec)$^{-1}$**	**Energy(MeV)**
Actinium-225 (Ac-225)	10.0 days	α 10	2.30×10^{-03}	5.286
		α recoil	2.30×10^{-03}	9.486×10^{-02}
		α 13	1.40×10^{-03}	5.443
		α recoil	1.40×10^{-03}	9.767×10^{-02}
		α 18	1.20×10^{-02}	5.580
		α recoil	1.20×10^{-02}	1.001×10^{-01}
		α 20	1.10×10^{-02}	5.609
		α recoil	1.10×10^{-02}	1.007×10^{-01}
		α 21	4.40×10^{-02}	5.637
		α recoil	4.40×10^{-02}	1.012×10^{-01}
		α 22	1.30×10^{-02}	5.682
		α recoil	1.30×10^{-02}	1.020×10^{-01}
		α 23	3.10×10^{-02}	5.724
		α recoil	3.10×10^{-02}	1.027×10^{-01}
		α 24	8.70×10^{-03}	5.731
		α recoil	8.70×10^{-03}	1.028×10^{-01}
		α 25	1.32×10^{-02}	5.732
		α recoil	1.32×10^{-02}	1.029×10^{-01}
		α 26	8.00×10^{-02}	5.732
		α recoil	8.00×10^{-02}	1.029×10^{-01}
		α 27	8.60×10^{-02}	5.791
		α recoil	8.60×10^{-02}	1.039×10^{-01}
		α 28	1.81×10^{-01}	5.793
		α recoil	1.81×10^{-01}	1.039×10^{-01}
		α 29	3.30×10^{-03}	5.805
		α recoil	3.30×10^{-03}	1.042×10^{-01}
		α 33	5.07×10^{-01}	5.83
		α recoil	5.07×10^{-01}	1.046×10^{-01}
		γ 1	8.50×10^{-02}	1.064×10^{-02}

		ce-L, γ 2	$6.58x10^{-02}$	$7.361x10^{-03}$a
		ce-M, γ 2	$1.76x10^{-02}$	$2.135x10^{-02}$a
		ce-N+, γ 2	$5.67x10^{-03}$	$2.485x10^{-02}$a
		ce-L, γ 3	$6.20x10^{-02}$	$1.806x10^{-02}$a
		ce-M, γ 3	$1.70x10^{-02}$	$3.205x10^{-02}$a
		ce-N+, γ 3	$6.20x10^{-03}$	$3.555x10^{-02}$a
		ce-L, γ 4	$5.99x10^{-02}$	$1.986x10^{-02}$a
		ce-M, γ 4	$1.61x10^{-02}$	$3.385x10^{-02}$a
		ce-N+, γ 4	$5.18x10^{-03}$	$3.735x10^{-02}$a
		γ 8	$4.30x10^{-03}$	$6.290x10^{-02}$
		ce-L, γ 8	$3.55x10^{-02}$	$4.426x10^{-02}$a
		ce-M, γ 8	$8.47x10^{-03}$	$5.825x10^{-02}$a
		ce-N+, γ 8	$2.80x10^{-03}$	$6.175x10^{-02}$a
		ce-L, γ 9	$6.15x10^{-03}$	$4.566x10^{-02}$a
		ce-M, γ 9	$1.60x10^{-03}$	$5.965x10^{-02}$a
		ce-L, γ 11	$2.31x10^{-03}$	$5.276x10^{-02}$a
		ce-L, γ 12	$4.00x10^{-03}$	$5.486x10^{-02}$a
		ce-M, γ 12	$1.00x10^{-03}$	$6.885x10^{-02}$a
		γ 13	$2.64x10^{-03}$	$7.390x10^{-02}$
		γ 16	$2.26x10^{-03}$	$8.740x10^{-02}$
		ce-L, γ 17	$4.20x10^{-03}$	$7.626x10^{-02}$a
		ce-M, γ 17	$1.18x10^{-03}$	$9.025x10^{-02}$a
		ce-L, γ 18	$1.12x10^{-03}$	$7.806x10^{-02}$a
		γ 19	$7.00x10^{-03}$	$9.960x10^{-02}$
		ce-L, γ 19	$1.61x10^{-02}$	$8.096x10^{-02}$a
		ce-M, γ 19	$3.92x10^{-03}$	$9.495x10^{-02}$a
		ce-N+, γ 19	$1.28x10^{-03}$	$9.845x10^{-02}$a
		γ 20	$1.00x10^{-02}$	$9.980x10^{-02}$
		ce-L, γ 21	$3.15x10^{-03}$	$8.216x10^{-02}$a
		γ 23	$2.16x10^{-03}$	$1.084x10^{-01}$
		ce-K, γ 23	$1.56x10^{-02}$	$7.263x10^{-03}$
		ce-L, γ 23	$4.97x10^{-03}$	$8.976x10^{-02}$a
		ce-M, γ 23	$1.25x10^{-03}$	$1.037x10^{-01}$a
		γ 24	$2.64x10^{-03}$	$1.115x10^{-01}$

		γ 37	$1.26x10^{-03}$	$1.452x10^{-01}$
		γ 38	$6.00x10^{-03}$	$1.501x10^{-01}$
		γ 40	$1.82x10^{-03}$	$1.539x10^{-01}$
		γ 41	$3.20x10^{-03}$	$1.573x10^{-01}$
		ce-K, γ 41	$5.41x10^{-03}$	$5.616x10^{-02}$
		ce-L, γ 41	$2.24x10^{-03}$	$1.387x10^{-02}$a
		γ 50	$4.50x10^{-03}$	$1.880x10^{-01}$
		γ 51	$1.23x10^{-03}$	$1.958x10^{-01}$
		ce-K, γ 51	$1.37x10^{-03}$	$9.466x10^{-02}$
		γ 56	$2.71x10^{-03}$	$2.169x10^{-01}$
		γ 63	$1.16x10^{-03}$	$2.535x10^{-01}$
Bismuth-213 (Bi-213)	45.61 minutes	α 1	$1.81x10^{-03}$	5.558
		α recoil	$1.81x10^{-03}$	$1.055x10^{-01}$
		α 2	$1.96x10^{-02}$	5.875
		α recoil	$1.96x10^{-02}$	$1.115x10^{-01}$
		β- 3	$5.86x10^{-03}$	$9.080x10^{-02*}$
		β- 8	$3.07x10^{-01}$	$3.204x10^{-01*}$
		β- 9	$2.29x10^{-03}$	$3.768x10^{-01*}$
		β- 3	$6.58x10^{-01}$	$4.922x10^{-01*}$
		γ 1	$4.29x10^{-03}$	$2.928x10^{-01}$
		γ 2	$1.67x10^{-03}$	$3.237x10^{-01}$
		γ 9	$2.92x10^{-03}$	$8.074x10^{-01}$
		γ 15	$2.59x10^{-03}$	1.100
Iodine-131 (I-131)	8.0252 days	β- 1	$2.08x10^{-02}$	$6.936x10^{-02*}$
		β- 2	$6.45x10^{-03}$	$8.694x10^{-02*}$
		β- 3	$7.23x10^{-02}$	$9.662x10^{-02*}$
		β- 4	$8.96x10^{-01}$	$1.916x10^{-01*}$
		β- 6	$3.90x10^{-03}$	$2.832x10^{-01*}$
		γ 1	$2.62x10^{-02}$	$8.019x10^{-02}$
		ce-K, γ 1	$3.14x10^{-02}$	$4.562x10^{-02}$
		ce-L, γ 1	$4.45x10^{-03}$	$7.473x10^{-02}$a
		γ 3	$2.69x10^{-03}$	$1.772x10^{-01}$
		γ 6	$6.12x10^{-02}$	$2.843x10^{-01}$
		ce-K, γ 6	$2.50x10^{-03}$	$2.497x10^{-01}$

		γ 11	$2.73x10^{-03}$	$3.258x10^{-01}$
		γ 13	$8.15x10^{-01}$	$3.645x10^{-01}$
		ce-K, γ 13	$1.56x10^{-02}$	$3.299x10^{-01}$
		ce-L, γ 13	$2.44x10^{-03}$	$3.590x10^{-01}$a
		γ 15	$3.59x10^{-03}$	$5.030x10^{-01}$
		γ 16	$7.16x10^{-02}$	$6.370x10^{-01}$
		γ 17	$2.17x10^{-03}$	$6.427x10^{-01}$
		γ 18	$1.77x10^{-02}$	$7.299x10^{-01}$
Lead-212 (Pb-212)	10.64 hours	β- 1	$5.08x10^{-02}$	$4.110x10^{-02*}$
		β- 2	$8.31x10^{-01}$	$9.350x10^{-02*}$
		β- 3	$1.19x10^{-01}$	$1.717x10^{-01*}$
		γ 1	$5.96x10^{-03}$	$1.152x10^{-01}$
		ce-K, γ 1	$3.45x10^{-02}$	$2.466x10^{-02}$
		ce-L, γ 1	$6.05x10^{-03}$	$9.880x10^{-02}$a
		γ 4	$5.96x10^{-03}$	$1.152x10^{-01}$
		ce-K, γ 4	$3.23x10^{-01}$	$1.481x10^{-01}$
		ce-L, γ 4	$5.60x10^{-02}$	$2.222x10^{-01}$a
		ce-M, γ 4	$1.32x10^{-02}$	$2.346x10^{-01}$a
		ce-N+, γ 4	$4.40x10^{-03}$	$2.377x10^{-01}$a
		γ 5	$3.30x10^{-02}$	$3.001x10^{-01}$
		ce-K, γ 5	$1.30x10^{-02}$	$2.096x10^{-01}$
		ce-L, γ 5	$2.25x10^{-03}$	$2.837x10^{-01}$a
Lutitium-177 (Lu-177)	6.647 days	β- 1	$1.16x10^{-01}$	$4.766x10^{-02*}$
		β- 3	$9.00x10^{-02}$	$1.117x10^{-01*}$
		β- 4	$7.94x10^{-01}$	$1.494x10^{-01*}$
		γ 1	$1.72x10^{-03}$	$7.164x10^{-02}$
		γ 2	$6.17x10^{-02}$	$1.129x10^{-01}$
		ce-K, γ 2	$5.12x10^{-02}$	$4.760x10^{-02}$
		ce-L, γ 2	$6.73x10^{-02}$	$1.017x10^{-01}$a
		ce-M, γ 2	$1.67x10^{-02}$	$1.103x10^{-01}$a
		ce-N+, γ 2	$4.80x10^{-03}$	$1.124x10^{-01}$a
		γ 4	$1.04x10^{-01}$	$2.084x10^{-01}$
		ce-K, γ 4	$5.70x10^{-03}$	$1.430x10^{-01}$
		γ 5	$2.01x10^{-03}$	$2.497x10^{-01}$

		γ 6	$2.10x10^{-03}$	$3.213x10^{-01}$
Phosphorus-32 (P-32)	14.268 days	β- 1	1.00	$6.950x10^{-01*}$
Radium-223 (Ra-223)	11.43 days	α 14	$1.50x10^{-03}$	5.287
		α recoil	$1.50x10^{-03}$	$9.575x10^{-02}$
		α 15	$1.30x10^{-03}$	5.339
		α recoil	$1.30x10^{-03}$	$9.668x10^{-02}$
		α 16	$1.30x10^{-03}$	5.366
		α recoil	$1.30x10^{-03}$	$9.717x10^{-02}$
		α 17	$2.22x10^{-02}$	5.434
		α recoil	$2.22x10^{-02}$	$9.840x10^{-02}$
		α 19	$1.00x10^{-02}$	5.502
		α recoil	$1.00x10^{-02}$	$9.963x10^{-02}$
		α 20	$9.00x10^{-02}$	5.540
		α recoil	$9.00x10^{-02}$	$1.003x10^{-01}$
		α 21	$2.52x10^{-01}$	5.607
		α recoil	$2.52x10^{-01}$	$1.015x10^{-01}$
		α 22	$5.16x10^{-01}$	5.716
		α recoil	$5.16x10^{-01}$	$1.035x10^{-01}$
		α 23	$9.00x10^{-02}$	5.747
		α recoil	$9.00x10^{-02}$	$1.041x10^{-01}$
		α 24	$3.10x10^{-03}$	5.858
		α recoil	$3.10x10^{-03}$	$1.061x10^{-01}$
		α 25	$1.00x10^{-02}$	5.871
		α recoil	$1.00x10^{-02}$	$1.063x10^{-01}$
		ce-K, γ 13	$2.18x10^{-03}$	$9.281x10^{-02}$a
		γ 16	$1.21x10^{-02}$	$1.223x10^{-01}$
		ce-K, γ 16	$7.47x10^{-02}$	$2.391x10^{-02}$
		ce-L, γ 16	$1.40x10^{-02}$	$1.043x10^{-01}$a
		ce-M, γ 16	$3.36x10^{-03}$	$1.178x10^{-01}$a
		ce-N+, γ 16	$1.17x10^{-03}$	$1.212x10^{-01}$a
		γ 19	$3.27x10^{-02}$	$1.442x10^{-01}$
		ce-K, γ 19	$1.27x10^{-01}$	$4.583x10^{-02}$
		ce-L, γ 19	$2.35x10^{-02}$	$1.262x10^{-01}$a
		ce-M, γ 19	$5.59x10^{-03}$	$1.398x10^{-01}$a

		ce-N+, γ 19	$1.95x10^{-03}$	$1.431x10^{-01}$a
		γ 21	$5.70x10^{-02}$	$1.542x10^{-01}$
		ce-K, γ 21	$1.85x10^{-01}$	$5.580x10^{-02}$
		ce-L, γ 21	$3.36x10^{-02}$	$1.362x10^{-01}$a
		ce-M, γ 21	$7.98x10^{-03}$	$1.497x10^{-01}$a
		ce-N+, γ 21	$2.78x10^{-03}$	$1.531x10^{-01}$a
		γ 22	$6.95x10^{-03}$	$1.586x10^{-01}$
		ce-K, γ 22	$2.03x10^{-02}$	$6.023x10^{-02}$
		ce-L, γ 22	$3.82x10^{-03}$	$1.406x10^{-01}$a
		γ 26	$1.53x10^{-03}$	$1.795x10^{-01}$
		ce-K, γ 26	$2.58x10^{-03}$	$8.114x10^{-02}$
		γ 35	$1.39x10^{-01}$	$2.695x10^{-01}$
		ce-K, γ 35	$9.29x10^{-02}$	$1.711x10^{-01}$
		ce-L, γ 35	$1.70x10^{-02}$	$2.514x10^{-01}$a
		ce-M, γ 35	$4.02x10^{-03}$	$2.650x10^{-01}$a
		ce-N+, γ 35	$1.37x10^{-03}$	$2.684x10^{-01}$a
		γ 38	$1.60x10^{-03}$	$2.882x10^{-01}$
		γ 39	$3.99x10^{-02}$	$3.329x10^{-01}$
		ce-K, γ 39	$1.60x10^{-02}$	$2.255x10^{-01}$
		ce-L, γ 39	$2.90x10^{-02}$	$3.058x10^{-01}$a
		γ 43	$2.22x10^{-03}$	$3.429x10^{-01}$
		γ 49	$4.87x10^{-03}$	$3.717x10^{-01}$
		ce-K, γ 49	$1.38x10^{-03}$	$2.733x10^{-01}$
		γ 57	$1.29x10^{-02}$	$4.450x10^{-01}$
		ce-K, γ 57	$2.25x10^{-03}$	$3.466x10^{-01}$
Rhenium-186 (Re-186)	3.7183 days	γ 1	$6.03x10^{-03}$	$1.226x10^{-01}$
		ce-L, γ 1	$5.55x10^{-03}$	$1.105x10^{-01}$a
		β- 3	$2.15x10^{-01}$	$3.061x10^{-01*}$
		β- 4	$7.10x10^{-01}$	$3.529x10^{-01*}$
		γ 1	$9.47x10^{-02}$	$1.372x10^{-01}$
		ce-K, γ 1	$4.16x10^{-02}$	$6.329x10^{-02}$
		ce-L, γ 1	$6.05x10^{-02}$	$1.242x10^{-01}$a
		ce-M, γ 1	$1.53x10^{-02}$	$1.341x10^{-01}$a
		ce-N+, γ 1	$4.63x10^{-03}$	$1.365x10^{-01}$a

Samarium-153 (Sm-153)	46.50 hours	β- 14	$3.13x10^{-01}$	$1.995x10^{-01*}$
		β- 16	$4.94x10^{-01}$	$2.253x10^{-01*}$
		β- 17	$6.00x10^{-03}$	$2.274x10^{-01*}$
		β- 18	$1.84x10^{-01}$	$2.643x10^{-01*}$
		γ 5	$4.73x10^{-02}$	$6.967x10^{-02}$
		ce-K, γ 5	$2.12x10^{-01}$	$2.115x10^{-02}$
		ce-L, γ 5	$3.45x10^{-02}$	$6.162x10^{-02}$a
		ce-M, γ 5	$7.52x10^{-03}$	$6.787x10^{-02}$a
		γ 6	$1.93x10^{-03}$	$7.542x10^{-02}$
		γ 7	$1.92x10^{-03}$	$8.337x10^{-02}$
		γ 8	$1.58x10^{-03}$	$8.949x10^{-02}$
		γ 10	$7.72x10^{-03}$	$9.743x10^{-02}$
		γ 11	$2.92x10^{-01}$	$1.032x10^{-01}$
		ce-K, γ 11	$4.24x10^{-01}$	$5.466x10^{-02}$
		ce-L, γ 11	$6.32x10^{-02}$	$9.513x10^{-02}$a
		ce-M, γ 11	$1.37x10^{-02}$	$1.014x10^{-01}$a
		ce-N+, γ 11	$3.95x10^{-03}$	$1.028x10^{-01}$a
Strontium-89 (Sr-89)	50.563 days	β- 2	1.00	$5.871x10^{-01*}$
Yttrium-90 (Y-90)	64.00 hours	β- 3	1.00	$9.337x10^{-01*}$
Zirconium-89 (Zr-89)	78.41 hours	β+ 1	$2.27x10^{-01}$	$3.955x10^{-01*}$
		γ ±	$4.55x10^{-01}$	$5.110x10^{-01}$
		γ 1	$9.90x10^{-01}$	$9.092x10^{-01}$
		ce-K, γ 1	$7.36x10^{-03}$	$8.921x10^{-01}$
		γ 3	$1.06x10^{-03}$	1.657
		γ 4	$7.45x10^{-03}$	1.713
		γ 5	$1.23x10^{-03}$	1.745

[+] Data from the Nuclear Decay Data in the MIRD Format at http://www.nndc.bnl.gov/mird/ - yields >1.00 x 10^{-3}

[*] Average Energy (MeV)

a Maximum Energy (MeV) for subshell