Advisory Committee on Medical Uses of Isotopes (ACMUI)
Sub-Committee on Proposed Rule

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

Subcommittee Members:
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Note
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. The Sub-Committee identifies many of its comments with respect to the relevant page and/or line numbers in a version of the foregoing document in which it has inserted line numbers.

The ACMUI has unanimously approved this current, final version of this report.

General Comments

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

a. Historical review of permanent implant brachytherapy misadministration/medical event.

In considering the criteria for an ME in permanent implant brachytherapy, it would be helpful to review the recent regulatory history of MEs for this form of therapy. In the current 10 CFR 35.2 (Definitions), "prescribed dose" for manual brachytherapy is defined as "…either the total source strength and exposure time or the total dose, as documented in the written directive." This definition implies that total source strength (activity) or exposure time is interchangeable with total dose. The current ME criteria in 10 CFR 35.3045 (a) (1) (i) do not include any dose unit and so do not appear to exclude use of total source strength (activity) or exposure time. The activity-based criterion for permanent implant brachytherapy MEs in proposed rule thus does not actually differ from that in the current.

To explore this further, previous Part 35 rulemakings were reviewed. NRC's final rule for "Quality Management Program and Misadministrations" published July 25, 1991 [58 FR 34104] established the first definition of a misadministration, which for brachytherapy is as follows.

"A brachytherapy radiation dose:

(i) Involving the wrong patient, wrong radioisotope, or wrong treatment site (excluding, for permanent implants, seeds that were implanted in the correct site but migrated outside the treatment site);

(ii) Involving a sealed source that is leaking;

(iii) When, for a temporary implant one or more sealed sources are not removed upon completion of the procedure; or

(iv) When the calculated administered dose differs from the prescribed dose by more than 20 percent of the prescribed dose." [58 FR 34120].

While item (iv) uses the term, "calculated administered dose," the document also provides the following discussion of a brachytherapy misadministration:

"Paragraph (6) applies to brachytherapy procedures other than those specified in paragraph (5) above. This paragraph is essentially the same as paragraph **(**d) in the proposed definition of prescription. This paragraph requires the authorized user (AU) to specify, before implantation, the radioisotope, the source strengths, and the number of sources, but does not require the total dose because detailed calculations are required to determine the total dose after the sources are implanted. However, following implantation but before completion of the procedure, AU must specify, among other parameters, the total source strength and exposure time. If the AU prefers, the total dose may be used instead of the total source strength and exposure time. This change, using total source strength and exposure time, provides an easy way of specifying the total dose and simplifies the determination of a misadministration. Since the total source strength is fixed when the sources are implanted, delivering the prescribed dose is a matter of using the correct (ie prescribed) exposure time. In other words, after implanting the correct sources, the exposure time (and total dose) will be correct if the sources are removed at the correct time." [58 FR 34115].

The foregoing discussion suggests that the current rule allows use of total source strength and exposure time to identify whether there was a misadministration.

In NRC's final rule for "Medical Use of Byproduct Material" published April 24, 2002 [67 FR 20250], the requirements of 35.3045 "…are based on the current requirements in Section35.33, Notifications, reports, and records of misadministrations" [67 FR 20363]. This rulemaking description does not indicate that NRC will no longer allow use of total source strength and exposure time in determination of a ME. Would that not mean that the 1991 statement allowing use of total source strength and exposure time also applies to identifying a brachytherapy ME? The ACMUI and its Rulemaking Sub-Committee unanimously recommend NRC staff allow 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.

b. 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 decision during the implant procedure.

c. There is some concern that the proposed ME definition may discourage practitioners from utilizing this therapy. The ACMUI and its Rulemaking Sub-Committee therefore unanimously recommend that NRC solicit information on whether the proposed ME definition for permanent implant brachytherapy will discourage licensees from using this therapy option or will otherwise adversely impact clinical practice, with the recognition that NRC may utilize language it deems most appropriate for soliciting this type of information from its stakeholders.

d. There is also concern with the OAS's position (page 29, lines 871-879, and page 77 ("Draft Compatibility Table for Proposed Rule")) that the draft rule re-defining MEs in permanent implant brachytherapy should be designated as Compatibility Category C for the Agreement States, thereby allowing them to retain the dose-based criteria for definition of a ME. The rationale for conversion from dose-based to activity-based criteria has been detailed, with the most important component of this rationale being the failure of dose-based criteria to sensitively and specifically capture clinically significant "misadministrations" in permanent implant brachytherapy. Retaining the current dose-based criteria (as specified in Section 35.3045), would still result in clinically insignificant occurrences being identified as MEs and thereby perpetuate the confusion associated with the current activity-based criteria. The ACMUI and its Rulemaking Sub-Committee recommend that the draft rule re-defining medical events in permanent implant brachytherapy be designated as Compatibility Category B. This recommendation was approved by the ACMUI with one dissenting vote.

e. Rather than ascribing the rationale for the ME criteria based on the absorbed dose to 5 cubic centimeters of contiguous normal tissue "…to the literature…," the following reference should be cited:

S Nag, H Cardenes, S Chang, I Das, B Erickson, G Ibbott, J Lowenstein, J Roll, B Thomadsen, M Varia. Proposed guidelines for image-based intracavitary brachytherapy for cervical carcinoma: Report from Image-Guided Brachytherapy Working Group Int J Radiat Oncol Biol Phys 60:1160-1172, 2004.

The ACMUI and its Rulemaking Sub-Committee unanimously recommend citation of this reference in the proposed rule.

2. Training and experience (T&E) requirements for authorized users (AU), medical physicists, Radiation Safety Officers (RSO), and nuclear pharmacist.

a. There is enthusiastic support for eliminating the preceptor statement requirement for Board-certified individuals.

b. With regard to the sentence on page 48, lined 1447-1448, why do AUs need to have work experience on the elution of generators? This topic should be covered as part of their didactic (ie classroom and laboratory) training. It is likely that the vast majority of § 35.200 AUs are not responsible for a generator system because they obtain unit dosages or bulk radionuclide from a commercial radiopharmacy. Would it not make more sense, therefore, that licensees approved to use generator systems show specific training on the requirement now listed under § 35.290 (c) (1) (ii)(G) for those individuals (AUs and others) who are responsible for proper operation and test of the generator as part of their license conditions? This could be similar to the way boiler-plate license conditions are used for sealed-source leak test requirements or for decay-in-storage requirements. The ACMUI and its Rulemaking Sub-Committee thus recommend

unanimously that (a) licensees approved to use generator systems show specific training on the requirement now listed under 35.290 (c) (1) (ii) (G) for those individuals (Authorized Users and others) who are responsible for proper operation and testing of the generator as part of their license conditions and (b) that Authorized Nuclear Pharmacists who have the adequate training and experience (T&E) are able to provide the supervised work experience for Authorized Users on the elution of generators.

c. With respect to the amended requirements for preceptor attestation for an individual seeking regulatory authorization as an RSO, AMP, ANP, or AU, the ACMUI and its Rulemaking Sub-Committee unanimously endorse 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).

d. The ACMUI has reservations about certain elements of Section 35.390 (Training for use of unsealed byproduct material for which a written directive is required) (pages 49-51) and of Section 35.396 (Training for the parenteral administration of unsealed byproduct material requiring a written directive) pages (53-55). Specifically, lines 1503 to 1508 (Section 35.390) state, "The current regulations include a broad category for parenteral administrations of 'any other' radionuclide. This broad category would be removed as any new parenteral administration of radionuclides not listed in this paragraph would be regulated under § 35.1000. This approach would allow the NRC to review each new proposed radionuclide for parenteral administration and determine the appropriate T&E for its use." And lines 1628-1632 (Section 35.396) state, "AUs authorized to use any of the categories for parenteral administration of radionuclides in § 35.390(b) (1) (ii) (G) would also have to meet the supervised work experience requirements in paragraph (d) of this section for each new parenteral administration listed in § 35.390(b) (1) (ii) (G) for which the individual is requesting AU status." The proposed radionuclide-by-radionuclide determination by the NRC of T&E requirements is unnecessary, places an unnecessary regulatory burden on practitioners, and may delay or prevent patient access to effective radionuclide-based diagnostics and therapeutics. There are only several types of radiations associated with radioactive decay: photons (x- and gamma-rays), beta particles (positrons and negatrons), electrons (internal conversion and Auger), and alpha particles, and there is no *fundamental* difference in the clinical applications and radiation safety among these radiations. The ACMUI believes the training and experience a physician receives to perform parenteral administration of a radiopharmaceutical, including the three cases of work experience, is sufficient in demonstrating that physician's competency to function as an AU for both beta-/gamma-emitting and alpha-emitting radiopharmaceuticals. NRC staff has not provided a compelling radiation-safety need for emission-specific T&E requirements. The ACMUI is concerned that this separation would have the opposite effect: the separation of beta-/gamma-emitting alpha-emitting radiopharmaceuticals expends licensee and regulatory staff resources in the prescriptive bookkeeping needed to track all these separate work experiences that the supervising AU and the physician being trained has had. In

addition, the ACMUI is concerned that the proposed separation does not address how AUs currently approved under § 35.390 and § 35.396 will be grandfathered to allow parenteral administration alpha-emitting radiopharmaceuticals and to act as supervising AUs for § 35.390 (b) (1) (ii) (G). Therefore, The ACMUI and its Rulemaking Sub-Committee recommend unanimously (with one abstention) that the work experience for parenteral administrations under § 35.390 (b) (1) (ii) (G) and § 35.396 **not** be separated between parenteral administration of a beta/gamma-emitting radiopharmaceutical versus an alpha-emitting radiopharmaceutical as proposed.

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 proposed regulations contain 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." See related Specific Comments below.

b. Some of the terminology NRC has historically used and now uses in the proposed rule is somewhat confusing. For clarification of meaning, it is suggested that 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.

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 unanimously 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. Once a board has been recognized by the NRC, the date of recognition is irrelevant. This point should be stated explicitly in the proposed rule.

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-89 (Rb-89) generators. Should other generator systems be included or should this section be generalized to all medical generator systems?

The current Food and Drug Administration (FDA) labeling requirements (ie 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 □Ci of Mo99 per mCi of Tc99m at the time of patient administration. The current FDA labeling is therefore more restrictive than the current NRC rule, while the proposed rule will match that of the FDA in terms of frequency of eluate testing (ie for each elution). Therefore, The ACMUI and its Rulemaking Sub-Committee unanimously recommend the NRC adopt the FDA-approved package insert for parent-breakthrough limits for radioisotope generators.

Pursuant to its recently revised labeling requirements for strontium-89 (Sr-89)/rubidium-89 (Rb-89) 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 comply with the FDA regulation. As discussed at the 4/17/2012 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 requirements regulation.

For generator breakthrough testing, conformity between the corresponding FDA regulations and NRC rules is highly recommended. This would be especially beneficial as new generators (eg 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. Of course, if the NRC feels it cannot inspect a licensee for compliance with the applicable FDA regulation at this time, then the proposed rule for breakthrough testing of Mo-99/Tc-99m generators is recommended.

b. The proposed NRC reporting requirement for out-of-tolerance generator elutions was debated at length by the ACMUI. 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 to the NRC and the manufacturers or distributers of medical generators any measurement that exceeds the limits specified in § 35.204(a) within 24 hours. The second requirement in § 30.50 would require manufacturers/distributors to report to the NRC when they receive such a notification from a licensee" (page 26 (lines 788-793), Section IV. f. (Requiring reporting and notification of failed Mo-99/Tc-99m and Sr-82/Rb-82 generators)). To lessen the reporting burden on licensees, the ACMUI considered reducing the reporting requirement for licensees to a single requirement, namely, reporting to the vendor. If licensees were required to report out-of-tolerance elution results to the vendor (which is the standard prevailing practice when out-of-tolerance generator elutions are found), then a requirement for the vendor to report such results to the NRC could be imposed. By a split vote, the ACMUI does *not* support the requirement in the proposed rule that licensees report to the NRC generator elutions with out-of-tolerance parent-breakthrough, as discussed below.

The ACMUI does not find the NRC's rationale - in lines 768-804 on pages 26 and 27 - for its proposed dual-reporting requirement (to the vendor and to the NRC) for out-of-tolerance generator elutions compelling. In the exposition of its rationale, the NRC states, for example, that, "The FDA may not investigate each reported incident and may take a considerable amount of time in investigating the cause of reported failures." Given the FDA's long-standing experience and expertise in the regulation of radiopharmaceuticals, however, it is the regulatory agency of choice for dealing with out-of-tolerance generator elutions. Further, the assertion that, "…some incidents of failed generators may not be reported to the FDA because certain manufacturers are not in the United States, and the generators are distributed by vendors who are not required to report to the FDA," is somewhat specious. If a drug product in used in the United States, it requires FDA approval. And, in either the new drug or an abbreviated new drug application, the manufacturing standard operating procedures (SOPs) and manufacturing site will be reviewed, inspected and approved by the FDA before the

product is actually marketed. If a licensee's generator is not performing to specifications and thus cannot be used for patient studies, the manufacturer will be notified immediately, either directly or indirectly through a vendor. The foregoing SOPs include protocols for documenting and reporting a product failure when the manufacturer is contacted by a customer/licensee, including how to form and implement a Deviation Investigation Team (DIT) to investigate such a failure. These SOPs also include a procedure for implementing and performing a Corrective and Preventative Action investigation if a DIT is unsuccessful. Finally, a formal mechanism in already in place for sharing of information among federal agencies, with a memorandum of understanding (MOU) dated December 4, 2002 between the FDA and the NRC - "The purpose of this MOU is to coordinate existing NRC and FDA regulatory programs for (1) medical devices, drugs, and biological products utilizing byproduct, source, or special nuclear material..." The MOU also calls for an annual meeting between the two agencies, providing an appropriate mechanism for addressing criteria for the evaluation process and the assessment of the regulatory response to issues of mutual responsibility.

c. With respect to Sr-82/Rb-82 generators, the proposed "reporting" rule does not actually address the underlying cause - the apparent failure of licensees to perform daily breakthrough testing - of the recent reported instances of excess radiostrontium breakthrough. Appropriate breakthrough testing at the two medical facilities involved very likely would have detected the out-of-tolerance breakthrough results and avoided the resulting large-scale disruption of Rb-82 myocardial perfusion studies. Has the NRC prepared an RIS or other document to emphasize the importance of and the proper method for breakthrough testing for this type of generator? Has it communicated with the Agreement States the importance of inspecting sites for not only regulatory compliance but also for demonstrated competency of a licensee's staff in performing breakthrough tests for Sr-82/Rb-82 generators? Has the NRC addressed training requirements for AUs who wish to use generators under Section 35.290? The current training requirements are specific to Mo-99/Tc99m generators; training requirements have not kept pace with new and different generators.

d. With respect to item c., it is suggested that NRC solicit comments in Supplementary Information Section IV. D. specifically on whether the proposed notification requirements will discourage licensees from using generators, potentially limiting development of generator-based radiopharmaceuticals and having an adverse economic impact on vendors of generator systems.

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

a. With the addition of the term, "ARSO," Section 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 and allowed to be named on medical licenses. Specific changes are suggested in the Specific Comments below.

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.

6. "Plain language" requirement

a. Section X. Plain Language (lines 2198-2200) states, "The NRC requests comment on the proposed rule with respect to the clarity and effectiveness of the language." Overall, the proposed rule is well-written and well-organized. It could be shortened, and improved, by eliminating redundancies and consolidating related sections, eliminating identical or nearly identical passages appearing multiple times throughout the draft rule. A further improvement would be the inclusion of a detailed "executive summary"-style section summarizing, perhaps in a "bullet" format, the key changes introduced in the draft rule. This would be in place of the current one-paragraph Summary.

7. Additional general comments

a. Elimination of the requirement to submit a second copy of the 313 application is excellent

b. Use of different sealed sources is a helpful change. However, licensees will have the need to easily access device registry documents. Can NRC provide access to copies of these registrations?

c. The gamma-knife change to 7-year full inspections is also helpful.

Specific Comments - Significant

Pg 10	Lines 323-324	The phrase, "…for the modalities that they practiced as of October 24, 2005…," should be changed to, "…for the modalities covered by their board certification as of October 24, 2005…"
Pg 10	Lines 325-326	The phrase, "…for the modalities that they practiced as of October 24, 2005…," should be changed to, "…for the modalities covered by their board certification as of October 24, 2005…"
Pg 10	Line 343	The phrase, "…for the modalities that they practiced as of October 24, 2005…," should be changed to, "…for the modalities covered by their board certification as of October 24, 2005…"
Pp 10-11	Lines 339-343	Amend Section 35.57 to recognize all individuals that were previously certified by boards recognized under the previous Subpart J as RSOs, teletherapy or medical physicists, AMPs, AUs , nuclear pharmacists, and ANPs for the modalities covered by their board certification as of October 24, 2005. The staff believes that these individuals should be eligible for grandfathering for the modalities that their board certification covered 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.

		Therefore, the NRC believes that preceptor attestations are not warranted for these "grandfathered" individuals so long as the provisions of § 35.59 are met and the individual requests authorizations only for the modalities the individual's board certification covered as of October 24, 2005.
Pg 29	Lines 866-868	This sentence appears to be incomplete or otherwise grammatically incorrect. In any case, its meaning is not clear. It should be revised and clarified.
Pg 32	Lines 960-963	This statement is not entirely accurate, as § 35.204 (b) requires "A licensee that uses molybdenum-99/technetium-99m generators for preparing a technetium-99m radiopharmaceutical shall measure the molybdenum-99 concentration of the *first* eluate after receipt of a generator to demonstrate compliance with paragraph (a) of this section." The proposed rule would require such a measurement after *every* elution, as noted earlier.
Pg 38	Lines 1155-1156	The phrase, "The maximum absorbed dose to any 5 contiguous cubic centimeters…," should be changed to, "The minimum absorbed dose to the maximally exposed 5 contiguous cubic centimeters…" Similar revisions are also suggested in the "Specific Comments - Minor" below.
Pg 39	Lines 1181-1182	It is suggested to revise this passage as follows. 2) adding a provision that would allow individuals identified as an AU, AMP, or ANP, on a medical license to be an RSO or an ASRSO not only on their current license, but also on a different medical license.
Pg 61	Lines 1852-1852	This sentence states the training must be provided by the device manufacturer or individuals certified by the device manufacturer. How will this requirement impact licensees? Will there be enough trainers for the number of unit operators? Will computer-based training be acceptable?
Pg 90	Line 2653	After this line, insert the following and renumber the items following this addition. 11. In § 35.15, redesignate paragraphs (c), (d), (e), (f), and (g) as paragraphs (d), (e), (f), (h), and (i), respectively, revise newly redesignated paragraphs (d) and (f), and add new paragraphs (c) and (g) to read as follows: § 35.15 Exemptions regarding Type A specific licenses of broad scope.

* * * * *

(c) The provisions of § 35.13(d);

(d) The provisions of § 35.13(f) regarding additions to or changes in the areas of use at the addresses identified in the application or on the license;

* * * * *

(f) The provisions of § 35.14(b) (1) for an authorized user, an authorized nuclear pharmacist, an Associate Radiation Safety Officer, or an authorized medical physicist;

(g) The provisions of § 35.14(b) (2) for a temporary Radiation Safety Officer;

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Pp 99-100	Lines 2944-2950	It is not clear what is meant at the end of this sentence by the phrase, "…any new material." Is this yet another use term that needs to be defined for its regulatory meaning as discussed in Item 3.b. in the General Comments above? It is uncertain, for example, what additional training an experienced, board-certified RSO would need and if a non-board-certified RSO would need a preceptor statement to document this T&E.

Specific Comments - Minor

Pg 1	Line 37	Here and throughout the document, hyphens should be inserted in "compound" adjectives such as "medical use."
Pg 1	Line 37	The phrase, "…molybdenum contamination for each elution…," should be changed to, "…molybdenum-99 contamination for each generator elution…"
Pg 6	Line 225	The phrase, "…on the dose administered to the patient," should be changed to, "…on the radiation absorbed dose delivered to various tissues/structures of the patients body."
Pg 7	Lines 230-231	With the foregoing revision, this sentence should be revised as follows, "The ME criteria would include absorbed doses to normal tissues located outside of the treatment site as well as within the treatment site."
Pg 7	Line 237	The phrase, "…to convert…," should be changed to, "…with the conversion…"
Pg 8	Line 261	The phrase, "…the agency…," should be changed to the word, "regulators."

Pg 8	Line 262	The comma between the words, “training” and “as,” should be deleted.
Pg 8	Line 267	The comma between the terms, “New York” and “in,” should be deleted.
Pg 8	Line 268	The comma between the terms, “Texas” and “in,” should be deleted.
Pg 8	Line 271	A comma should be inserted between the words, “stakeholders” and “to.”
Pg 11	Line 353	The comma between the words, “regulations” and “and,” should be deleted.
Pg 11	Line 372	Is the term, “noticed,” appropriate in the context in which it is being used?
Pg 11	Line 387	The phrase, “…these definitions…,” should be changed to, “…the definition of an ME…”
Pg 12	Line 399	The comma between the terms, “ACMUI” and “as,” should be deleted.
Pg 12	Line 401	The phrase, “…for distinguishing truly significant events from those related to deviations from the WD but otherwise clinically inconsequential.”
Pg 13	Lines 406-407	The phrase, “…, as there is no suitable clinically used dose metric available for judging the occurrence of MEs,” should be changed to, “…, as dose is generally not a reliable metric for identifying clinically significant MEs,” should be appended to the end of this sentence
Pg 13	Line 413	The comma between the terms, “brachytherapy” and “the,” should be deleted.
Pg 13	Line 421	The comma and the word, “and,” should be transposed.
Pg 14	Line 433	The phrase, “…public involvement in…,” should be changed to, “…for further public comment on…”
Pg 14	Line 433	The term, “regulation,” should be changed to, “MEs.”
Pg 14	Line 438	The phrase, “…, noted earlier…,” should be deleted.
Pg 14	Line 439	A hyphen should be inserted between the terms, “source strength” and “based.”
Pg 14	Lines 439-442	This sentence should be revised as follows, “The final report also included a quantitative consideration of the target site

		source distribution, the "octant approach," for if the distribution of implanted sources was irregular enough (i.e., "bunched") relative to the prescribed distribution to qualify as an ME."
Pg 14	Lines 442-443	The "dose-related ME criterion for the treatment site" should be specified.
Pg 14	Line 445	The word, "by," should be changed to the phrase, "…in a…"
Pg 14	Line 447	The phrase, "…expressed criticism…," should be changed to, "…criticized…"
Pg 14	Line 450	The comma between the words, "site" and "removed," should be changed to the word, "and."
Pg 14	Line 451	The comma between the words, "dose" and "was," should be deleted.
Pg 15	Line 457	A comma should be inserted between the terms, "2012" and "to."
Pg 15	Line 474	The comma between the words, "sources" and "for," should be changed to the word, "and."
Pg 15	Line 477	The comma between the words, "site" and "and," should be deleted. A hyphen should be inserted between the words, "dose" and "based."
Pg 15	Line 482	The term, "written directive," should be changed to the abbreviation, "WD."
Pg 16	Line 488	The comma between the terms, "ACMUI" and "for," should be deleted.
Pg 16	Line 499	The phrase, "…the high variation in dose sometimes seen in doses…," should be changed to, "…the pronounced spatial variation in dose sometimes seen with 'point' sources (i.e., seeds)…"
Pg 16	Line 501	The phrase, "…the size of the normal tissues,…," should be changed to, "…the specified volume of the normal tissue affected,…"
Pg 17	Line 514	A hyphen should be inserted in the term, "60-day."
Pg 17	Line 515	The phrase, "…come back…," should be changed to, "…return to the treatment center…"

Pg 17	Line 524	The comma between the words, “sources” or “or,” should be deleted. The comma between the closing parenthesis and the word, “A,” should be deleted.
Pg 17	Line 529	A comma should be inserted between the words, “locations” and “results.”
Pg 17	Line 531	Hyphens should be inserted in the terms, “0.5-sievert” and “50-rem.”
Pg 18	Line 541	The comma at the end of this line should be deleted.
Pg 18	Line 543	A hyphen should be inserted in the term, “post-procedure.”
Pg 18	Line 560	The phrase, “brachytherapy where…,” should be changed to, “brachytherapy procedures, where…”
Pg 19	Line 591	The comma between the terms, “2008” and “with,” should be deleted.
Pg 19	Line 593	Commas should be inserted before and after the phrase, “…if not corrected…”
Pg 20	Line 597	The term, “authorized individuals,” should be changed to, “preceptors.”
Pg 20	Lines 614-617	This sentence should be revised as follows, “The ACMUI advised that training of residents is a collective process and entails the collective judgment of an entire residency program faculty whereas preceptor attestation is an individual process.
Pg 20	Line 618	The comma between the terms, “2008” and “with,” should be deleted.
Pg 22	Line 652	Here and elsewhere in the draft rule, a hyphen should be inserted between the words, “board” and “certified.”
Pg 22	Line 680	The between the terms, “who” and “RSO,” should be deleted.
Pg 22	Line 691	The phrase, “…or other service-provider sites…,” should be inserted between the words, “hospitals” and “are.”
Pg 24	Line 734	The phrase, “…at the time of administration,” should be inserted at the end of the sentence ending with, “99m.”
Pg 24	Line 737	The word, “several,” should be changed to, “multiple.”
Pg 25	Line 746	A period should be inserted at the end of this line.

Pg 25	Lines 753-760	Are there any relevant references which may be cited to support the statements in this paragraph?
Pg 25	Line 756	The phrase, "…failed subsequent elutions," should be changed to, "…excessive Mo-99 concentrations in subsequent elutions."
Pg 25	Line 769	The term, "radioactive drugs," should be changed to, "radiopharmaceuticals."
Pg 25	Line 776	The word, "received," should be changed to, "undergone."
Pg 25	Line 777	The word, "radionuclides," should be changed to, "radionuclidic contaminants."
Pg 27	Line 804	The word, "vendors," is misspelled.
Pg 28	Line 857	The comma between the words, "event" and "is," should be deleted.
Pg 30	Line 908	The phrase, "…the high variation in dose sometimes seen in point doses…," should be changed to, "…the pronounced spatial variation in dose sometimes seen with 'point' sources (i.e., seeds)…"
Pg 31	Line 940	The semi-colon between the words, "issues" and "Section," should be changed to a colon.
Pg 32	Line 963	A period should be inserted at the end of this line.
Pg 33	Lines 989-990	Here and subsequently in the draft rule, the phrase, "by the NRC or Agreement State…," should be changed to, "…by the NRC or an Agreement State."
Pg 36	Line 1091	A comma should be inserted between the terms, "RSO" and "who."
Pg 37	Line 1118	Should the word, "allow," be changed to, "require"?
Pg 38	Lines 1147-1148	The phrase, "…include determining post implant source position verification and normal tissue dose assessment…," should be changed to, "…include performing post-implant source-position verification and normal-tissue dose assessment…"
Pg 38	Line 1154	The word, "minimum," should be inserted between the words, "The" and "absorbed."
Pg 38	Line 1166	A hyphen should be inserted in the term, "60-calendar day."

Pg 39	Line 1182	The comma between the terms, “ANP” and “on,” should be deleted.
Pg 40	Line 1182	The comma between the words, “on” and “therefore,” should be changed to a semi-colon.
Pg 40	Lines 1226-1228	This sentence (in particular, the phrase, “…same new medical license”) is confusing. It should be re-worded and clarified.
Pg 46	Line 1394	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 47	Line 1418	The word, “several,” should be changed to, “multiple.”
Pg 48	Line 1453	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 51	Line 1557	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 53	Line 1598	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 54	Line 1645	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 56	Lines 1707-1708	The phrase, “…to provide high confidence that…,” should be changed to, “…to ensure that…”
Pg 57	Line 1736	Here and elsewhere, a hyphen should be inserted between the words, “single” and “discipline.”
Pg 58	Line 1744	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 60	Line 1816	Here and elsewhere, a hyphen should be inserted between the words, “photon” and “emitting.”
Pg 60	Line 1820	The comma between the terms, “SSDR” and “however,” should be changed to a semi-colon.
Pg 63	Line 1909	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 64	Line 1924	The semi-colon between the words, “management” and “and,” should be deleted.
Pg 64	Line 1961	The word, “have, “between the words, “provide” and “criteria,” should be deleted.
Pg 65	Line 1971	The comma between the terms, “ME” and “an,” should be deleted.

Pg 65	Line 1981	The word, “radiation, should be deleted.
Pg 65	Line 1986	The comma at the end of this line should be changed to a period.
Pg 66	Line 1995	Here and elsewhere when used at an adjective, the term, “organ at risk,” should be changed to, “organ-at-risk.”
Pg 66	Line 2016	A hyphen should be inserted between the terms, “20” and “percent.”
Pg 67	Line 2037	The phrase, “…failed generators…,” should be changed to, “…out-of-tolerance generator elutions…”
Pg 67	Line 2044	The comma at the end of this line should be changed to a semi-colon.
Pg 67	Line 2045	The comma between the words, “notified” and “and,” should be changed to a semi-colon.
Pg 70	Line 2127	The phrase, “…, and, thus,…,” should be changed to, “…and thus…”
Pg 78	Line 2213	The word, “failures,” should be changed to, “deficiencies.”
Pg 79	Line 2242	The comma between the words, “regulations and “meet,” should be deleted.
Pg 82	Line 2336	The hyphen at the end of this line should be changed to a colon.
Pg 87	Line 2526	The hyphen at the end of this line should be changed to a colon.
Pg 91	Line 2695	The hyphen at the end of this line should be changed to a colon.
Pg 93	Line 2750	The hyphen at the end of this line should be changed to a colon.
Pp 93-94	Lines 2761-2765	This item is confusing (grammatically incomplete?) as written. It should be revised and clarified.
Pg 94	Line 2769	The word, “mean,” should be inserted between the words, “The” and “mean.”
Pg 94	Line 2771	The phrase, “The maximum absorbed dose to any 5 contiguous cubic centimeters…,” should be changed to, “The mean absorbed dose to the maximally exposed 5 contiguous cubic centimeters…”

Pg 94	Line 2784	The hyphen at the end of this line should be changed to a colon.
Pg 94	Line 2798	A comma should be inserted between the words, “examination” and “administered.”
Pg 95	Line 2805	The hyphen at the end of this line should be changed to a colon.
Pg 95	Line 2816	The hyphen at the end of this line should be changed to a colon.
Pg 96	Line 2832	The hyphen at the end of this line should be changed to a colon.
Pg 105	Line 3108	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 106	Line 3152	The hyphen at the end of this line should be changed to a colon.
Pg 106	Line 3169	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 107	Line 3183	The hyphen at the end of this line should be changed to a colon.
Pg 108	Line 3212	The hyphen at the end of this line should be changed to a colon.
Pg 108	Line 3219	The comma between the words, “characteristics” and “or.”
Pg 109	Line 3224	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 110	Line 3290	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 112	Line 3348	The hyphen at the end of this line should be changed to a colon.
Pg 112	Line 3361	The hyphen at the end of this line should be changed to a colon.
Pg 113	Line 3375	The hyphen at the end of this line should be changed to a colon.
Pg 113	Line 3380	The comma between the words, “dosages” and “and,” should be deleted.

Pg 113	Line 3385	The comma between the words, “safely” and “and,” should be deleted.
Pg 113	Line 3387	The comma between the words, “subjects” and “that,” should be deleted.
Pg 114	Line 3413	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 114	Line 3425	Here and subsequently, the term, “Sealed Source and Device Registry,” should be replaced by the previously introduced abbreviation, “SSDR.”
Pg 114	Line 3449	A hyphen should be inserted between the words, “full” and “time.”
Pg 114	Line 3465	The phrase, “…to provide high confidence that…,” should be changed to, “…to ensure that…”
Pg 116	Line 3491	The comma between the words, “experience” and “under,” should be deleted.
Pg 116	Line 3493	The comma between the terms, “§ 35.400” and “involving,” should be deleted. The hyphen at the end of this line should be changed to a colon.
Pg 116	Line 3507	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 118	Line 3561	The hyphen at the end of this line should be changed to a colon.
Pg 118	Line 3572	The hyphen at the end of this line should be changed to a colon.
Pg 120	Line 3625	The hyphen at the end of this line should be changed to a colon.
Pg 121	Line 3673	The hyphen at the end of this line should be changed to a colon.
Pg 122	Line 3692	The word, “or,” between the words, “Education” and “the,” should be changed to a comma.
Pg 123	Line 3747	The hyphen at the end of this line should be changed to a colon.
Pg 123	Line 3758	The comma between the words, “fraction” and “by,” should be deleted.

Pg 124	Line 3762	The hyphen at the end of this line should be changed to a colon.
Pg 124	Line 3782	The hyphen at the end of this line should be changed to a colon.
Pg 125	Line 3790	The phrase, “An absorbed dose…,” should be changed to, “A mean absorbed dose…”
Pg 125	Line 3794	The phrase, “An absorbed dose…,” should be changed to, “A mean absorbed dose…”