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.