POLICY ISSUE
NOTATION VOTE

December 27, 2005 SECY-05-0234

FOR: The Commissioners

FROM: Luis A. Reyes
Executive Director for Operations

SUBJECT: ADEQUACY OF MEDICAL EVENT DEFINITIONS IN 10 CFR 35.3045, AND COMMUNICATING ASSOCIATED RISKS TO THE PUBLIC

PURPOSE:

The purpose of this paper is to obtain Commission approval for the staff's recommended course of action.

SUMMARY:

In Staff Requirements Memorandum (SRM)-M040302B dated March 16, 2004, the Commission directed the staff: (1) to provide recommendations concerning the current definition of a medical event (ME); (2) to provide recommendations on how to effectively communicate the associated risks, if any, to the public; and (3) to confirm that there was an appropriate basis for applying the 20 percent reporting threshold for MEs to each medical use modality in the revised 10 CFR Part 35 rule that became effective in October 2002. The Commission also directed the staff to involve the Advisory Committee on the Medical Uses of Isotopes (ACMUI) in the development of these recommendations.

This paper discusses the basis for the current definition of an ME, confirms that there was an appropriate basis for applying the 20 percent reporting threshold for MEs to each medical use modality, and recommends, with one exception, that the current dose-based definition be

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retained for the various usage modalities. The staff also recommends that for permanent implant brachytherapy, the Commission approve the staff's plan to revise the ME definition and the associated requirements for written directives (WDs) to be activity-based, instead of dose-based. Finally, this paper also discusses and provides the staff's recommendations on several approaches the ACMUI suggests for improving public understanding of the risks associated with MEs.

BACKGROUND:

For all medical uses, without exception, the variance criterion threshold for licensee submission of an ME report is an administered total dose (or dosage) that differs from the prescribed dose (or dosage), as defined in the WD, by ± 20 percent. Since WDs are required primarily for administrations intended for therapeutic purposes, ± 20 percent variance corresponds to patient intended target doses reduced by or exceeded by approximately 0.4 Gray (Gy) (40 rads) to 12 Gy (1200 rads). The basis for this ME variance criterion reporting threshold, as discussed below, is that variances of this magnitude may reflect quality assurance (QA) problems with the licensees' programs and also have the potential, though not the certainty, to result in harm to the involved individuals. This ± 20 percent criterion, and others relating to reporting of MEs, appears in 10 CFR 35.3045. In addition, 10 CFR 35.40 provides the requirements for a WD which, for permanent implant brachytherapy only, allow the authorized user (AU) to revise a WD "after implantation but before completion of the procedure."

Several medical use events in 2003 that are described in Enclosure 1, as well as advice from the ACMUI, prompted the staff to reconsider the appropriateness and adequacy of the regulations for WDs and MEs. During its March 2004 meeting, the ACMUI considered the issue of defining MEs involving permanent implant brachytherapy. It concluded that the ± 20 percent variance from the prescription criterion in the existing rule was appropriate if both the prescription and the variance could be expressed in units of activity, rather than in units of dose, as there is no suitable clinically used dose metric available for judging the occurrence of MEs. In June 2004, the staff concluded that, for permanent implant brachytherapy, total source strength is an acceptable alternative to total dose for the purpose of determining the occurrence of MEs (i.e., total dose is equivalent to total source strength for the expression of prescribed dose and administered dose in the WD). Subsequently, the ACMUI used this interpretation of the requirements for 10 CFR 35.40 for permanent implant brachytherapy WDs in its consideration of the adequacy of ME definitions in 10 CFR 35.3045.

Following receipt of SRM-040302B, the staff began its interactions with the ACMUI on the issues of the adequacy of ME definitions, and how to effectively communicate to the public associated risks, if any, during the ACMUI's fall meeting in October 2004. At that meeting, the ACMUI established a Medical Event Subcommittee (MESC), and a staff member was assigned to serve as liaison to the MESC and ACMUI during the development of ACMUI recommendations to the staff on these issues. The ACMUI subsequently considered these issues: 1) as the principal subject of its mid-cycle teleconference in January 2005 and during a March 2005 teleconference; 2) during the ACMUI spring meeting in April 2005; and 3) as the

principal subject of a teleconference in June 2005. During this final teleconference, the ACMUI received and approved, with modification, the recommendations prepared by the MESC. The final ACMUI recommendations on these issues (Enclosure 2) were conveyed to the staff on July 19, 2005. The recommendations included one recommendation on definitions of MEs for all medical use modalities except permanent implant brachytherapy; six recommendations on ME definition and WD requirements for permanent implant brachytherapy; and two general recommendations plus four specific recommendations on improving public understanding of risks associated with MEs.

The staff's proposed responses to the ACMUI's recommendations on these issues were discussed with the ACMUI at its recent meeting in October 2005. At this meeting, the ACMUI offered one additional recommendation (to not release Event Summary information until an ME has been confirmed) and one suggestion (to footnote each Event Summary with information on what MEs represent) to improve public understanding of the risks associated with MEs. The additional recommendation and suggestion are addressed in this paper. All of the above-described ACMUI meetings were open to the public and noticed in the *Federal Register*. Further, the public participated in discussion of these matters during the meetings.

DISCUSSION:

The discussion is divided into three independent areas: (1) basis for the ±20 percent reporting threshold for MEs; (2) recommendations concerning the current definition of an ME; and (3) improving public understanding of the risks associated with MEs.

Basis for the ± 20 Percent Reporting Threshold for MEs

As part of the general revision of 10 CFR Part 35 that was concluded in 2002, the staff considered the appropriateness and adequacy of the dose/dosage variance criterion thresholds for misadministrations[1] and intended to retain them, provided no issues developed to indicate that a change was needed. During discussions by the ACMUI, by the Part 35 Revision Working Group, and at Part 35 revision public workshops, no rigorous evidence-based rationale for retaining the ± 20 percent variance threshold was presented. In large part, the threshold was retained because: (1) it was in the then-current version of Part 35; (2) the reporting frequency associated with that threshold did not appear to be causing a significant burden for licensees; (3) there was a general consensus that an error of 20 percent or more definitely had a significant potential, though not a certainty, to cause harm; and (4) exceeding the threshold could indicate a deficiency in the licensee's program for ensuring that byproduct material or radiation from byproduct material is administered as directed by the AU even if the dose variation did not necessarily indicate a significant risk to the patient.

[1]± 20% for all modalities except gamma stereotactic radiosurgery at ± 10 % variance from prescription.

At that time, the consensus of the ACMUI was that a dose error of 20 percent in a cancer treatment regimen could lead to inadequate treatment of the cancer (underdosing) or to an increased likelihood of complications (overdosing). However, a dose variance threshold of 10 percent was considered to be too low for reporting MEs, since such differences were well within the range of standard-of-care variations from one practitioner to another. In contrast, for the difference-in-dose criterion thresholds for MEs,[2] a diagnostic radiopharmaceutical dosing error of more than 20 percent that resulted in either of the difference-in-dose thresholds being only slightly exceeded would probably only rarely lead to actual harm. However, the absolute magnitude of the dosage error would likely be large enough to warrant reporting. The consensus of the ACMUI and the Part 35 Revision Working Group was that the U.S. Nuclear Regulatory Commission (NRC) would have a legitimate interest in over-dosages causing excess effective dose equivalents exceeding 0.05 Sv (5 rem) or excess organ, tissue, or skin doses exceeding 0.5 Sv (50 rem).

Finally, the ACMUI and the Part 35 Revision Working Group recognized that there was not a sufficient basis in the scientific literature to justify the selection of different thresholds for each modality based on the risk of harm. Different reporting criteria for different modalities would have been technically complex to develop and extremely confusing to licensees.

Recommendations Concerning the Current Definition of an ME

Consistent with SRM-M040203B, the ACMUI considered the current definition of an ME in 10 CFR 35.3045 at its October 2004 meeting and recommended retention of the ± 20 percent delivered dose variation from prescription as an appropriate threshold for ME reporting for all modalities except permanent implant brachytherapy, for which the use of delivered dose variation from prescription is problematic. The final ACMUI recommendations (July 2005) reaffirm its October 2004 recommendation. The ACMUI rationale for this recommendation is that the ± 20 variance threshold is a reasonable threshold for identifying events indicative of treatment delivery problems in accurately realizing AUs' clinical intentions. The staff agrees with the ACMUI rationale for retaining this threshold and notes that no events involving medical use have resulted in this threshold being questioned. Accordingly, the staff endorses and supports this ACMUI recommendation.

On this issue, the ACMUI also recommended as general "guiding principles" that NRC consider MEs as a QA performance index indicative of technical or QA problems in accurately realizing clinical intentions of AUs, but not as an indicator of patient harm, or the probability of patient harm. The staff endorses and supports this ACMUI position, which is consistent with the position NRC stated in the supplementary information accompanying publication of the 2002 Part 35 rule, 67 FR 20330 (April 24, 2002).

[2] A difference in effective dose equivalent of 0.05 Sievert (Sv) (5 rem) from prescription or a difference in organ, tissue, or skin dose of 0.5 Sv (50 rem) from prescription.

The ACMUI's final recommendations document provided a basis and rationale for each of several principles, or recommendations, for guiding the staff in reformulating the ME reporting rule and associated definitions for permanent implant brachytherapy. Below are the ACMUI recommendations relating to ME definitions and requirements and to WDs for permanent implant brachytherapy. The basis and rationale associated with each recommendation are provided in the enclosed ACMUI final recommendations. Overall, ACMUI recommends that for permanent implant brachytherapy WDs and MEs be activity-based, not dose-based, because 1) there is no suitable clinically used dose metric available for judging the occurrence of MEs and 2) clinicians have better control over activity being implanted than dose resulting from the implant. The staff endorses and supports all of these ACMUI recommendations.

1. For all permanent implants, MEs should be defined in terms of the total source strength implanted in the treatment site, not in terms of absorbed dose.

2. Any implant in which the total source strength implanted in the treatment site deviates from the WD by more than 20 percent (in either direction) should be classified as an ME. As in the current ME rule, ACMUI intends that seed migration be specifically excluded as grounds for a treatment-site-accuracy ME.

3. Implants in which more than 20 percent of the total source strength documented in the preimplantation WD is implanted in tissue or organs adjacent to the treatment site [within 3 centimeters (cm) (1.2 in.) of the treatment site boundary] should be classified as MEs. Seeds that were correctly implanted, but subsequently migrated, are excluded as grounds for an ME.

4. Implants should be classified as MEs if:
   a. sealed radioactive sources (seeds) are implanted in distant [beyond 3 cm (1.2 in.) from the treatment site boundary] tissue or organs;
   b. the excess dose to the distant tissue or organ exceeds 0.5 Sv (50 rem); and
   c. the excess dose to the tissue or organ is at least 50 percent greater than the dose that would have been delivered if the seeds had been implanted in the correct tissue volume.

   Seeds that were correctly implanted but subsequently migrated are excluded as grounds for an ME.

5. An implant is an ME if the dose calculations used to determine the total source strength documented in the WD, to achieve the AU's intention for absorbed dose to the treatment site, are in error by more than 20 percent in either direction.

6. 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 after the implantation procedure and immediate post-operative period.[3]

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[3] For outpatient treatments, completion of the WD prior to release of the patient from the facility. For inpatient treatments, completion of the WD before the patient leaves the operating room or recovery area.

Taken together, the staff believes that these six ACMUI recommendations provide a satisfactory approach for addressing the issues raised by the two medical use events reported in 2003 that were discussed in Enclosure 1. The staff believes that the dose-based regulations for WDs (in 10 CFR 35.40) and for MEs (in 10 CFR 35.3045) for permanent implant brachytherapy use should be revised to be activity-based, following these recommendations of the ACMUI.

Improving Public Understanding of the Risks Associated with MEs

The ACMUI's final recommendations document also provided four suggestions for improving public understanding of the risks associated with MEs. The ACMUI's specific suggestions for achieving this objective are listed in Enclosure 3. The basis and rationale associated with each of these suggestions are provided in Enclosure 2. While the staff supports ACMUI's "guiding principles" as likely to improve public understanding of the risks associated with MEs, the staff does not endorse and support these four specific ACMUI suggestions, for the reasons described in Enclosure 3.

At its recent meeting in October 2005, the ACMUI offered one additional recommendation and one suggestion on the issue of improving public understanding of the risks associated with MEs. These items are also listed in Enclosure 3. The staff endorses and supports, with modification as explained in Enclosure 3, the intent of this ACMUI recommendation, to not disclose/release event information to the public until the event has been confirmed to be a reportable ME. The staff also endorses and supports the intent of the ACMUI suggestion, to footnote each Event Summary released to the public as a reportable ME to indicate that thresholds in NRC's ME definitions, if exceeded, are not necessarily indicative of patient harm.

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To improve public understanding of the risks associated with MEs, the staff also proposes the following NRC actions. These suggestions reflect concepts and language provided by the ACMUI in its ME definition "guiding principles," listed in the enclosure.

1. Publicize that NRC's ME definitions provide thresholds for identifying events indicative of technical or QA problems in accurately realizing the clinical intentions (prescriptions) of AUs.

2. Publicize that thresholds in NRC's ME definitions, if exceeded, are not necessarily indicative of patient harm.

The staff recommends that this information be conveyed through: 1) an article in the NMSS Licensee Newsletter; 2) issuance of a Regulatory Information Summary; 3) letters to and/or discussions with professional organizations such as the American Association of Physicists in Medicine, the American Society for Therapeutic Radiology and Oncology, the Society of Nuclear Medicine, and others; and/or 4) a footnote to each Event Summary released to the public as a reportable ME.

COMMITMENTS:

There are no commitments beyond those that would be implemented if the Commission approves the recommendations below.

RECOMMENDATIONS:

Based on the background and discussion above, the staff recommends that the Commission:

1. Retain the ± 20 percent delivered dose variation from prescription, in 10 CFR 35.3045(a), as an appropriate threshold for ME reporting for all medical use modalities except permanent implant brachytherapy.

2. Approve development of a rulemaking plan (contingent upon the annual Common Prioritization Process) to modify both the WD requirements in 10 CFR 35.40(b)(6) and the ME reporting requirements in 10 CFR 35.3045 for permanent implant brachytherapy medical use, to convert from dose-based to activity-based, to reflect the six guiding principles, listed above, recommended by the ACMUI for this modality.

3. Approve the following actions to improve public understanding of the risks associated with MEs:
   a. The staff will publicize that NRC's ME definitions provide thresholds for identifying events that are indicative of technical or QA problems in accurately realizing the clinical intentions (prescriptions) of AUs, and that thresholds in NRC's ME definitions, if exceeded, are not necessarily indicative of patient harm; and

   b. Event information supplied by a licensee to the NRC Operations Center, pursuant to the next-calendar-day reporting requirement in 10 CFR 35.3045(c), will not be disclosed/released to the public until the event has been confirmed to be a reportable ME, or 5 calendar days have passed.

RESOURCES:

Recommendation 1 does not require resources, as no implementation is required. Recommendation 2, to develop a rulemaking plan, is estimated to require a total of 0.5 FTE over the course of two years to accomplish. However, the determination of the timing of a new rulemaking is dependent upon the annual Common Prioritization Process, which will be initiated for the FY07-08 Planning Period in the Spring of 2006. This process involves ranking all anticipated rulemakings on a common scale by a team comprised of members of the Rulemaking Coordinating Committee (RCC) and additional representatives of any other Offices involved in proposing new rules.

Based on resources allocated for rulemaking, the team determines how many of the rules can be carried out during the two year window under consideration. Changes can be accommodated through a prioritization of any proposed additional rule, and if necessary, an add/shed to make resources available to pursue it. At this time, the impact of a re-prioritization, if necessary, is not known. Resources needed to complete the rulemaking will be sought during the Planning Budgeting and Performance Management (PBPM) process for FY 2008 and beyond, as applicable. Recommendation 3 does not require additional resources. Needed resources of <0.1 FTE can be absorbed into existing workload without an adverse impact.

The information on resources and schedule reflect the current environment. If a significant amount of time (greater that 30 days) passes or the Commission provides the staff direction that differs from or adds to the staff's recommended action(s), this section of the paper would need to be revisited after issuance of the draft SRM.

COORDINATION:

The Office of the General Counsel has reviewed this paper and has no legal objection. The Office of the Chief Financial Officer has reviewed this paper for resource implications and has no objections.

/RA by Martin J. Virgilio Acting for/

Luis A. Reyes
Executive Director
for Operations

Enclosures:
1. Medical Use Events in 2003
2. Recommendations of the ACMUI on the Definition of Medical Event (ML052220224)
3. ACMUI's Specific Suggestions for Improving Public Understanding of the Risks Associated with Medical Events

Medical Use Events in 2003 That Prompted the Staff to Reconsider the Appropriateness and Adequacy of the Regulations for WDs and MEs

A medical use event involved the implantation of 40 Iodine-125 (I-125) sources for permanent implant brachytherapy in the wrong implantation site. The staff determined that this occurrence was not a ME because: 1) the AU revised the WD in the operating room after the erroneous source placement was discovered but before completion of the procedure and also documented the actual number of sources implanted into the prostate (34 instead of the intended 74); and 2) the unintended dose to the bladder (the wrong site) did not exceed 50 percent of the dose expected to this organ from a properly conducted procedure because the 40 I-125 sources in the bladder were promptly removed when their incorrect placement was discovered. However, the staff considered the written directive rule to be flawed because 10 CFR 35.40 permits the AU to revise the WD for permanent implant brachytherapy, thereby avoiding reporting the incident as an ME.

An event nearly identical to the one just described occurred in October 2005 at the same facility, involving erroneous placement of 45 (of 90) I-125 sources into the bladder instead of the prostate. In this event, the AU discovered the incorrect placement, removed the sources from the bladder, and revised the WD before the patient left the operating room. Although the staff is still evaluating this event, the staff anticipates that this event will not constitute a reportable ME, again because 10 CFR 35.40 permits the AU to revise the WD for permanent implant brachytherapy, thereby avoiding reporting the incident as an ME.

Another event in 2003 also involved the implantation of I-125 sources, for permanent implant brachytherapy of the prostate, into the wrong site. At this facility, 21 patients received source implants to the wrong site between January 22, 2001 and January 10, 2002, because of a systematic error. The licensee identified these occurrences in June 2003, and the staff determined that they were MEs. The dose to the prostate ranged from 0 percent to 76 percent of the intended dose using a definition of target-organ dose for the prostate recommended by the ACMUI in November 2003.

The measure used for determining if a prostate brachytherapy treatment misadministration/ME had occurred was the dose received by 90 percent of the target volume (D90), in comparison to the prescribed dose.* Although the ME criterion for underdosing of -20 percent (D90 < 80 percent of the prescribed dose) is generally satisfactory, D90s exceed 120 percent of the prescribed dose for many standard treatments. Such treatments would therefore be inappropriately classified as overdosing MEs (+ 20 percent) if the criterion D90 > 120 percent of the prescribed dose is used. Accordingly, the staff recognized the need to develop an appropriate criterion for comparison to the dose-based reporting requirement in 10 CFR 35.3045. To determine such a criterion, the staff consulted the ACMUI and requested its recommendation.

*The regulation requires that the delivered dose be compared to the prescribed dose. Of the various measures used for specifying the practitioner's intention, the one that is commonly used and is dose-based is D90. The NRC is obligated to use "industry standards" when they exist and can be used in regulation; D90 is such a "standard."

UNITED STATES
NUCLEAR REGULATORY COMMISSION
WASHINGTON, D.C. 20555-0001

ADVISORY COMMITTEE
ON THE MEDICAL
USES OF ISOTOPES

July 19, 2005

MEMORANDUM TO: Charles L. Miller, Director
Division of Industrial and Medical
Nuclear Safety
Office of Nuclear Material Safety
and Safeguards

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

SUBJECT: SUBMISSION OF GUIDING PRINCIPLES FOR NUCLEAR REGULATORY COMMISSION STAFF USE IN FORMULATING MEDICAL EVENT CRITERIA FOR PERMANENT IMPLANT BRACHYTHERAPY PROCEDURES

On June 28, 2005, the Medical Event Subcommittee (MESC) of the Advisory Committee on the Medical Uses of Isotopes (ACMUI) held a public teleconference meeting to discuss a set of guiding principles for staff use while the staff writes a rule that will define medical events resulting from permanent implant brachytherapy procedures.

During the discussion, the MESC refined the principles and submitted them to the full ACMUI for a vote. All principles were unanimously passed by the full ACMUI.

Please see the attached to review the principles. Request that you submit these principles to your staff, as guidance to assist staff in defining a rule to capture medical events resulting from permanent implant brachytherapy procedures.

Primary contact for any questions is Jeffrey F. Williamson, PhD, Chair, MESC, at (804) 628-1047. Alternate contact is Leon S. Malmud, Chair, ACMUI, at (215) 707-7078.

Attachment: Recommendations of the ACMUI on the Definition of Medical Event for Permanent Interstitial Brachytherapy

Recommendations of the ACMUI on the Definition of Medical Event for Permanent Interstitial Brachytherapy

This document outlines the recommendations of the Advisory Committee on Medical Use of Isotopes (ACMUI) regarding the need to revise the Medical Event (ME) reporting requirement and associated definitions for permanent brachytherapy. These recommendations are based upon a report formulated by ACMUI's Medical Event Subcommittee (MESC), which was chaired by Jeffrey Williamson, Ph.D. and consisting of ACMUI members Subir Nag, M.D., Ralph Lieto, M.S., and David Diamond, M.D.; invited consultant Louis Potters, M.D.; and NRC Staff Liaison Ronald Zelac, Ph.D. MESC unanimously approved forwarding these recommendations to ACMUI for further consideration during a closed teleconference held on 13 June 2005.

Because of the technical difficulty in formulating its recommendations in proposed rule language, ACMUI's recommendations are presented in the form of ordinary-language descriptions, principles, and examples. However, in the opinion of ACMUI, the approach outlined below does constitute a consistent and complete alternative to the current permanent implant ME regulation that the NRC staff can use as the basis for drafting an alternative ME rule and associated definitions.

A Status of current ME rule and associated definitions

1) ACMUI understands that the NRC Office of General Counsel (OGC) has ruled that an authorized user (AU) may revise a permanent implant Written Directive (WD) (In Part 35 language "complete the WD") at any time during the interval between completion of seed insertion (called "implantation" in 10CFR35) and availability of the post-implant dose distribution. Availability of the post-implant dose distribution has been accepted by OGC to be the "completion of the procedure" for permanent implants; other interpretations are possible since "completion of the procedure" is not defined by 10CFR35. Moreover, this interpretation of "completion of the procedure" is necessary if (a) the WD is specified in terms of absorbed dose and (b) the ME definition is based upon the discrepancy between prescribed absorbed dose and delivered absorbed dose.
2) For permanent implant WDs, the current rule states that AUs must specify the total absorbed dose prior to implantation, but may specify either the total source strength actually implanted or the absorbed dose by the end of the procedure. The practical impact of OGCs recent interpretation is that "dose," "total dose," and "total source strength" maybe used interchangeably in permanent implant WD's both prior to implantation and prior to completion of the procedure.
3) ACMUI does not believe that a 20% ME criterion is reasonable for absorbed dose WDs that are compared to absorbed dose distributions based upon any form of post-implant imaging.

   Rationale: The 20% dose threshold is comparable to the variation encountered in normal medical practice, due mainly to the limited control the authorized user has over the positioning of seeds and hence the dose delivered by permanent implants. Raising the relative absorbed dose threshold, e.g., to 50%, would reduce the number of clinically acceptable implants deemed Medical Events but at the expense of not capturing implants that do exhibit technical errors of quality assurance (QA) significance. The variations in post-implant absorbed dose distributions relative to the originally prescribed dose are due to

- Limited AU control over seed positioning
- Legitimate intraoperative adaptations of the preplanned source distribution
- Discrepancies between imaging modalities used for seed placement (ultrasound) and post-implant evaluation (x-ray CT) as well as physician organ contouring variations
- Postoperative changes such as prostate edema and seed migration
- Variable interval between seed implantation and post-implant imaging

4) The wrong site criterion (50% dose discrepancy of at least 50 Rem) is workable only for wrong site implantations far from the intended site. For identifying implants with excessive seed placement in organs adjacent to the treatment site, this dose-based wrong site criterion has all of the problems described in 3). Moreover, for many implantation sites and procedures, the current criterion cannot be evaluated explicitly, since what constitutes the intended adjacent organ dose is not clear or may not be specified in advance of the implantation procedure. Intended adjacent organ doses are not documented in the WD and not all implant procedures involve preoperative planning.

B Consensus principles for guiding NRC staff in reformulating the ME reporting rule and associated definitions

1) For all permanent implants, ME should be defined in terms of the total source strength implanted in the treatment site, not in terms of absorbed dose

Rationale: This proposed criterion focuses on what the AU can control, namely into which organ or treatment site the sources are implanted, instead of the absorbed dose distribution, over which AU control is limited. In addition, for the most commonly practiced forms of image-guided source implantation, definitive dose distributions may not be available until several weeks after completion of the procedure. On the other hand, the number of sources implanted in the treatment site (and hence total source strength) can be assessed, e.g., via intraoperative imaging for prostate implants, before releasing the patient from licensee control, will capture the majority of technical errors of interest to NRC, and is relatively insensitive to small, clinically acceptable, errors in positioning radioactive seeds relative to their planned locations.

2) Treatment-site accuracy ME pathway: Specifically ACMUI recommends that any implant in which the total source strength implanted in the treatment site deviates from the written directive by more than 20% (in either direction) should be classified as a ME. Several comments on this "treatment site accuracy" ME pathway are in order.
   a) The intent of this proposal is to provide the AU option of positioning up to 20% of the prescribed number of seeds into tissue or organs adjacent to the treatment volume (treatment site). Often, a small number radioactive seeds need to be placed 2-10 mm outside the prostate in order to provide adequate dosimetric coverage. In addition, the 20% latitude also accounts for variations in treatment-site definition, difficulties in visualizing the target organ by intraoperative imaging, and other phenomena that contribute to uncertainty in estimating the fraction of seeds implanted in the treatment site.
   b) As in the current ME rule, ACMUI intends that seed migration be specifically excluded as grounds for a treatment-site accuracy ME.

c) The technology for image-guided seed positioning and verification is most developed and mature for prostate brachytherapy. However, even in this clinical setting, the precision with which the fraction of seeds implanted in the prostate can be determined from post-implant CT or intraoperative ultrasound 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 volume that can be used to precisely determine whether the implant is a treatment-site accuracy ME. In such cases, only grossly erroneous MEs can be determined with certainty. NRC enforcement policy must be based upon realistic expectations of the precision that can be achieved in ME determination in different clinical settings.

3) Wrong-site ME pathway: The ACMUI recommends that the revised "wrong site" ME criterion distinguish between two scenarios: tissue or organs immediately adjacent to the treatment site and organs that are distant from the treatment site. For permanent implants, tissues that are more than 3 cm from the treatment site boundary can be considered distant, as the dose has fallen to subtherapeutic levels (1-5% of the prescribed dose).

a) Adjacent tissue wrong site ME: Implants in which more than 20% of the total source strength documented in the preimplantation WD is implanted in tissue or organs adjacent to the treatment site should be classified as MEs.

In this setting, a 20% threshold strikes a reasonable balance between permitting seed implantation outside of the target to boost peripheral doses [a medically legitimate objective] and detecting gross mispositioning of seeds into an adjacent organ rather than the intended treatment site.

b) Distant organ/tissue wrong site ME: For erroneous implantation of radioactive seeds in an organ distant from the intended treatment site, ACMUI recommends that such implants be classified as MEs if (i) seeds are actually implanted in a distant organ, (ii) the excess dose to the distant organ exceeds 50 Rem, and (iii) the excess dose to the organ is at least 50% greater than the dose that would have been delivered had the seeds been implanted in the correct tissue volume.
This definition is very similar to the wrong site pathway in the current ME definition except that it is invoked only when seeds are placed in the distant organ. An example of a distant organ ME is implanting the seeds in the left kidney when the right kidney was intended. Such an error could arise if the wrong medical record is used to confirm the treatment site or if the surgeon mistakenly exposed the kidney on the wrong side of the patient.

c) For both adjacent and distant wrong-site MEs, it is important to exclude seeds that were correctly implanted but subsequently migrated as grounds for an ME. Because a seed may occasionally migrate a large distance from the correctly implanted treatment site, it may be difficult to distinguish between true distant site MEs and seed migration by means of post-implant imaging alone.

4) Given a source-strength-based ME criterion of 20% in either direction (described in section B.3)), it is reasonable to require that the AU complete any revisions to the WD for permanent implants before the patient is released from licensee control.

Rationale: Using intraoperative imaging, a competent brachytherapist will be able to determine whether the fraction of seeds implanted in the treatment site agrees with the written directive within 20%. Hence the preimplantation WD can be revised at the time of the procedure to account for any medically necessary plan adaptations. This revision would effectively limit the AUs authority to revise the WD to the implantation procedure or the immediate post-operative period.

5) Dose-based ME pathway for permanent implants: In addition to incorporating the activity-based ME pathway (described above) into Part 35, ACMUI recommends retaining a limited dose-based ME criterion. **An implant is a ME if the dose calculations used to determine the total source strength documented in the WD are in error by more than 20% in either direction.**

For example, suppose that an AU intended to deliver a dose of 145 Gy to the prostate using ^{125}I seeds. Based upon pretreatment ultrasound imaging of the prostate, treatment-planning software is used estimate the source strength/seed (e.g., 0.44 mCi) and number of seeds (e.g., 100) needed to deliver 145 Gy to the contoured treatment volume. Suppose the dose-calculation algorithm erroneously used a ^{103}Pd seed dose rate constant (0.68), rather than the value (0.94) appropriate to iodine seed model to be implanted. This would overestimate the activity per seed by 38% (e.g., assuming that the correct ^{125}I monotherapy activity/seed is 0.32 mCi, the planning system would predict that 100 seeds of 0.44 mCi are needed to deliver 145 Gy to the target. Suppose that this dose-calculation error went undetected and that the AU recorded 100 seeds of 0.44 mCi/seed in the WD and actually implanted these seeds into the treatment site. This byproduct material administration would be a ME under the proposed dose-based criterion.

Rationale:

- In mainstream prostate brachytherapy practice, the AU describes his or her treatment intention in units of absorbed dose to a target volume. Through treatment planning, the source strength, number of seeds and seed arrangement are identified that realize this prescription. Preplanning can be a complex activity with the potential for mistakes that could result in large dose-delivery errors. Even nomogram-based systems seek to deliver a certain dose to a specified target volume. Defining ME solely in terms of correctly implanting the source strength specified in the WD would make all treatment-planning errors, many of which could adversely affect the patient's clinical outcome, exempt from regulatory oversight.
- In the current ME rule (and the previous misadministration rule), dose calculations that mediate between the AUs goal to deliver a certain dose and treatment device settings (treatment time, number of sources, etc), are currently subject to regulatory oversight for all modalities including permanent brachytherapy. Eliminating this oversight would be viewed as NRC backing away from patient safety. A single well-

publicized error or series of errors due to dose-calculation errors would be very embarrassing if NRC had no regulatory authority in this area.

- The "limited" ME dose pathway proposed here would focus only on preplanning or intraoperative planning, not post-implant evaluation. Hence, it avoids the difficulties of the current ME definition.

C Risk Communication

1) Problem definition: From the regulated community's point of view, ME reporting stigmatizes the licensee and all but assures increased regulatory scrutiny, which is viewed as punitive. Even though many ME reports do not result in license violations, licensees view the process as punitive because (a) regulatory intrusion into the patient-physician relationship; (b) placing the event reporting process in the public record; and (c) reactive inspections following ME reports appear to equate even minor MEs with nuclear reactor events having much greater potential public safety consequences. A perceived punitive regulatory response, along with the ambiguity of some ME criteria and their lack of medical relevance, results in potential under-reporting and almost certainly discourages reporting of borderline or ambiguous cases that might be helpful to NRC in constructing a more complete picture of error pathways. ACMUI affirms that there is no scientific basis for treating medical events (MEs) as a surrogate or harbinger of patient harm, or even of increased probability of patient harm. The SC believes that efforts to revise ME definitions to improve its correlation with potential or actual harmful effects is misguided and undercuts its value as QA performance index. Provided that ME incidence is decoupled from the concept of patient harm, the current 20% is a reasonable if arbitrary threshold for identifying events indicative technical or QA problems in accurately realizing the AUs clinical intentions.
2) The role of the 10CFR35.3045 ME reporting rule as a technical quality performance indicator should be decoupled from its use as a potential patient harm index. To this end, the patient reporting requirement 35.3045(e) should be amended to require informing the patient and/or friends and relatives only if the licensee determines that the ME may have harmed the patient, could potentially harm the patient, or is materially relevant to the patient's future medical treatment decisions.
3) The SC recommended that NRC staff strive to make the ME reporting and subsequent enforcement processes more like the regulated community's own QA practice of followup and QA process review that occurs following detection of a delivery error or potential error.

   Rationale: Comprehensive institutional QA programs are based upon three broad principles:

   a) Avoid making the occurrence of a medical error grounds for actual or perceived disciplinary action. Medical health professionals should be encouraged to report errors, not discouraged from doing so.
   b) Avoid increasing an institution's legal liability associated with its QA deliberations and process improvements made in response to a medical error. Regulatory actions that make quality improvement activities a source of institutional liability discourage adherence to comprehensive quality assurance standards and undermine the quality of patient care.
   c) Encourage use of medical error reports as input to systematic efforts to improve planning, delivery, safety, QA, and documentation processes.

4) ACMUI recommendations for making ME reports more like industry standard error reporting

   a) To the extent possible, NRC's ME reporting and followup procedures should be designed to not increase Licensee liability. Keeping ME reports, or at least the

Licensee's identity out of the public record, is probably the single most useful improvement NRC could make in this regard.

b) NRC is encouraged to develop a more graded and risk-informed process for responding to ME reports that ties the intensity and immediacy of its inspection response to individual patient risk and public health implications of the event. For example, for relatively minor MEs, where public health and safety is not in question, NRC could minimize reactive inspections of Licensee pending a satisfactory investigation and quality-improvement response on the part of the Licensee. Thus, ACMUI recommends that NRC manage minor MEs much like recordable events in Old Part 35.

c) Change the 24 hour Operations Center reporting procedure. The current process which requires verbally reporting MEs to the Operations Center within 24 hours and appears to equate Medical Events, most of which do not cause actual harm to the patient, with serious nuclear reactor events, which the potential to affect large numbers of people. Reports to the Operations Center are immediately available to the World Wide Web. This results in adverse publicity and adds to the liability concerns raised above. Thus for all but the most serious MEs, an alternative and more appropriate reporting mechanism should be devised. Specifically, the ACMUI recommends that MEs that have not harmed the patient; have little potential for harming the patient, and are not materially relevant to the patient's future medical treatment decisions, as evaluated by the Licensee, be reported to NRC by means of written notification within 7 days of their discovery.

ACMUI's Specific Suggestions for Improving Public Understanding of the Risks Associated with Medical Events

From ACMUI final recommendations document, received July 19, 2005

1. The patient reporting requirement in 10 CFR 35.3045(e) should be amended to require informing the patient and/or friends and relatives of the ME only if the licensee determines that the ME may have harmed the patient, could potentially harm the patient, or is materially relevant to the patient's future medical treatment decisions.

Staff does not support this ACMUI recommendation because the Commission has repeatedly stated and endorsed its position that a patient or human research subject involved in any ME should be notified of the occurrence, based on the individual's right to know information about himself or herself that is contained in records both inside and outside the Federal sector [43 FR 2927 (May 7, 1978); 63 FR 43516 (August 13, 1998); 67 FR 20332 (April 24, 2002)]. Further, this requirement codifies existing medical ethical standards obligating physicians to provide complete and accurate information to their patients, so the patients can be actively involved in any decisions about any remedial or prospective health care that may be appropriate following MEs, as indicators of technical or QA problems in prescription delivery.

2. NRC staff should strive to make the ME reporting and subsequent enforcement processes more like the regulated community's own QA practice of followup and QA process review that occurs after detection of a delivery error or potential error. Specific suggestions for accomplishing this objective are as follows.

    a. NRC's ME reporting and follow-up procedures should be designed so as to not increase licensee liability. Keeping ME reports, or at least the licensee's identity, out of the public record is probably the single most useful improvement NRC could make in this regard.

Staff does not support this ACMUI recommendation because it is counter to the Commission's policy of public openness and transparency in the conduct of its business, except in cases of National security or personal privacy of patients and human research subjects. Further justification for continuing the public release of ME information is NRC's concern that technical or QA failures identified through ME reports might result in harm to individuals at the reporting licensee's facility or at other licensee facilities if ME reporting thresholds are significantly exceeded and should therefore be publicized.

    b. NRC is encouraged to develop a more graded and risk-informed process for responding to ME reports that ties the intensity and immediacy of its inspection response to individual patient risk and public health implications of the event. For example, for a relatively minor ME, where public health and safety are not in question, NRC could minimize reactive inspection of the licensee pending a satisfactory investigation and quality-improvement response on the part of the licensee.

Enclosure 3

NRC's approach to ME assessment in Management Directive 8.10, "NRC Medical Event Assessment Program," is already graded and risk-informed. For example, NRC already has a variable time frame for initiation of ME assessments that reflects the known or potential seriousness of each occurrence, with generally acceptable delay times ranging from 2 working days (for the most serious events) to 10 working days, or longer. Also, the degree and type of follow-up are based on the type of ME reported, with NRC taking enforcement action only when appropriate.

Once the ME assessment is initiated, the purpose of the inspector's site visit is to confirm and/or gather information to ensure that all required facts are available to complete the assessment. The staff continues to believe that this assessment is necessary for all MEs so that (1) the NRC is aware of events that trigger the thresholds for MEs, to determine what actions, if any, need to be taken to prevent recurrence; (2) other licensees can be made aware of generic problems that result in MEs; and (3) patients can, when appropriate based on the ME reporting criterion being significantly exceeded, make timely decisions regarding remedial and prospective health care. Staff believes that the most effective and efficient approach to ensure the timely availability of information necessary for completion of these assessment process tasks is the assessment group inspector's visit of the site, to confirm and/or gather information. Even for an ME that the licensee considers to be relatively minor, staff does not support this ACMUI recommendation.

c. NRC is encouraged to change the 24-hour Operations Center reporting procedure. Specifically, MEs that have not harmed the patient, have little potential for harming the patient, and are not materially relevant to the patient's future medical treatment decisions, as evaluated by the licensee, are to be reported to NRC by means of written notification within 7 days of their discovery.

The Commission has previously endorsed staff's position opposing different reporting periods, depending on the licensee's initial assessment of the event [67 FR 20331 (April 24, 2002)] for several reasons. First, a requirement that allows for different reporting periods, depending on the initial assessment of the event, would lead to differing interpretations and confusion as to whether the magnitude of the event requires notification of the NRC no later than the next calendar day. In addition, there may be a medical event where the seriousness of the consequences would not be immediately apparent and which, therefore, would not be reported. Further, medical events need to be evaluated as soon as possible to determine if any immediate follow-up or corrective actions are necessary.

Additionally, the 24-hour reporting requirement, intended to permit NRC to conduct a *timely*, thorough, systematic, and formal assessment is consistent with NRC's 24-hour reporting requirements for other events involving licensed material. For example, 10 CFR 30.50, "Reporting Requirements" [byproduct material]; 10 CFR 40.60, "Reporting Requirements" [source material]; and 10 CFR 70.50, "Reporting Requirements" [special nuclear material] all require 24-hour reporting of: (1) an unplanned contamination event that requires access to the contaminated area to be restricted for more than 24 hours and involves a quantity of material greater than five times the lowest annual limit on intake specified in Appendix B of 10 CFR Part 20 for the material; (2) an event in which equipment is disabled or fails to function as designed when the equipment is required by regulation or license condition to prevent releases exceeding regulatory limits, to prevent exposures to radiation and radioactive materials exceeding

regulatory limits, or to mitigate the consequences of an accident, and the equipment is required to be available and operable when it is disabled or fails to function, and no redundant equipment is available and operable to perform the required safety function; (3) an event that requires unplanned medical treatment at a medical facility of an individual with spreadable radioactive contamination on the individual's clothing or body; (4) an unplanned fire or explosion damaging any licensed material or any device, container, or equipment containing licensed material, when the quantity of material involved is greater than five times the lowest annual limit on intake specified in Appendix B of Part 20 for the material; and the damage affects the integrity of the licensed material or its container.

The 24-hour reporting requirements for all these material use events, which enable NRC to promptly assesses the potential health and safety consequences for individuals or actual impact on licensed operations, serve a parallel purpose to NRC's 24-hour reporting requirement for medical use events, which enable NRC to promptly evaluate the circumstances of the MEs to determine if any immediate follow-up or corrective actions are necessary.

From ACMUI October 2005 meeting

> Recommendation: NRC should treat event information supplied by a licensee to the NRC Operations Center, pursuant to the next-calendar-day reporting requirement in 10 CFR 35.3045(c), and contained in an Event Summary, as preliminary raw data, and the Event Summary as a draft document. This information should not be disclosed/released to the public until the event has been confirmed to be a reportable ME.

This recommended procedure, as applicable to events reported by NRC medical use licensees, parallels a procedure NRC follows, upon Agreement State request, for releasing event information reported by an Agreement State for any type of event. Therefore, the staff endorses and supports the intent of this ACMUI recommendation. However, similar to Event Summaries received by NRC from Agreement States, there must be a limit on the delay time for fact-finding and assessment, before release of information to the public, if appropriate. Therefore, if the event has not been confirmed to be a reportable ME within 5 calendar days from initial reporting by the licensee, the staff recommends that the information available on the event at that time should be released to the public since it represents a potential ME.[1]

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[1]It has been suggested by Regional staff from each region, who are involved in implementing Part 35, that any delay in releasing information on potential MEs is inappropriate, since licensee-supplied information on other types of events at NRC-licensed facilities is released promptly upon receipt by NRC. NMSS/IMNS does not accept this position, since 1) there is often more informational uncertainty (re: the need for reporting) for events involving medical use than there is for most events involving other uses, and 2) for consistency, Event Summaries for NRC medical use licensees should be handled by NRC in the same way as Event Summaries for Agreement State medical use licensees. Whether, for further consistency, Event Summaries for other types of events reported by NRC licensees should be considered for delayed release when there is uncertainty, due to the need to acquire additional information (e.g., to analyze a personal dosimeter), as to the appropriateness of reporting, is outside the scope of this paper, unless the Commission directs otherwise.

Suggestion: NRC should footnote each Event Summary disclosed/released to the public as a reportable ME to indicate that NRC's ME definitions provide thresholds for identifying events that are indicative of technical or QA problems in accurately realizing the clinical intentions (prescriptions) of AUs and that thresholds in NRC's ME definitions, if exceeded, are not necessarily indicative of patient harm, or even of increased probability of patient harm.

The staff endorses and supports the intent of this ACMUI suggestion.