

PR 35  
(73FR45635)

November 6, 2008 (4:30pm)  
OFFICE OF SECRETARY  
RULEMAKINGS AND  
ADJUDICATIONS STAFF

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Submission via the Federal eRulemaking Portal

November 5, 2008

Re: Advisory Committee on the Medical Uses of Isotopes (ACMUI) comments on the Proposed Rule for Medical Use of Byproduct Material—Amendments/Medical Event Definitions (RIN 3150-A126, NRC-2008-0071) [See 73 FR 45635 (August 6, 2008)]

At their meeting on October 27, 2008, the ACMUI reviewed the proposed rule on medical use of byproduct material for permanent implants. The ACMUI notes that these rules were developed based primarily on the preplanned technique of prostate brachytherapy whereas the rules will nonetheless apply to all types and techniques of permanent brachytherapy in any organ of the body. This could create some unforeseen unintended consequences.

General comments:

The ACMUI supports rule § 35.40 for the written directive (WD) to be source strength-based rather than being dose based. The ACMUI recommends that the word "activity" be replaced by the more technically acceptable term "source strength" whenever it is applied to permanent brachytherapy in the document. The ACMUI also notes that although the proposed rules were based on the recommendations of the ACMUI, the ACMUI was not offered an opportunity to review the proposed rules before the proposed rules were published in the *Federal Register*. The ACMUI requests that, in future, the ACMUI be given an opportunity to review proposed rules before publication.

Specific concerns:

The ACMUI is concerned that the proposed language §35.3045(a)(2) could result in inadvertently and inappropriately categorizing some properly executed, medically acceptable, implants as "medical events" (ME) as follows:

1. The proposed language for § 35.3045(a)(2) (i) on page 45643, column 3 would deem it an ME if the total source strength administered differed by 20 percent or more from the total source strength documented in the preimplantation WD. Further, it is noted that the preimplantation WD cannot be changed since the preimplantation WD serves as the basis for determining if an ME has occurred.

The ACMUI wishes to clarify that many Authorized Users (AU) perform real-time adaptive interactive planning whereby the written directive and the source strength to be implanted are based on the actual volume dynamically obtained during the procedure rather than be based on the preimplant volume (Reference: Nag S, Ciezki JP, Cormack R, Doggett S, DeWyngaert K, Edmundson GK, Stock RG, Stone NN, Yu Y, Zelefsky M. Intraoperative Planning and Dosimetry for Permanent Prostate Brachytherapy: Report of The American Brachytherapy Society. *Int J Radiat Oncol Biol Phys* 2001;51:1422-30). Real-time planning is a more accurate method of implantation as it takes into account any alterations in the prostate volume and shape that occur between the time of the preplan and the implant procedure and therefore represents the actual prostate volume and implant situation. Hence for those performing real-time adaptive planning implantation, the total source strength to be implanted is determined intraoperatively

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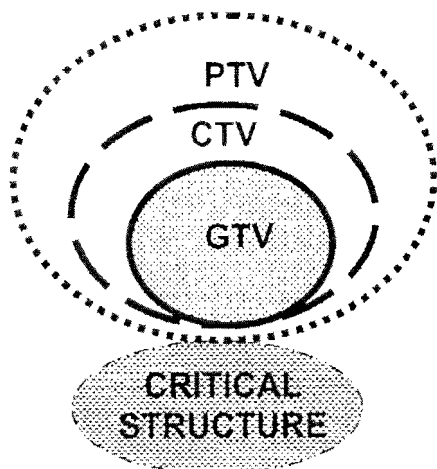
SECY-02

during the implantation procedure and not preimplant. Further, even those performing permanent brachytherapy using preplanned techniques will often modify their plan if, intraoperatively, they find that the gland volume differs markedly from the volumes determined during the preplan. Hence the basis for ME should be the total source strength implanted after administration but before the patient leaves the post-treatment recovery area.

The ACMUI therefore recommends that: § 35.3045 (a)(2)(i) be modified to read "The administration of byproduct material or radiation from byproduct material for permanent implant brachytherapy (excluding sources that were implanted in the correct site but migrated outside the treatment site) results in the total source strength administered differing by 20 percent or more from the total source strength documented in the written directive." {i.e. **delete "preimplantation"**} It should be clarified that, in the WD, the source strength implanted refers to the source strength implanted after administration but before the patient leaves the post-treatment recovery area. This wording would therefore apply both to those using the preplanned technique and those using real time adaptive technique. Similarly, the word "preimplantation" should be deleted from "preimplantation written directive" in sections § 35.3045 (a)(2)(ii), (iii) and (iv).

2. The proposed language for § 35.3045(a)(2) (ii) ) on page 45643, column 3 would deem it an ME if the total source strength implanted outside the **treatment site** and within 3 cm (1.2 in) of the boundary of the treatment site exceeded 20 percent of the total source strength documented in the preimplantation WD.

The definition of "treatment site" described in § 35.2 as "the anatomical description of the tissue intended to receive a radiation dose, as described in a written directive" leads to some ambiguity regarding the exact volume that "treatment site" refers to in § 35.3045(a)(2)(ii). There are various standard radiation oncology volumes already defined in International Commission on Radiation Units and Measurements (ICRU) report #62, including the gross tumor volume (GTV), clinical target volume (CTV), and planning target volume (PTV) [ICRU Report 62. Prescribing, Recording, and Reporting Photon Beam Therapy. Bethesda, MD: International Commission on Radiation Units and Measurements (ICRU), 1999.] The GTV is the gross demonstrable extent and location of tumor growth as determined by clinical examination and/or by imaging techniques. The CTV is the tissue volume that contains the GTV and surrounding subclinical microscopic malignant disease. The PTV adds a margin to the CTV account for uncertainties in source positioning, set up errors, internal organ motion, isodose constrictions, etc to ensure that the CTV will be fully covered by the treatment plan. These expansion margins are non-uniform and depend on the clinical situation and treatment modality. Radiation oncologists use a larger margin if there is high degree of uncertainty and/or if there are no adjacent critical structures. Conversely, the margins are smaller if the boundary is distinct and/or if there are adjacent critical structures as illustrated in the following diagram.



**Volume abbreviations:**  
**GTV = gross tumor volume**  
**CTV = clinical target volume**  
**PTV = planning target**

Therefore, it is apparent that using the definition of "treatment site" in § 35.2 as "the anatomical description of the tissue intended to receive a radiation dose, as described in a written directive" raises ambiguities in terms of the proposed ME reports as it is unclear whether the "treatment site" refers to the gross tumor volume or includes the margins in the clinical target volume or those in the planning target volume. Further, the NRC will be interfering into medical judgment if it dictates the amount of source strength the authorized user can place in the expansion margin, which is a clinical decision. The ACMUI therefore recommends that the definition of "treatment site" in § 35.2 and § 35.3045(a)(2)(ii) be clarified to reflect that it is the planning target volume and includes the gross tumor, the clinical target volume, plus a planning target margin as defined by the AU.

3. The proposed language for § 35.3045 (a)(2)(iii) on page 45643, column 3 would deem it an ME if any brachytherapy source(s) were implanted beyond 3 cm (1.2 in) from the outside boundary of the treatment site, except for brachytherapy source(s) at other sites noted in the preimplantation written directive. Further in page 45638 column 2 it is noted that with the exception of sealed sources that migrate after implantation, even a single brachytherapy source implanted beyond 3 cm from the outside boundary of the treatment site would constitute an ME.

The ACMUI wishes to emphasize that in the normal course of some brachytherapy implants, a few seeds can end up beyond 3 cm (1.2 in) from the outside boundary of the treatment site due to a number of factors.

- a. In the prostate, seeds can be deposited into the periprostatic blood vessels and then travel to distant organs such as the lung. This is correctly recognized by the NRC, which excludes sources that were implanted in the correct site but have migrated outside the treatment site from medical event criteria. However, the deposited seeds could also travel to the adjacent pelvic area via the pelvic vessels and be more than 3 cm away from the prostate. This case could be determined to be an ME as it would be impossible to distinguish whether it was wrongly deposited there or was correctly placed but migrated there.

- b. In prostate implants, a few seeds can sometimes be implanted into the urethra or adjacent bladder. Most of these seeds normally are excreted in the urine. However, sometimes they move within the bladder or urethra and lodge more than 3 cm from the prostate.
- c. In permanent implants of any organ, some seeds can be unknowingly sucked along the needle track while the needle is being retracted and may end up more than 3 cm from the organ in the direction of the needle track. In the prostate, they would end up inferior to the prostate.
- d. In permanent implants of any organ, patients could inadvertently move during the needle retraction causing some seeds to be deposited more than 3 cm from the treatment site.
- e. While most permanent brachytherapy is done in the prostate, these rules will apply to other sites of permanent implant in addition to prostate. At other sites, for example the tumor beds after resection and deep seated liver tumors, the margins are indistinct and there are greater uncertainties. Therefore clinicians routinely implant beyond the tumor or tumor bed if there are no critical structures in that area. Further, sometimes (especially after tumor resection) there may be no tissues to anchor the seeds to and so they are placed in gelfoam or vicryl mesh and attached to the tumor bed. Some of these seeds do dislodge and then can travel in an adjacent free cavity and be deposited more than 3 cm away (e.g., in the abdominal, pelvic, or thoracic cavity). It would be virtually impossible to determine whether they were implanted there or were dislodged and migrated there and therefore could be deemed to be an ME.

The ACMUI recommends that section § 35.3045(a)(2) (ii) be modified to "The total source strength implanted outside the treatment site (including the gross tumor, the clinical target volume plus a variable planning margin as defined by the AU) exceeding 20 percent of the total source strength documented in the written directive". This would take into account source migrations, seeds being dislodged, sucked out, etc, but would still hold accountable cases in which the target organ was grossly misidentified and the wrong area was implanted. Accordingly, § 35.3045 (a)(2)(iii) will become superfluous and therefore would be eliminated.

Other comments:

1. In §35.40(B)(6), it should be clarified that for any two part WD, **an** AU (rather than **the** AU) needs to sign and date both the before administration and after implantation parts of the WD. This would clarify the intent of the regulation that **an** AU (and not necessarily the same AU) needs to approve all required information on the WD.

2. In §35.3045(a), the ACMUI wishes to comment on new wording that potentially affects any administration of byproduct material requiring a WD. The proposed language for §35.3045(a) on Federal Register, page 45643, column 2 currently reads, "A licensee shall report as a medical event any administration requiring a written directive if a written directive was not prepared or any event..." Not having a written directive prior to administration of byproduct material is already a violation of NRC

regulations. 10 CFR §§35.40(a) and 35.41 require having a WD prior to administration and the program and procedures to provide "high confidence" for verifying the written directive is done. Creating MEs that are already regulatory violations serves only to add the number of reported deviations and establishes a undesirable precedent for making any medical regulation violation an ME.

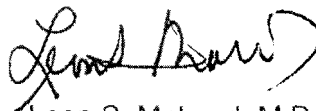
Therefore, the ACMUI recommends that when a WD is required, administrations without a WD are to be reported as **regulatory violations** and may or may not constitute an ME.

Summary:

The ACMUI is very much concerned that the proposed rules may inadvertently result in the unintended consequence that some properly executed, medically acceptable, brachytherapy implants may be inappropriately deemed to be medical events when, in reality, they sometimes occur in the course of normal medical practice, and are beyond the control of the AU. Further, the ACMUI is concerned that some practitioners will simply abandon permanent brachytherapy procedures rather than risk having medical events. This will be detrimental to patient care. Specifically, the ACMUI recommends that:

1. The word "preimplantation" be deleted from "preimplantation written directive" in sections § 35.3045 (a)(2) (i), (ii), (iii) and (iv).
2. § 35.3045(a)(2) (ii) ) be clarified to read "The total source strength implanted outside the treatment site (including the gross tumor, the clinical target volume plus a variable planning margin as defined by the Authorized User exceeding 20 percent of the total source strength documented in the written directive".
3. § 35.3045 (a)(2)(iii) will become superfluous and therefore should be eliminated.
4. The word "activity" should be replaced by the term "source strength" whenever it is applied to permanent brachytherapy in the document.
5. §35.40(B)(6) should be clarified that for any two part WD, **an** AU (though not necessarily **the** same AU) needs to approve all required information on both parts of the WD.
6. The ACMUI should be given an opportunity to review proposed rules before they are published.
7. When a WD is required, administrations without a WD are to be reported as regulatory violations and may or may not constitute an ME.

Thank you for affording us this opportunity to provide comments on the NRC's preliminary draft rule changes to 10 CFR 35.40 and 35.3045 related to medical events in brachytherapy.



Leon S. Malmud, M.D.  
Chairman, Advisory Committee  
on the Medical Uses of Isotopes

## Rulemaking Comments

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**From:** Carol Gallagher  
**Sent:** Thursday, November 06, 2008 2:22 PM  
**To:** Rulemaking Comments  
**Subject:** Comment on Medical Use of Byproduct Material Proposed Rule  
**Attachments:** malmud.pdf

Attached for docketing is a comment from Leon Malmud on the above noted proposed rule (73 FR 45635) that I received on 11/5/08.

Carol

Received: from HQCLSTR01.nrc.gov ([148.184.44.79]) by OWMS01.nrc.gov  
([148.184.100.43]) with mapi; Thu, 6 Nov 2008 14:21:38 -0500  
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From: Carol Gallagher <Carol.Gallagher@nrc.gov>  
To: Rulemaking Comments <Rulemaking.Comments@nrc.gov>  
Date: Thu, 6 Nov 2008 14:21:31 -0500  
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