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/

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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

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