UNITED STATES
NUCLEAR REGULATORY COMMISSION
OFFICE OF FEDERAL AND STATE MATERIALS
AND ENVIRONMENTAL MANAGEMENT PROGRAMS
WASHINGTON, D.C. 20555

December 5, 2007

NRC REGULATORY ISSUE SUMMARY 2007-27
IMPROVING PUBLIC UNDERSTANDING OF THE RISKS ASSOCIATED WITH MEDICAL EVENTS

ADDRESSEES

All U.S. Nuclear Regulatory Commission (NRC) medical use licensees. All Radiation Control Program Directors, and State Liaison Officers.

INTENT

NRC is issuing this Regulatory Issue Summary (RIS) to help improve public understanding of the risks associated with medical events (MEs), as described in 10 CFR 35.3045. No specific action or written response is required. NRC is providing this RIS to Agreement States for their information and for distribution to their medical licensees, as appropriate.

BACKGROUND

On April 24, 2002, the Commission published a final rule in the *Federal Register* amending 10 CFR Part 35, "Medical Use of Byproduct Material," in its entirety (67 FR 20250). The revision includes a section, 10 CFR 35.3045, "Report and Notification of a Medical Event," that provides criteria for reporting and notifying individuals about an ME. The requirements in this section of the final rule are based on those in the previous 10 CFR 35.33, "Notifications, Reports, and Records of Misadministrations." An ME is defined in 10 CFR 35.2, "Definitions," as an event that meets the criteria in 10 CFR 35.3045(a) or (b). The final rule can be viewed on the NRC public web site, at http://www.nrc.gov/reading-rm/doc-collections/cfr/part035/.

In Staff Requirements Memorandum (SRM)-M040302B dated March 16, 2004, the Commission directed the staff to, among other tasks, provide recommendations on how to effectively communicate to the public the risks, if any, associated with MEs. The Commission also directed the staff to involve the Advisory Committee on the Medical Uses of Isotopes (ACMUI) in the development of its recommendations.

ML071360295

In SECY–05-0234, dated December 7, 2005, the NRC staff submitted recommendations to improve public understanding of the risks associated with MEs, and in SRM-SECY-05-0234, dated February 15, 2006, the Commission approved those recommendations. The staff's recommendations were based on certain "guiding principles," a recommendation, and a suggestion developed by the ACMUI. The SRM can be viewed on the NRC public web site, at http://www.nrc.gov/reading-rm/doc-collections/commission/srm/2005/2005-0234srm.html. This RIS is one of the mechanisms that the Commission approved for improving public understanding of the risks associated with medical events (MEs).

SUMMARY OF ISSUE

For all medical uses, without exception, there are two criteria that apply to reporting an ME. These criteria appear in 10 CFR 35.3045(a). One criterion is the percent variation of delivered dose from prescribed dose exceeding a threshold; it is referred to as the "variance threshold." The other criterion is the difference between the delivered dose and the prescribed dose (or dose that would have resulted from the prescribed dosage) exceeding a threshold; it is referred to as the "difference-in-dose threshold."

The variance threshold for licensee submission of an ME report is an administered total dose (or dosage) that differs by ± 20 percent from the prescribed dose (or dosage) defined in the authorized user (AU) physician's written directive (WD). Since WDs are required primarily for administrations intended for therapeutic purposes, a ± 20 percent variance can correspond to intended target doses reduced by or exceeded by approximately 0.5 Gray (Gy) (50 rads) to 18 Gy (1800 rads).[1] The basis for this variance threshold for reporting an ME, 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 patients or human research subjects.

The basis for the variance threshold for reporting an ME, in part, reflects a general consensus among the members of the ACMUI active during the general revision of 10 CFR Part 35 concluded in 2002, and among recent past and current members of the ACMUI. The consensus is that a variance in total delivered dose, or dosage, of 20 percent or more from that intended (prescribed) (1) has a significant potential, though not a certainty, to cause harm to the involved patient or research subject and (2) could indicate a deficiency in the licensee's program for ensuring that byproduct material is used as directed by the AU, even if the variance did not necessarily indicate a significant risk to the involved patient or research subject. The ACMUI rationale for this position is that the ± 20% variance threshold is a reasonable threshold for identifying events indicative of treatment delivery problems in accurately realizing AUs' clinical intentions. NRC staff agrees with the ACMUI rationale for this variance threshold criterion for ME reporting and notes that no events involving medical use have resulted in this threshold being questioned.

[1]Both Gray and rad are units of radiation dose, reflecting the amount of energy deposited in a given quantity of matter, in this case, tissue.

The consensus of the ACMUI was that a total 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 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 thresholds criterion for MEs,[2] a diagnostic radiopharmaceutical over-dosing error that resulted in either the excess effective dose equivalent slightly exceeding 0.05 Sv (5 rem) or the excess organ, tissue, or skin dose slightly exceeding 0.5 Sv (50 rem) would only rarely, if ever, result in actual harm to the patient or research subject. However, the absolute magnitude of the dosage error would likely be large enough (considerably exceeding 20%) to warrant reporting. The consensus of the ACMUI was that the NRC would have a legitimate interest in over-dosages where either of these difference-in-dose thresholds for ME reporting was exceeded.

The ACMUI recommended in July 2005, as general "guiding principles," that NRC consider MEs as performance indicators of technical or QA problems in accurately realizing clinical intentions of AUs, but not as indicators of actual or probable patient harm. NRC 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, at 67 FR 20330 (April 24, 2002).

At its meeting in October 2005, the ACMUI offered an additional recommendation and a suggestion on the issue of improving public understanding of the risks associated with MEs. The NRC staff generally supports the ACMUI recommendation not to disclose/release event information to the public until the event has been confirmed to be a reportable ME, but with one modification. Specifically, in the interest of openness and timeliness, the NRC has determined that information should be provided to the public about events reported as MEs when the events have been confirmed to be MEs or after five calendar days have passed, even if the events have not yet been confirmed as MEs. The staff also endorses and has implemented the intent of the ACMUI suggestion to footnote each Event Summary released to the public as a reportable ME to indicate that the thresholds in NRC's ME criteria, if exceeded, are not necessarily indicative of patient harm.

In summary:

1. NRC's ME criteria provide thresholds for identifying events indicative of technical or QA problems in accurately achieving the clinical intentions (prescriptions) of AUs;
2. Thresholds in NRC's ME criteria, if exceeded, are not necessarily indicative of patient harm.

---

[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.

This summary has been incorporated into an NRC fact sheet, available on the NRC public web site, located at http://www.nrc.gov/reading-rm/doc-collections/fact-sheets/risks-assoc-medical-events.html.

BACKFIT DISCUSSION

This RIS requires no action or written response. Any action on the part of addressees in accordance with the guidance contained in this RIS is strictly voluntary and, therefore, is not a backfit under any regulatory requirement in Title 10, Code of Federal Regulations. Consequently, the staff did not perform a backfit analysis.

FEDERAL REGISTER NOTIFICATION

A notice of opportunity for public comment on this RIS was not published in the *Federal Register* because this RIS is informational and does not represent a departure from current regulatory requirements.

PAPERWORK REDUCTION ACT STATEMENT

This Regulatory Issue Summary contains information collection requirements that are subject to the Paperwork Reduction Act of 1995 (44 U.S.C. 3501 et seq.). These information collections were approved by the Office of Management and Budget, approval number; 3150-0010.

Public Protection Notification

The NRC may not conduct or sponsor, and a person is not required to respond to, a request for information or an information collection requirement unless the requesting document displays a currently valid OMB control number

CONGRESSIONAL REVIEW ACT

This RIS is not a rule as designated by the Congressional Review Act (5 U.S.C. §§ 801-886) and, therefore, is not subject to the Act.

CONTACT

This RIS requires no specific action or written response. If you have any questions about this summary, please contact the individual listed below or the appropriate regional office.

/RA/

Janet R. Schlueter, Director
Division of Materials Safety
and State Agreements
Office of Federal and State Materials
and Environmental Management Programs

Technical Contact: Ronald Zelac, FSME
(301) 415-7635
E-mail: rez@nrc.gov

Enclosure: List of Recently Issued NMSS/FSME
Generic Communications

CONTACT

This RIS requires no specific action or written response. If you have any questions about this summary, please contact one of the individuals listed below or the appropriate regional office.

/RA/

Janet R. Schlueter, Director
Division of Materials Safety
and State Agreements
Office of Federal and State Materials
and Environmental Management Programs

Technical Contact: Ronald Zelac, FSME
(301) 415-7635
E-mail: rez@nrc.gov

Enclosure: List of FSME/NMSS
Generic Communications (2007)

OFFICE	MSSA/MSEA	Tech. Editor	DMSSA/MSEA	DMSSA/MSEA	DMSSA/MSEA
NAME	RZelac	QTE via email	CFlannery	AMcIntosh	SWastler
DATE	11/6/07	11/08/07	11/16/07	11/08/07	/ /07

OFFICE	OIS	OGC - NLO	OGC - CRA	DMSSA	DMSSA
NAME	TDonnell	FCameron	TRothschild	RLewis	JSchlueter
DATE	5/17/07	10/09/07	10/18/07	12/5/07	12/5/07

OFFICIAL RECORD COPY

List of Issued FSME/NMSS Generic Communications (2007)			
Date	GC No.	Subject	Addressees
02/02/07	IN-07-03	Reportable Medical Events Involving Patients Receiving Dosages of Sodium Iodide Iodine-131 less than the Prescribed Dosage Because of Capsules Remaining in Vials after Administration	All U.S. Nuclear Regulatory Commission medical use licensees and NRC Master Materials Licensees. All Agreement State Radiation Control Program Directors and State Liaison Officers.
02/28/07	IN-07-08	Potential Vulnerabilities of Time-reliant Computer-based Systems Due to Change in Daylight Saving Time Dates	All U. S. Nuclear Regulatory Commission licensees and all Agreement State Radiation Control Program Directors and State Liaison Officers.
03/13/07	IN-07-10	Yttrium-90 Theraspheres® and Sirspheres® Impurities	All U.S. Nuclear Regulatory Commission (NRC) Medical Licensees and NRC Master Materials Licensees. All Agreement State Radiation Control Program Directors and State Liaison Officers.
04/04/07	IN-07-13	Use of As-Found Conditions to Evaluate Criticality-related Process Upsets at Fuel Cycle Facilities	All licensees authorized to possess a critical mass of special nuclear material.
05/02/07	IN-07-16	Common Violations of the Increased Controls Requirements and Related Guidance Documents	All licensees who are implementing the U.S. Nuclear Regulatory Commission (NRC) Order Imposing Increased Controls (EA-05-090), issued November 14, 2005 and December 22, 2005.
05/21/07	IN-07-19	Fire Protection Equipment Recalls and Counterfeit Notices	All holders of operating licenses for nuclear power reactors and fuel cycle facilities; except those licensees for reactors that have permanently ceased operations and who have certified that fuel has been permanently removed from the reactor vessel; and except those licensees for decommissioned fuel cycle facilities.
06/11/07	IN-07-20	Use of Blank Ammunition	All power reactors, Category I fuel cycle facilities, independent spent fuel storage installations, conversion facility, and gaseous diffusion plants.

Date	GC No.	Subject	Addressees
07/19/07	IN-07-25	Suggestions from the Advisory Committee on the Medical Use of Isotopes For Consideration to Improve Compliance With Sodium Iodide I-131 Written Directive Requirements in 10 CFR 35.40 and Supervision Requirements in 10 CFR 35.27	All U.S. Nuclear Regulatory Commission (NRC) medical-use licensees and NRC Master Materials Licensees. All Agreement State Radiation Control Program Directors and State Liaison Officers.
08/08/07	IN-07-23	Inadvertent Discharge of Halon 1301Fire-suppression System from Incorrect and/or Out-of-date Procedures	All holders of operating licenses for nuclear power reactors, except those who have permanently ended operations and have certified that fuel has been permanently removed from the reactor vessel. All holders of licenses for fuel cycle facilities.
08/13/07	IN-07-26	Combustibility of Epoxy Floor Coatings at Commercial Nuclear Power Plants	All holders of operating licenses for nuclear power reactors and fuel cycle facilities except licensees for reactors that have permanently ceased operations and who have certified that fuel has been permanently removed from the reactor vessel.
09/13/07	IN-07-30	Radiological Controls Create Criticality Safety Accident Scenario for Fissile Solution Container Transport at Fuel Cycle Facility	All licensees authorized to possess a critical mass of special nuclear material.
09/28/07	IN-07-33	Exposures To Members Of The Public Caused By Inadequate Controls Over Well Logging Sources	All U.S. Nuclear Regulatory Commission Well Logging Licensees, All Agreement State Radiation Control Program Directors and State Liaison Officers.
10/15/07	IN-07-32	Out-of-Service Equipment Connected to In-service Process Line Results in Fissile Solution Spill at Fuel Cycle Facility	All licensees authorized to possess a critical mass of special nuclear material
10/17/07	IN-07-35	Varian Medical Systems Varisource HDR Events: Iridium-192 Source Pulled From Shielded Position	All U.S. Nuclear Regulatory Commission medical use licensees and NRC Master Materials Licensees authorized to possess or use a Varian Medical Systems VariSource High Dose Rate Remote Afterloader (VariSource HDR). All Agreement State Radiation Control Program Directors and State Liaison Officers.
03/01/07	RIS-07-03	Ionizing Radiation Warning Symbol	All U.S. Nuclear Regulatory Commission licensees and certificate holders. All Radiation Control Program Directors and State Liaison Officers.

Date	GC No.	Subject	Addressees
03/09/07	RIS-07-04	Personally Identifiable Information Submitted to the U.S. Nuclear Regulatory Commission	All holders of operating licenses for nuclear power reactors and holders of and applicants for certificates for reactor designs. All licensees, certificate holders, applicants, and other entities subject to regulation by the U.S. Nuclear Regulatory Commission of the use of source, byproduct, and special nuclear material.
03/20/07	RIS-07-05	Status and Plans for Implementation of NRC Regulatory Authority for Certain Naturally-occurring and Accelerator-produced Radioactive Material	All NRC materials licensees, Radiation Control Program Directors, State Liaison Officers, and NRC's Advisory Committee on the Medical Uses of Isotopes.
04/05/07	RIS-07-07	Clarification of Increased Controls for Licensees That Possess Collocated Radioactive Material During Transportation Activities	All U.S. Nuclear Regulatory Commission licensees issued NRC's Order Imposing Increased Controls and all Radiation Control Program Directors and State Liaison Officers
05/04/07	RIS-07-09	Examples of Recurring Requests for Additional Information (RAIs) for 10 CFR Part 71 and 72 Applications	All holders of, and applicants for, a: (1) 10 CFR Part 71 certificate of compliance (CoC) for a radioactive material transportation package; (2) 10 CFR Part 72 CoC for a spent fuel storage cask; and (3) 10 CFR Part 72 specific license for an independent spent fuel storage installation (ISFSI).
06/27/07	RIS-06-27, Suppl. 1	Availability of NRC 313A Series of Forms and Guidance for Their Completion	All U.S. Nuclear Regulatory Commission medical-use licensees and NRC Master Materials licensees. All Radiation Control Program Directors and State Liaison Officers.
05/15/07	RIS-07-10	Subscriptions To New List Server For Automatic Notifications Of Medical-Related Generic Communications, Federal Register Notices And Newsletters	All U.S. Nuclear Regulatory Commission medical-use licensees and NRC Master Materials licensees. All Radiation Control Program Directors and State Liaison Officers.

Date	GC No.	Subject	Addressees
08/31/07	RIS-07-13	Verification of the Authenticity of Materials Possession Licenses	All U.S. Nuclear Regulatory Commission materials licensees. All Agreement State Radiation Control Program Directors and State Liaison Officers.
09/07/07	RIS-07-18	Data for Updating the Interim Inventory of Radioactive Sources	All U.S. Nuclear Regulatory Commission (NRC) Part 40, Part 50, Part 70, Part 72, and Part 76 licensees and certificate holders who are authorized to possess sources of radioactive material at the Category "3.5" activity or higher.
10/04/07	RIS-07-22	Status Update For Implementation Of NRC Regulatory Authority for Certain Naturally-Occurring and Accelerator-Produced Radioactive Material	All U.S. Nuclear Regulatory Commission materials licensees, radiation control program directors, State liaison officers, and the NRC's Advisory Committee on the Medical Uses of Isotopes.
10/04/07	RIS-07-23	Date For Operation Of National Source Tracking System	All licensees authorized to possess Category 1 or Category 2 quantities of radioactive materials. All Radiation Control Program Directors and State Liaison Officers.