Advisory Committee on the Medical Use of Isotopes (ACMUI)

Report on Abnormal Occurrence Criteria for Medical Use

April 15, 2013

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Charge: To review the refined abnormal occurrence criteria for events involving patients or human research subjects and to provide recommendations to the NRC staff.

Recommendations:

The following changes are recommended to Appendix A: Abnormal Occurrence Criteria in the current Abnormal Occurrence Revised Policy Statement[1].

1. **In section I. A., add new paragraph 4. to read as follows:**

   4. These criteria do not apply to events included in criteria III.C. involving medical administrations using byproduct material to patients or human research subjects.

2. **In section III. C., redefine title; replace paragraphs 1. and 2. with the following paragraphs 1. and 2.:**

   C. For Events Involving Patients or Human Research Subjects

      1. Medical event involving a patient or human research subject that, as determined by a consultant physician(s) deemed qualified by NRC or an Agreement State, results in one or more of the following:

         a. Unintended or unexpected permanent functional damage to an organ.

         b. Unintended or unexpected permanent functional damage to a physiological system.

         c. A significant unexpected adverse health effect.

         d. Death.

[1] Nuclear Regulatory Commission, "Revised Policy Statement on Abnormal Occurrence Criteria," 71 FR 60198, October 12, 2006, http://www.gpo.gov/fdsys/pkg/FR-2006-10-12/pdf/E6-16871.pdf (accessed March 25, 2013).

2. Notification under 10 CFR 35.3047 of an event involving an unintended dose to an embryo/fetus or a nursing child that results in a significant adverse health impact to the embryo/fetus or child, as determined by a consultant physician(s) deemed qualified by NRC or an Agreement State.

Need for Medical Abnormal Occurrence Criteria Update:

The Nuclear Regulatory Commission (NRC) is required to annually report abnormal occurrences to Congress as defined in Section 208 of the Energy Reorganization Act of 1974[2]. This section states:

> "For the purposes of this section an abnormal occurrence is an unscheduled incident or event which the Commission determines is significant from the standpoint of public health or safety."

Establishment of the NRC Policy Statement on Abnormal Occurrence Criteria[3] provides explanation of how the Commission determines the incidents or events to be significant and included in the annual abnormal occurrence (AO) report. The NRC Staff and the Advisory Committee on the Medical Use of Isotopes (ACMUI) have discussed concerns that the medical use-related incidents and events being included in AO reports may not be significant from the standpoint of public health or safety. During an ACMUI teleconference in December 2011[4], the ACMUI endorsed their 2008 position, which is summarized by the following: AOs for medical licensees should be events which result in death or threaten life; AOs should not capture those occurrences that are accepted risks of the treatment; AOs should be of significant adverse effect; AO criteria should be qualitative and not quantitative[5].

At the September 2012 ACMUI meeting[6], the NRC Staff asked the Committee to consider their proposal to add dose-based criteria for medical licensee AO criteria (see Attachment 1) to allow the NRC Staff a screening tool to decide which medical events should then be evaluated by a consultant physician to determine significant adverse effect. During discussion of this proposal, the ACMUI again voiced their concerns of using dose-based criteria to judge medical AOs. The ACMUI established a subcommittee to develop recommendations concerning the AO criteria related to medical use incidents and events.

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[2] U.S. Energy Reorganization Act of 1974, as Amended (Public Law 93-438), pages 252-253, http://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr0980/v1/sr0980v1.pdf#page=241 (accessed March 25, 2013).

[3] Nuclear Regulatory Commission, "Revised Policy Statement on Abnormal Occurrence Criteria," 71 FR 60198, October 12, 2006, http://www.gpo.gov/fdsys/pkg/FR-2006-10-12/pdf/E6-16871.pdf (accessed March 25, 2013).

[4] Official Transcript of Proceedings, Nuclear Regulatory Commission Advisory Committee on the Medical Use of Isotopes Teleconference, December 15, 2011, http://pbadupws.nrc.gov/docs/ML1206/ML12062A278.pdf (accessed March 25, 2013).

[5] Meeting Summary, Nuclear Regulatory Commission Advisory Committee on the Medical Use of Isotopes Teleconference, December 15, 2011, http://pbadupws.nrc.gov/docs/ML1135/ML11355A253.pdf (accessed April 4, 2013).

[6] Official Transcript of Proceedings, Nuclear Regulatory Commission Advisory Committee on the Medical Use of Isotopes Teleconference, September 21, 2012, http://pbadupws.nrc.gov/docs/ML1232/ML12324A222.pdf (accessed April 4, 2013).

Development of Recommendations:

The Subcommittee reviewed medical use-related abnormal occurrences reported to Congress in the past five years, as summarized in this table, discussed the NRC Staff's proposed criteria, and came to the conclusions as described here. Additional Subcommittee discussion points pertinent to these conclusions are included in Attachment 2.

Abnormal Occurrences Reported to Congress

FY	All AO	AO I.A.2. ① from Medical Use	AO III.C. ② from Medical Use
2011[7]	24	2	19
2010[8]	15	3	12 ③
2009[9]	9	2	7
2008[10]	10	2	8 ③
2007[11]	11	1	10

① Each AO listed here involved one I-131 therapy patient who was found to be in early stage pregnancy following her therapy. No medical licensee reported more than one patient.

② Each AO listed here involved one or two radiation therapy patients per medical licensee, except as noted.

③ One AO in this total involved three or more radiation therapy patients at one medical licensee.

[7] NUREG-0090, Vol. 34, "Report to Congress on Abnormal Occurrences – Fiscal Year 2011," Nuclear Regulatory Commission, http://pbadupws.nrc.gov/docs/ML1214/ML12142A194.pdf (accessed March 25, 2013).
[8] NUREG-0090, Vol. 33, "Report to Congress on Abnormal Occurrences – Fiscal Year 2010," Nuclear Regulatory Commission, http://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr0090/v33/sr0090v33.pdf (accessed March 25, 2013).
[9] NUREG-0090, Vol. 32, "Report to Congress on Abnormal Occurrences – Fiscal Year 2009," Nuclear Regulatory Commission, http://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr0090/v32/sr0090v32.pdf (accessed March 25, 2013).
[10] NUREG-0090, Vol. 31, "Report to Congress on Abnormal Occurrences – Fiscal Year 2008," Nuclear Regulatory Commission, http://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr0090/v31/sr0090v31.pdf (accessed March 25, 2013).
[11] NUREG-0090, Vol. 30, "Report to Congress on Abnormal Occurrences – Fiscal Year 2007," Nuclear Regulatory Commission, http://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr0090/v30/sr0090v30.pdf (accessed March 25, 2013).

Title Change for Medical Use AO Criteria

The Subcommittee agreed with the NRC Staff's proposed medical use AO criteria title, "For Events Involving Patients or Human Research Subjects." This title change makes clear that these AO criteria refer only to incidents related to medical administrations using byproduct materials, and that other parts of a medical licensee's program are subject to the other AO criteria applicable to material licensees.

Use of Screening Criteria for Medical Use AO Criteria

At the September 2012 ACMUI meeting[12], the NRC Staff voiced concern that without dose-based AO criteria, all medical events may require the NRC to have every medical event reviewed by a medical consultant, resulting in significant costs and time delays. The Committee's discussions at that meeting and continued discussions by the Subcommittee led the Subcommittee to conclude that dose-based screening criteria would not provide the NRC Staff a reliable method to identify medically significant incidents in all cases and therefore should not be included in the AO criteria.

The Subcommittee discussed the NRC Staff's request to establish screening criteria for identifying those medical events that require an additional medical consultant review. ACMUI's annual review of the medical events and the Subcommittee's review of the AO reports for the past five years indicate there are few medical events reported each year that have the potential to cause significant harm. The Subcommittee believed that requiring an additional medical consultant review of every medical event to determine the significance of the event would be an unnecessary expenditure of resources. The Subcommittee explored the use of alternative screening criteria, such as setting a minimum number or rate of individuals significantly harmed by a medical event(s) reported by a medical licensee in one AO report year (see Attachment 2, Discussion Points 2 and 3 for additional information on these discussions). The NRC Staff informed the Subcommittee that a screening criterion using a threshold number of individuals would not be acceptable from a regulatory point of view. In addition, the Subcommittee was unable to come to a unanimous consensus on what the threshold number of individuals should be for an AO definition.

The Subcommittee concluded that there are no practical and implementable screening criteria which could be included with the NRC Staff's proposed AO criteria definition of significant harm (see Attachment 1, Item 2). However, the Subcommittee suggested that the NRC Staff could rely on the existing NRC policy regarding the use of medical consultants[13] as a reasonable and practical screening tool to determine the need for a consultant physician (see Attachment 3).

[12] Official Transcript of Proceedings, Nuclear Regulatory Commission Advisory Committee on the Medical Use of Isotopes Meeting, September 21, 2012, http://pbadupws.nrc.gov/docs/ML1232/ML12324A222.pdf (accessed March 25, 2013).

[13] NRC Inspection Manual Chapter 1360: "Use of Physician and Scientific Consultants in the Medical Consultant Program", IMC 1360-04.02, November 2, 2006, http://pbadupws.nrc.gov/docs/ML0627/ML062720195.pdf (accessed March 25, 2013).

Embryo/Fetus or Nursing Child Dose

The Subcommittee also reviewed the reporting criteria of abnormal occurrences involving medical licensee notification of unintended dose to an embryo/fetus or nursing child. The past five years of AO reports included notifications of unintended dose to an embryo/fetus that were due to I-131 therapy patients unknowingly being pregnant at the time of their therapy despite appropriate pre-treatment pregnancy screening. These incidents were reported as abnormal occurrences due to the low dose threshold criterion defined the "For All Licensees" AO criteria I.A.3.

The Subcommittee did not believe use of the "For All Licensees" criteria I.A.3 is appropriate in judging a medical use AO, even though dose to the embryo/fetus or child may be considered a public dose. The Subcommittee considered it inappropriate because the mother is undergoing a medical treatment and the unintended dose to the embryo/fetus or child should not be considered separate from the medical administration. In a regulatory sense, this is consistent with how the NRC requires embryo/fetus or nursing child dose reporting to be done under the medical use regulations[14] rather than under the protection against radiation regulations[15]. The Subcommittee recommended that the "For All Licensees" AO criteria I.A. be modified to exclude events that are included in criteria III.C involving medical administrations using byproduct material to patients or human research subjects. This recommended modification is made in a similar way the "For All Licensees" criteria I.B. excludes transportation events. The Subcommittee recommended that the AO criteria III.C. also include the unintended dose reported under 10 CFR 35.3047 to an embryo/fetus or a nursing child which results in a significant medical harm to the embryo/fetus or child because this abnormal occurrence can only happen as a result of medical administration to a patient or human research subject.

[14] 10 CFR 35.3047, "Report and notification of a dose to an embryo/fetus or a nursing child," http://www.nrc.gov/reading-rm/doc-collections/cfr/part035/part035-3047.html (accessed March 25, 2013).
[15] 10 CFR 20.2203(a)(2)(iv), "Reports of exposures, radiation levels, and concentrations of radioactive material exceeding the constraints or limits," http://www.nrc.gov/reading-rm/doc-collections/cfr/part020/part020-2203.html (accessed March 25, 2013).

Attachment 1

Medical AO Draft Criteria Discussed at the September 2012 ACMUI Meeting

For Events Involving Patients or Human Research Subjects

1. A medical event that results in an unintended dose to the target or a dose other than the dose to the intended target that is:

    a. Greater than or equal to 1 Gy (100 rad) to a major portion of the bone marrow or to the lens of the eye; **or**
    b. Greater than or equal to 2.5 Gy (250 rad) to the gonads; **or**
    c. Greater than or equal to 10 Gy (1,000 rad to any other unintended organ or tissues other than the treatment site; **and**

2. Results in a significant impact on patient health that would result in **one or more** of the following, as determined by a consultant physician(s) deemed qualified by NRC or an Agreement State:

    a. Unintended or unexpected permanent functional damage to an organ.
    b. Unintended or unexpected permanent functional damage to a physiological system.
    c. A significant unexpected adverse health effect.
    d. Death

Attachment 2

Additional Subcommittee Discussion Points
Concerning Medical Use Abnormal Occurrence Criteria

In developing recommendations for medical use abnormal occurrence (AO) criteria, the Subcommittee discussed the following points.

1. **What is the difference between medical events or notifications of embryo/fetus or child dose versus abnormal occurrences?**

   The Subcommittee recognized that regulations for medical events and notifications of unintended embryo/fetus or child dose provide indicators of errors in a medical administration using byproduct materials worthy of close evaluation by the licensee and the regulators. The fact that these incidents may not be considered abnormal occurrences does not diminish the seriousness of the incident, the requirements to evaluate cause and corrective action, or the need for regulatory enforcement. Medical licensees have demonstrated a good safety record with low incident rates less than 0.3 % for medical events affecting the medical treatment of 50 to 100 patients a year[16]. In most cases, these medical events do not result in a significant adverse effect to the patient or human research subject.

   In the end, the Subcommittee distinguished regulatory criteria defining medical events and notifications of unintended embryo/fetus or child dose as being chosen to protect the individual member of the public, while AO criteria are used to define which of these medical events and notifications should be considered as significant from the standpoint of public health and safety for the annual report to Congress.

2. **Could a minimum number of medical use-related event reports per licensee to be considered as a screening criterion for abnormal occurrence definition?**

   The Subcommittee explored the meaning of "public health or safety" used in the definition of an abnormal occurrence by considering the definitions of the following terms:

[16] Byproduct Material Events Subcommittee Report, Nuclear Regulatory Commission Advisory Committee on the Medical Use of Isotopes Meeting, April 2011, http://pbadupws.nrc.gov/docs/ML1109/ML11095A086.pdf (accessed April 4, 2013).

Public[17] –

1. of, belonging to, or concerning the people as a whole; of or by the community at large
3. as regards community, rather than private, affairs

Public Health[18] –

The science and practice of protecting and improving the health of a community, as by preventive medicine, health education, control of communicable diseases, application of sanitary measures, and monitoring of environmental hazards.

Public Health Ethics[19] -

Public health ethics involves a systematic process to clarify, prioritize and justify possible courses of public health action based on ethical principles, values and beliefs of stakeholders, and scientific and other information.

The Subcommittee considered that incidents or events should have the potential for significant medical harm to more than one individual to be considered as significant from a public health or safety standpoint. The NRC has used this sort of threshold criteria for determining whether an Incident Investigation Team (IIT) or an Augmented Inspection Team (AIT) is warranted for a Medical Event Assessment (MEA)[20].

The Subcommittee discussed what might be an appropriate number of individuals for a threshold criterion. One Subcommittee member felt any number greater than one would not be acceptable because of the adverse medical consequence criteria. Another Subcommittee member suggested two individuals would be the appropriate threshold criterion because one adverse event could happen anywhere, and not signify a threat to public health, but a second similar adverse event could indicate a failure in the cause analysis and correction process. The remaining Subcommittee members thought three individuals would be an appropriate threshold criterion, but also suggested that the Commission should consider providing summary information of medical use-related events resulting in medical harm not meeting this AO criterion as part of the AO report under the AO criteria IV. Other Events of Interest.

The NRC Staff told the Subcommittee that this sort of screening criterion would not be acceptable from a regulatory point of view. They noted that the regulatory philosophy of the NRC considers harm to any individual. As noted in Discussion Point 1, every medical event is subject to regulation and therefore no event posing harm to an individual would avoid regulatory scrutiny. The majority of

[17] Webster's New World College Dictionary, http://www.yourdictionary.com/public (accessed March 25, 2013).
[18] The American Heritage® Medical Dictionary, http://medical.yourdictionary.com/public-health (accessed March 25, 2013).
[19] Centers for Disease Control and Prevention, http://www.cdc.gov/od/science/integrity/phethics/ (accessed March 25, 2013)
[20] NRC Medical Event Assessment Program Directive 8.10, July 6, 1994, http://pbadupws.nrc.gov/docs/ML0414/ML041410592.pdf (accessed April 8, 2013)

Subcommittee members did not see a conflict between using a threshold number of individuals as a screening criterion and the NRC's regulatory philosophy.

3. Could a measure of rate be used rather that an absolute number of events reported in a year by a medical licensee?

The Subcommittee discussed whether consideration should be included for an AO criterion that evaluates the difference between a small clinic medical licensee reporting multiple events out of a low number of medical administrations a year versus a large university hospital medical licensee reporting the same number of events out of a much higher number of medical administrations. The Subcommittee concluded that use of a rate-based AO criterion would be impractical because medical licensees are not required to report the number of medical administrations per year. The Subcommittee did recognize that the evaluation of this kind of event rate is an important aspect of the NRC or Agreement State inspection of the medical licensee's compliance and subsequent enforcement actions.

Attachment 3

NRC INSPECTION MANUAL
Manual Chapter 1360

Use of Physician and Scientific Consultants
in the Medical Consultant Program
(http://pbadupws.nrc.gov/docs/ML0627/ML062720195.pdf)

1360-04 POLICY ON USE OF MEDICAL CONSULTANTS

04.01 The time frame for initial activation of the procedures in this Manual Chapter should be based on the initial assessment of the severity of the event. This assessment will typically be performed by the regional office with input from MSSA/FSME, as necessary.

The following guidelines may be used when establishing the time frame for activation[1]:

a. Radiation Exposure Incident resulting in a fatality - 2 working days after NRC is informed of the event.

b. Radiation Exposure Incident determined to:

    1. be a medical event; and

    2. result in a total dose in excess of the prescribed total dose to a patient – 5 working days after the event is determined to be a medical event by NRC.

c. Radiation Exposure Incident determined to:

    1. be a medical event where the reporting requirement was based on the fractionated dose; and

    2. result in an overexposure that exceeds the prescribed total dose or three times the fractionated dose, whichever occurs first - 10 working days after the event is determined to be a medical event by NRC.

d. Radiation Exposure Incident (other than a medical event) that has not resulted in a fatality - 10 working days after NRC is informed of the event.

[1] The specified time frame assumes that the radiation exposure incident occurred within the last 2 months. If the radiation exposure incident occurred in the past, consideration should be given to extending the time frame.

04.02 Medical Consultants must be used under the following circumstances:

a. Incidents where an individual has received one or more of the following doses:

    1. A suspected total effective dose equivalent of 0.25 sievert (Sv) (25 rem) or more.

    2. A suspected lens of the eye dose equivalent of 0.75 Sv (75 rem) or more.

    3. A shallow-dose equivalent to the skin or extremities of 2.5 Gray (250 rad or more.

    4. A suspected committed effective dose of 2.5 Sv (250 rem) or more to any individual organ or tissue other than the lens of the eye.

b. Incidents where an individual is demonstrating physical symptoms (erythema, nausea, vomiting, etc.) consistent with radiation syndromes, and the source of the radiation may be attributable to NRC-licensed radioactive material.

c. Incidents where NRC staff believe permanent functional damage to an organ or a physiological system is possible.

d. Incidents where a nursing infant or an embryo/fetus may have been inadvertently exposed to radiation or radioactive material as a result of the intentional or unintentional exposure of the mother of the nursing infant or an embryo/fetus to radiation or radioactive material.

e. A medical consultant shall be contacted for all medical events involving an overexposure in accordance with Management Directive 8.10, "NRC Medical Event Assessment Program." With the exception of the case identified in item c. above (for which site visits are required), a site visit by the medical consultant will not normally be required. A site visit by the medical consultant would be appropriate if the region and consultant agree that a site visit is necessary for NRC to understand the event, its causes, and its ramifications to the NRC's programs. Section 05.04e describes documentation required when the medical consultant determines that a site visit or consulting services are not necessary.

04.03 Medical Consultants may be used under the following circumstances:

a. Incidents where members of the public or occupationally exposed individuals may have been exposed to radiation during a radiation exposure incident.

b. Incidents where the staff believes that the assistance of a medical consultant would be beneficial to fulfilling the NRC mission.