



**UNITED STATES
NUCLEAR REGULATORY COMMISSION**

REGION III
2443 WARRENVILLE ROAD, SUITE 210
LISLE, IL 60532-4352

October 28, 2011

EA 11-228
NMED 110133 (closed)

Mr. Steven Benedict, Director
Occupational Safety & Environmental Health
Regents of the University of Michigan
1239 Kipke Drive
Ann Arbor, Michigan 48109

**SUBJECT: NRC REACTIVE INSPECTION REPORT NO. 03001988/201101(DNMS) –
REGENTS OF THE UNIVERSITY OF MICHIGAN**

Dear Mr. Benedict:

On March 15-16, 2011, with continued U.S. Nuclear Regulatory Commission (NRC) in-office review through October 6, 2011, an NRC inspector conducted a reactive inspection at the University of Michigan in Ann Arbor, Michigan. The in-office review was to review your written procedures concerning the administration of licensed material to patients and receipt and review of the NRC medical consultant's report. The purpose of the inspection was to review the circumstances, root and contributing causes, and proposed corrective actions for a medical event that occurred on March 9, 2011. The enclosed report presents the results of the inspection.

Based on the results of the inspection, one apparent violation was identified and is being considered for escalated enforcement action in accordance with the NRC Enforcement Policy. The current Enforcement Policy is included on the NRC's Website at (<http://www.nrc.gov/about-nrc/regulatory/enforcement/enforce-pol.html>). The apparent violation concerns the failure to develop adequate written procedures to provide high confidence that each Yttrium-90 TheraSpheres administration was in accordance with the written directive as required by Title 10 of the Code of Federal Regulation (CFR) 35.41.

The circumstances surrounding the apparent violation, the significance of the issues, and the need for lasting and effective corrective action were discussed with selected members of your staff at a preliminary exit meeting on March 16, 2011, and at a final telephonic exit meeting on October 6, 2011. As a result, it may not be necessary to conduct a Predecisional Enforcement Conference (PEC) in order to enable the NRC to make an enforcement decision.

Before the NRC makes its enforcement decision, we are providing you an opportunity to either: (1) respond to the apparent violation addressed in this inspection report within 30 days of the date of this letter; or (2) request a PEC. If a PEC is held, it will be open for public observation and the NRC will also issue a press release to announce the conference. A PEC should be held within 30 days of the date of this letter.

The NRC has concluded that information regarding the reason for the violation and the corrective actions taken and planned to correct the violation and prevent recurrence is already adequately addressed on the docket in your 15-day report dated March 21, 2011. In addition, since your facility has not been the subject of escalated enforcement actions within the last two inspections, and based on our understanding of your corrective actions as documented above, a civil penalty may not be warranted in accordance with Section 2.3.4 of the Enforcement Policy. Therefore, you are not required to either respond in writing or to attend a PEC unless the description herein does not accurately reflect your corrective actions or your position. However, please contact Tamara E. Bloomer at 630-829-9627 within ten days of the date of this letter to notify the NRC as to whether you plan to provide no further response, provide a written response, or request a PEC.

If you choose to provide a written response, it should be clearly marked as a "Response to an Apparent Violation in Inspection Report No. 03001988/2011001(DNMS); EA-11-228" and should include for each apparent violation: (1) the reason for the apparent violation, or, if contested, the basis for disputing the apparent violation; (2) the corrective steps that have been taken and the results achieved; (3) the corrective steps that will be taken to avoid further violations; and (4) the date when full compliance will be achieved. Your response may reference or include previously docketed correspondence, if the correspondence adequately addresses the required response. If an adequate response is not received within the time specified or the NRC has not granted an extension of time, the NRC will proceed with its enforcement decision or schedule a PEC.

If you choose to request a PEC, the conference will afford you the opportunity to provide your perspective on the apparent violation and any other information that you believe the NRC should take into consideration before making an enforcement decision. The topics discussed during the conference may include: information to determine whether a violation occurred, information to determine the significance of a violation, information related to the identification of a violation, and information related to any corrective actions taken or planned to be taken.

In presenting your corrective actions, you should be aware that the promptness and comprehensiveness of your actions will be considered in assessing any civil penalty for the apparent violation. In addition, please be advised that the number and characterization of any apparent violations may change as a result of further NRC review. You will be advised by separate correspondence of the results of our deliberations on this matter.

In accordance with 10 CFR 2.390 of the NRC's "Rules of Practice," a copy of this letter and its enclosures will be available electronically for public inspection in the NRC Public Document Room or the NRC's Agencywide Documents Access and Management System (ADAMS). ADAMS is accessible from the NRC Website at <http://www.nrc.gov/reading-rm/adams.html>.

S. Benedict

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To the extent possible, your response should not include any personal privacy, proprietary, or safeguards information so that it can be made available to the Public without redaction.

Sincerely,

/RA/

Anne T. Boland, Director
Division of Nuclear Materials Safety

Docket No. 030-01988
License No. 21-00215-04

Enclosure:
Inspection Report No. 03001988/201101(DNMS)

cc w/encl: Mark L. Driscoll, Radiation Safety Officer
Jean M. Moran, Ph.D. Associate Division
Director of Clinical Physics Assistant Professor of Radiation Oncology
Department of Radiation Oncology
State of Michigan

S. Benedict

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Sincerely,

/RA/

Anne T. Boland, Director
Division of Nuclear Materials Safety

Docket No. 030-01988
License No. 21-00215-04

Enclosure:
Inspection Report No. 03001988/201101(DNMS)

cc w/encl: Mark L. Driscoll, Radiation Safety Officer
Jean M. Moran, Ph.D. Associate Division Director of Clinical Physics Assistant
Professor of Radiation Oncology Department of Radiation Oncology
State of Michigan

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U.S. NUCLEAR REGULATORY COMMISSION

REGION III

Docket No.: 030-01988

License No.: 21-00215-04

Report No.: 03001988/2011001(DNMS)

EA No.: 11-228

Licensee: Regents of the University of Michigan

Location: 1239 Kipke Drive
Ann Arbor, Michigan

Date of Inspection: March 15-16, 2011, with continued
in-office review through October 6, 2011

Preliminary Site
Exit Meeting: March 16, 2011

Final Exit Meeting: October 6, 2011

Inspector: Michael M. LaFranzo, Senior Health Physicist

Reviewed By: Tamara E. Bloomer, Chief
Materials Inspection Branch
Division of Nuclear Materials Safety

Enclosure

EXECUTIVE SUMMARY

**Regents of the University of Michigan
Ann Arbor, Michigan
Inspection Report No. 03001988/2011001(DNMS)**

The U.S. Nuclear Regulatory Commission (NRC) conducted a reactive inspection on March 15 through 16, 2011, to review the circumstances, root and contributing causes, and corrective actions associated with a medical event that University of Michigan (the licensee) reported to the NRC on March 10, 2011. The medical event involved a single patient undergoing Yttrium-90 (Y-90) TheraSphere therapy for treatment of the left lobe of the patient's liver. The patient was prescribed a treatment dose of 74.4 Gray (Gy) to the left lobe of the liver using 60.5 millicuries of Y-90 TheraSpheres. The dose to the patient's liver was determined to be approximately 159.4 Gy or 114 percent above the prescribed dose. The licensee determined that no Y-90 TheraSpheres were administered outside of the treatment site. The licensee identified the medical event during post-analysis of the treatment.

The root cause of the medical event was due to miscommunication between the medical physicist, authorized user and interventional radiologist. Contributing factors for the medical event were unclear written instructions to the medical physicist regarding treatment site and the use of documentation that made various aspects of the administration confusing.

The licensee did not anticipate any long-term medical effects on the patient as a result of the medical event. No additional treatment is planned for the patient. The NRC contracted a medical consultant to review the medical event and determine if any adverse health consequences to the patient are expected. The medical consultant determined that there should be no effects of the additional dose on the patient.

The inspector identified an apparent violation of NRC requirements involving a failure to develop, implement, and maintain written procedures to provide high confidence that each administration is in accordance with the written directive for Y-90 TheraSpheres administrations as required by Title 10 of the Code of Federal Regulations (CFR) 35.41(a) and (b)(2). To reduce the likelihood of recurrence of a similar event, the licensee initiated several immediate and long-term corrective actions. A summary of the licensee's corrective actions included:

- a. The radiation oncology department modified the Interventional Radiology (IR) worksheet to clearly designate the necessary diagnostic, pathological, and anatomical information needed to prepare for such a treatment and to require signature by the interventional radiologist.
- b. A revised IR worksheet now also includes a separate section which the radiation oncologist must also complete and sign and a separate worksheet must be completed and submitted to the medical physicist for each infusion treatment.
- c. The written directive form for Y-90 TheraSpheres has been modified to require entry of the specific treatment site in terms of right lobe, left lobe or whole liver to be consistent with the modified IR worksheet.

- d. The prescribing physician and a second medical physicist will be required to complete and sign a separate Y-90 TheraSpheres Infusion Checklist when reviewing the draft written directive.
- e. The Operating Room checklist has been modified to include confirmation immediately before the procedure that the treatment infusion site and associated volume described in the written directive are correct.

Report Details

1 Program Scope and Inspection History

This licensee was a broad-scope license authorized for medical and research activities. The licensee was authorized by NRC License No. 21-00215-04 to use a variety of byproduct materials for diagnostic and therapeutic nuclear medicine, including Y-90 TheraSpheres brachytherapy administrations. The licensee averages 10-12 patients/year using brachytherapy Y-90 TheraSpheres therapy.

A routine safety and security inspection was conducted August 23-27, 2010 with continuing NRC review through October 12, 2010; one Severity Level IV violation of NRC requirements occurred concerning security.

A reactive safety inspection was conducted on October 29, 2009 concerning a medical event which occurred on October 14, 2009; one Severity Level IV violation of NRC requirements was identified concerning 10 CFR 35.41(a) – Failure to develop, implement and maintain written procedures, concerning an administration of 180.5 millicuries of I-131, to provide high confidence that the administration was in accordance with the written directive.

A routine safety and security inspection was conducted March 10-13, 2008; no violations of NRC requirements were identified.

2 Sequence of Events and Licensee Investigation

2.1 Inspection Scope

The inspector reviewed the sequence of events that resulted in the medical event and the licensee's investigation report. In addition, the inspector toured the facility, interviewed selected staff, and reviewed patient treatment records and procedures.

2.2 Observations and Findings

On December 15, 2010, the licensee performed an infusion of Y-90 TheraSpheres, as a brachytherapy treatment, into the right lateral lobe of an adult male patient. The administration was implemented as required and the licensee decided that a second treatment would take place in the future to administer Y-90 into the left lateral lobe.

On March 9, 2011, the licensee performed an infusion of Y-90 TheraSpheres, as a brachytherapy treatment, into the left lateral lobe of the same adult male patient. Prior to the treatment, the medical physicist used an IR Worksheet developed in December 2010, and email correspondence from the authorized user, to determine the treatment location and volume size that corresponds with the dose to be delivered to the patient. The December 2010 IR Worksheet, documented the left lateral lobe of the liver to be 411.12 cc and the right lobe and left medial segment of the liver to be 1333.64 cc.

The documents used by the medical physicist to determine the treatment site and target volume were confusing relative to which volume was to be used for this procedure. As a result, the medical physicist used the target volume from the December 15, 2010, administration, to determine the target volume (1333.64 cc), which was incorrect. This resulted in a proposed dosage to the left lateral lobe approximately twice that of the written directive (the licensee determined that the left lateral lobe volume to be 637 cc at the time of the March treatment). The medical physicist prepared the written directive and ordered the Y-90 TheraSphere dose. The medical physicist explained to the inspector that this error was also the result of using documentation prepared for the treatment in December 15, 2010.

Prior to the administration on March 4, 2011, the authorized user reviewed and signed the written directive with the documented incorrect treatment site and target volume. The authorized user explained to the inspector that she did not review the entire document for accuracy but performed a cursory review for prescribed dose (which was correct) and Lung Shunt Fraction.

In discussions with the medical physicist and authorized user, it was clarified that the interventional radiologist was the individual who developed the treatment plan. The treatment plan included the size of the treatment location, which is necessary to determine the correct activity to the patient as documented in the written directive. However, the interventional radiologist did not review the written directive nor did the medical physicist or authorized user review the treatment plan prior administration which would have identified the incorrect target volume.

As a result of the authorized user not properly reviewing the treatment plan, an activity of approximately 60.5 millicuries of Y-90 TheraSpheres was delivered resulting in a dosage of approximately 159.4 Gy instead of the prescribed 74.4 Gy, more than double the intended dose.

Title 10 CFR Section 35.41(a)(2) requires, for any administration requiring a written directive, that the licensee develop, implement, and maintain written procedures to provide high confidence that each administration is in accordance with the written directive.

Title 10 CFR 35.41(b)(2) requires, in part, that, as a minimum, the procedures required by 10 CFR 35.41(a) address verifying that the administration is in accordance with the treatment plan, if applicable, and the written directive.

Based upon the information available, proper reviews by the authorized user, medical physicist and/or the interventional radiologist would have resulted in the identification of the error within the written directive. However, the licensee's written procedures did not specifically address all the reviews necessary to ensure the administration was implemented in accordance with the written directive. Therefore, the licensee's written procedures were inadequate to address the review of the written directive and the treatment plan between the medical physicist, authorized user and interventional radiologist to provide high confidence that the administration was implemented in accordance with the written directive.

The licensee's failure to have adequate procedures for the administration of Y-90 to the liver is an apparent violation of 10 CFR 35.41(a)(2) and 10 CFR 35.41(b)(2), which requires that the licensee develop, implement, and maintain written procedures to provide high confidence that each administration is in accordance with the written directive and, at a minimum, include verification that the administration is in accordance with the treatment plan, which is applicable, and the written directive.

The inspector also reviewed five other Y-90 cases performed by the licensee and did not identify any issues that would have constituted a medical event.

2.3 Conclusions

The inspector identified an apparent violation of 10 CFR 35.41(a) and 10 CFR 35.41(b)(2) concerning the licensee's failure to develop adequate procedures to provide high confidence that Y-90 TheraSphere administrations were performed in accordance with the written directive. The inspector concurred with the licensee's root cause determination. The licensee did not expect any adverse medical effects for the patient because of the medical event.

3 **Licensee Corrective Actions**

3.1 Inspection Scope

The inspector reviewed the licensee's proposed corrective actions to preclude similar events. The review included the licensee's written report dated March 21, 2011, regarding the medical event, interviews of selected licensee personnel, and the licensee's revised policies and procedures.

3.2 Observations and Findings

The inspector determined that the licensee initiated several immediate and long-term corrective actions to prevent recurrence of a similar medical event. The corrective actions, documented in the licensee's policies and procedures, included, but not limited to:

- a. The radiation oncology department modified the Interventional Radiology (IR) worksheet to clearly designate the necessary diagnostic, pathological, and anatomical information needed to prepare for such a treatment and to require signature by the interventional radiologist. For purposes of measuring volume, the form now clearly designates liver segments right lobe, left lobe and total liver volume. This consistency will be carried over into a modified written directive.
- b. The revised IR worksheet now also includes a separate section which the radiation oncologist must also complete and sign. The radiation oncologist must specify, in writing, the specific treatment site and the exact segment volume to use. In addition, the oncologist will include the date and time of the planned infusion. A separate worksheet must be completed and submitted to the medical physicist for each infusion treatment planned-even if the medical data supplied by the radiologist will remain unchanged for purposes of preparing a draft written directive.

- c. The written directive form for I-90 TheraSpheres has been modified to require entry of the specific treatment site in terms of right lobe, left lobe or whole liver to be consistent with the modified IR worksheet.
- d. The prescribing physician and a second medical physicist will be required to complete and sign a separate TheraSphere Infusion Checklist when reviewing the draft written directive. This checklist requires both individuals to confirm that the treatment site and the treatment volume identified in the written directive are consistent with the information supplied in the IR worksheet.
- e. The Operating Room checklist has been modified to include confirmation immediately before the procedure that the treatment infusion site and associated volume described in the written directive are correct.

3.3 Conclusions

The inspector determined that the licensee developed corrective actions to address the violation and prevent similar medical events.

4 Independent Patient Dose Assessment

4.1 Inspection Scope

The NRC contracted a medical expert consultant to assess probable deterministic effects of the radiation exposure to the patient as a result of the medical event. The inspector reviewed the Medical Consultant's report dated September 1, 2011.

4.2 Observations and Findings

The medical expert consultant noted that the patient has received two treatments to his/her liver. The first treatment was to the right lobe, as prescribed, and the second treatment to the left lobe that reflected the incident as an overdose relative to the written directive.

The medical expert consultant stated that based upon clinical, peer reviewed and published studies, the delivered overdose of approximately 155 Gy is not considered high relative to toxicity and untoward potential events. Doses delivered using the same type of delivery system, which were noted as high as 521 Gy, have been administered to the liver without adversity.

4.3 Conclusions

The medical expert consultant determined the patient should not have any effects of the additional dose as a result of the medical event.

5 Notifications and Reports

5.1 Inspection Scope

The inspector interviewed selected licensee staff and reviewed the licensee's notification to the NRC Operations Center and the associated 15-day written report to ensure compliance with NRC reporting requirements.

5.2 Observations and Findings

On March 9, 2011, the licensee determined that the administered dose to the patient's left lateral lobe of the liver was in excess of 100% of the prescribed dose for a Y-90 TheraSphere administration. This case is considered a medical event because the left lateral lobe of the liver received a dose that differed from the prescribed dose by more than 0.50 Sv and the total dose delivered differed from the prescribed dose by more than 20%. As part of the licensee's 15 day report, the licensee determined that the dose administered to the left lateral lobe of the liver was approximately 159.6 Gy and the prescribed dose was 74.4 Gy. Title 10 CFR 35.3045(a)(ii) requires a licensee to report any medical event where the dose received differs from the prescribed dose by more than 0.5 Sv (50 rem) to an organ and the total dosage delivered differs from the prescribed dosage by 20% or more. Title 10 CFR 35.3045(c) requires a licensee to notify the NRC Operations Center no later than the next calendar day after discovery of the medical event. The licensee's Radiation Safety Officer notified the NRC Operations Center of the event on March 10, 2011, (EN No. 46665). The patient and the referring physician for the medical event were notified on March 9, 2011, in accordance with 10 CFR 35.3045(e). The licensee's 15-day report, dated March 21, 2011 contained the information required by 10 CFR 35.3047(d).

5.3 Conclusions

The licensee made all of the notifications and submitted the reports required by 10 CFR 35.3045 within the specified time period. The inspector determined that the licensee included all of the required information.

6 Exit Meeting

On March 16, 2011, at the completion of the onsite inspection, the inspector discussed the findings in this report with licensee management. The inspector held a final exit meeting by telephone on October 6, 2011, where the inspector discussed the sequence of events that led to the medical event, the root and contributing causes of the event, and the licensee's corrective actions. The licensee did not identify any information reviewed during the inspection and proposed for inclusion in this report as proprietary in nature.

PARTIAL LIST OF PERSONS CONTACTED

- * Ian Stienman – Associate Director/Fire Marshal
 - * Mark Discoll – Radiation Safety Officer
 - * Dennin Palmieni – Senior Health Physicist
 - * Neil Whiteside – Health Physicist
 - * Joann Prisciandaro – Medical Physicist
 - * Jean M. Moran, Ph.D., Associate Division Director of Clinical Physics,
Assistant Professor of Radiation Oncology, Department of Radiation Oncology
 - * Russell S. Garcia – Health Physicist
 - * Stan Uitti – Health Physicist
 - * Joe Miklos – Coordinator, Senior Health Physicist
- * Attended the March 15 and 16, 2011, preliminary entrance/exit meeting