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VIA E-Mail to: rulemaking.comments@nrc.gov

October 23, 2008

Annette L. Vietti-Cook
Secretary of the Commission
U.S. Nuclear Regulatory Commission
Washington, DC 20555-0001

ATTN: Rulemakings and Adjudications Staff

**Re: Comments on Proposed Rule for Medical Use of Byproduct Material—
Amendments/Medical Event Definitions (RIN 3150-AI26, NRC-2008-0071) [See 73 FR
45635 (August 6, 2008)]**

Dear Ms. Vietti-Cook:

The American Society for Therapeutic Radiology and Oncology (ASTRO) agrees with many of the U.S. Nuclear Regulatory Commission’s (NRC’s) proposed rule modifications to 10 CFR 35.40 and 35.3045 to establish separate medical event criteria and written directive requirements for permanent implant brachytherapy and commends the efforts of the NRC in proposing changes for the benefit of patients’ health and safety. ASTRO urges the NRC to base its enforcement policy upon realistic expectations of the precision that can be achieved in medical event (ME) determination in different clinical settings. ASTRO welcomes the opportunity to participate in this rulemaking process by offering the following comments.

ASTRO is the largest radiation oncology society in the world, with approximately 10,000 members who specialize in treating patients with radiation therapies. As a leading organization in radiation oncology, biology and physics, the Society is dedicated to the advancement of the practice of radiation oncology by promoting excellence in patient care, providing opportunities for educational and professional development, promoting research and disseminating research results and representing radiation oncology in a rapidly evolving healthcare environment.

Timing of Written Directive and Medical Events

ASTRO is concerned that the proposed rule language for § 35.40(b)(6) and §35.3045(a)(2) does not take into account clinical practice realities, and accordingly, could inappropriately include certain medically acceptable implants as “medical events.” The proposed rules will apply to all types of permanent brachytherapy in any part of the body. Yet, the precision with which the sources implanted in some organs, particularly those other than the prostate, can be determined from post-implant or intraoperative imaging may be limited, due either to image artifacts or operator variability in defining the treatment site. For some treatment sites, e.g., postoperative brachytherapy of a tumor bed, there is no well-encapsulated or radiographically visible target

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volume that can be used to precisely determine the target volume. The prostate is well-encapsulated and easily seen on ultrasound. Tumors in other sites, however, are more diffuse and may not have a capsule to define the boundary—making it difficult to precisely demarcate the treatment site. When the tumor has been surgically resected, only microscopic residual tumor remains, which is not imageable, and defining the treatment site is problematic.

Seeds cause artifacts which make it difficult to define the boundary—but this happens at all sites including the prostate.

The proposed language for § 35.3045 reads:

- (a) A licensee shall report as a medical event any administration requiring a written directive if a written directive was not prepared or any event, except for an event that results from patient intervention, in which –
 - (2) 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 –
 - (i) The total source strength administered differing by 20 percent or more from the total source strength documented in the pre-implantation written directive.

Under the proposed rule, making changes to the pre-implantation written directive (WD) would constitute a prohibited revision of the WD. Current regulations require that revisions to the WD be made before implantation begins. As stated, the reason the pre-implantation WD cannot be changed is that the pre-implantation WD serves as the basis for determining if an ME has occurred. ASTRO emphasizes that many authorized users (AUs) perform real-time, adaptive, interactive planning, whereby the written directive and the source strength to be implanted are based on the actual volume dynamically determined during the procedure rather than based on the pre-implant volume.¹

ASTRO believes that real-time planning is a more accurate method of implantation because it takes into account any alterations in the prostate volume and shape that occur between the time of the pre-plan and the implant procedure and therefore represents the actual prostate or other organ volume and implant situation. While real-time planning is most developed and most commonly used in the prostate, it can also be used in brachytherapy procedures not involving the prostate as long as the organ is easily imaged in real time.

¹ (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).

For those performing real-time adaptive planning implantation, the total source strength to be implanted is determined intraoperatively during the implantation procedure and not pre-implant. Further, even those performing permanent brachytherapy using preplanned techniques will often modify their plan if intraoperatively they find major discrepancies in the gland or organ volume from the volumes determined during the preplan.

Accordingly, ASTRO recommends modification of the proposed language to provide that the WD refer to the total source strength implanted after administration, but before the patient leaves the post-treatment recovery area rather than an arbitrary pre-implantation WD. ASTRO notes that this approach is also reflected in the ACMUI recommendations cited in the Federal Register Notice of this rulemaking that, "The AU is to complete any revisions to the WD for permanent implants to account for any medically necessary plan adaptations before the patient is released from licensee control following the implantation procedure and immediate post-operative period."

ASTRO recommends that the word "pre-implantation" be deleted and that the proposed language of § 35.3045 (a) be modified to:

- (2) 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 –
 - (i) the total source strength administered differing by 20 percent or more from the total source strength documented in the written directive.

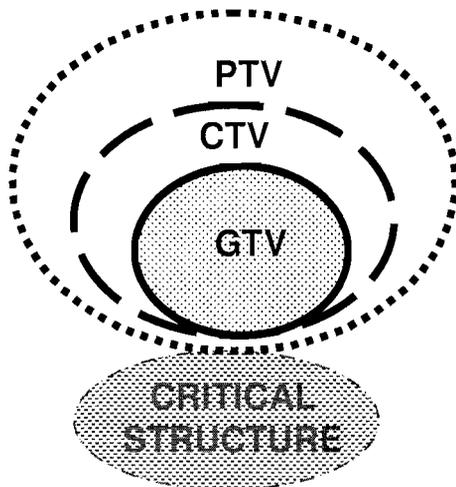
ASTRO believes that this modification is critical to clarify that the source strength implanted as stated in the WD refers to the source strength implanted after administration but before the patient leaves the post-treatment recovery area. This wording would therefore apply both to those using the pre-planned technique and those using real time adaptive technique.

Definition of Treatment Site

The proposed language for § 35.3045 reads:

- (a) A licensee shall report as a medical event any administration requiring a written directive if a written directive was not prepared or any event, except for an event that results from patient intervention, in which –
 - (2) 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 –
 - (ii) The total source strength implanted outside the treatment site and within 3 cm (1.2 in) of the boundary of the treatment site exceeding 20 percent of the total source strength documented in the pre-implantation written directive.

ASTRO wishes to point out that 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 volumes already defined in radiation oncology, including the gross tumor volume, which is the volume that contains tumor. Two other margins are added to the gross tumor volume during the brachytherapy planning process. One margin is added to account for the subclinical spread of tumor, which is termed the “clinical target volume,” and a second margin is added to account for uncertainties in source positioning, tumor boundaries, isodose constrictions, etc., which is termed the “planning target volume.”



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

These expansion margins are not constant but change for different clinical situations. 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.

ASTRO believes that the proposed regulations cross into clinical decision-making by specifying margin parameters and the source strength to be placed in the margin. The NRC will be interfering into medical judgment if it dictates the amount of source strength the authorized user can place in the margins. Using the definition found at § 35.2 of “treatment site” 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 medical event reports and notifications 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.

ASTRO recommends that the definition of “treatment site” in § 35.2 be changed to

“the anatomical description of the tissue intended to receive a radiation dose, including gross tumor, the clinical target volume, plus a variable planning target volume, as described by the AU in a written directive.”

ASTRO further recommends that § 35.3045 (a)(2)(ii) be revised as follows:

(ii) The total source strength administered outside the treatment site (including the gross tumor, the clinical target volume plus a variable planning target volume as defined by the AU) and within 3cm (1.2 in) of the boundary of the treatment site exceeding 20 percent of the total source strength documented in the ~~pre-implantation~~ written directive.

ASTRO believes that this definition of medical event, would allow the NRC to prevent poor implants without interfering with the physician’s clinical judgment.

ASTRO is concerned that under the proposed § 35.3045 (a)(2)(iii), a single brachytherapy source 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 pre-implantation written directive, would be deemed a medical event. Further it is noted with the exception of sealed sources that migrate after implantation, a single brachytherapy source implanted beyond 3 cm from the outside boundary of the treatment site would constitute an ME.

The proposed language for § 35.3045 (a)(2)(iii) reads:

(iii) Brachytherapy source(s) 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 pre-implantation written directive.

ASTRO notes that under its suggested alternative language, section § 35.3045 (a)(2)(iii) will become superfluous and therefore could be eliminated when § 35.3045(a)(2)(ii) is modified per the ASTRO suggestion as this modification would take into account source migrations, as well as seeds being dislodged, or sucked out along needle track. However, AUs would still be held accountable where the target organ was grossly misidentified and the wrong area was implanted.

ASTRO believes that these suggested modifications to the proposed rule language are necessary because in the normal course of some medically acceptable brachytherapy implant procedures, a few seeds may come to rest beyond 3 cm (1.2 in) from the outside boundary of the treatment site due to a number of factors, including the following:

- In prostate procedures, seeds can be deposited into the periprostatic blood vessels and then travel to distant organs like the lung. This is correctly recognized by the NRC proposed regulation which exclude sources that were implanted in the correct site but migrated outside the treatment site from medical event. 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. In

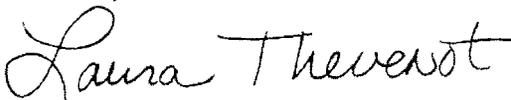
this case, it could be determined to be a medical event as it would be impossible to distinguish whether it was wrongly deposited there or was correctly placed but migrated there.

- Sometimes, also in prostate implant procedures, a few seeds are implanted into the urethra or adjacent bladder. Most of these seeds normally are extruded out in the urine. However, occasionally they move within the bladder or urethra and lodge more than 3 cm from the prostate.
- In implant procedures, some seeds can be sucked along the needle track while the needle is being retracted and may end up more than 3 cm inferior to the prostate or other target organ.
- During any implant procedure, patients could inadvertently cough or otherwise move during the needle retraction causing some seeds to be deposited more than 3 cm from the treatment site.
- While most permanent brachytherapy implant procedures are done on the prostate, the proposed rules will apply to other sites of permanent implant as well as the 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. Some of these seeds do dislodge and then can travel more than 3 cm away in a free cavity (e.g., in the abdominal, pelvic or lung cavity). It would be virtually impossible to determine whether they were deposited there or were dislodged and migrated there and therefore could be deemed a medical event.

Conclusion

In conclusion, ASTRO asks the NRC to modify the proposed regulations in accordance with the recommendations set forth in this letter. Thank you for affording ASTRO this opportunity to provide comments on the NRC's proposed rule changes to 10 CFR 35.40 and 35.3045 related to medical events in permanent implant brachytherapy--medical use of byproduct material--amendments/medical event definitions. Please contact Richard Martin at 703-839-7366 or richardm@astro.org if you have any questions.

Sincerely,



Laura I. Thevenot
Chief Executive Officer

Rulemaking Comments

From: Richard Martin [richardm@astro.org]
Sent: Thursday, October 23, 2008 10:22 AM
To: Rulemaking Comments
Cc: Emily Wilson
Subject: Comment Medical Use of Byproduct Material--Amendments/Medical Event Definitions (RIN 3150-A126, NRC-2008-0071)
Attachments: AstroNrcPermBrachyCommentOctober 23.pdf

Dear Sir or Madam:

Please find attached the American Society for Therapeutic Radiology and Oncology (ASTRO) comment letter on 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)].

If you have questions or need additional information, call me directly. Thank you for your assistance.

Sincerely,

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