June 12, 2009

NMED No. 090481

Marcia Gonzales, J.D.
Executive Director Research Compliance
IUPUI /Indiana University Medical Center
Office of Research Administration
620 Union Drive, Suite 104
Indianapolis, IN 46202

SUBJECT: NRC REACTIVE INSPECTION REPORT NO. 03001609/2009-03(DNMS) - IUPUI/INDIANA UNIVERSITY MEDICAL CENTER

Dear Ms. Gonzales:

This refers to the reactive inspection conducted on May 14, 2009, in response to a medical event involving an underdose from a TheraSphere® therapy treatment with yttrium-90 microspheres that occurred on April 29, 2009, at IUPUI/Indiana University Medical Center. The purpose of the inspection was to review the circumstances, causes, and corrective actions related to this event. At the conclusion of the on-site inspection, the inspection findings were discussed with selected members of your staff. The enclosed report presents the results of this inspection.

The inspection report identifies areas examined during the inspection. Within these areas, the inspection consisted of a selective examination of procedures and representative records, observations, and interviews with personnel. Based upon the inspection, no violations of NRC regulatory requirements were identified.

In accordance with 10 CFR 2.390 of the NRC's "Rules of Practice," a copy of this letter and its enclosures will be made available electronically for public inspection in the NRC Public Document Room or from the NRC's document system (ADAMS), accessible from the NRC Web site at http://www.nrc.gov/reading-rm/adams.html.

We will gladly discuss any questions you have concerning this inspection.

Sincerely,

/RA/

Kenneth J. Lambert, Acting Chief
Materials Inspection Branch

Docket No. 030-01609
License No. 13-02752-03

Enclosure:
Inspection Report No. 03001609/2009-03(DNMS)

cc w/encl: Mack Richard, MS, Radiation Safety Officer

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cc w/encl: Mack Richard, MS, Radiation Safety Officer

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REGION III

Docket No.:	030-01609
License No.:	13-02752-03
Report No.:	03001609/2009-03(DNMS)
Licensee:	IUPUI/Indiana University Medical Center
Location:	Indianapolis, Indiana
Date:	May 14, 2009
Inspector:	Robert P. Hays, Health Physicist
Approved by:	Kenneth J. Lambert, Acting Chief Materials Inspection Branch Division of Nuclear Materials Safety

NMED No. 090481
Enclosure

EXECUTIVE SUMMARY

IUPUI/Indiana University Medical Center
Indianapolis, Indiana
NRC Inspection Report 03001609/2009-03(DNMS)

This was a reactive, announced inspection to review the circumstances, causes, and licensee corrective actions associated with a reported medical event that occurred at IUPUI/Indiana University Medical Center on April 29, 2009, and was reported to the NRC by the licensee on April 30, 2009. The reported medical event involved a 26.4 percent underdose to the patient utilizing TheraSphere® yttrium-90 microspheres. The typical dose range for a TheraSphere® procedure is 80 to 120 Gray (Gy). Although the patient was administered 26.4 percent less than the prescribed dosage, the calculated dose the patient actually received was 86.6 Gy, which is within the desired range. The licensee did not anticipate any negative effects to the patient as a result of the reported medical event.

The root cause of the medical event was a quantity of microspheres collecting and sticking to the septum of the dose vial. For each patient treatment involving micropheres, the licensee follows a written checklist that includes detailed step-by-step instructions for the procedure. The step-by-step instructions were provided by the microsphere manufacturer. Each step of the checklist to administer the microspheres was followed in the specified order. To complete the patient treatment, one of the final steps of the procedure was a direct radiation measurement of the delivery box containing the dose vial. The radiation measurement indicated that some of the microspheres remained in the dose vial. The licensee attempted to empty the dose vial by flushing the vial with sterile flushing solution. Three subsequent flushings of the dose vial did not change the radiation measurement. Post treatment calculations by the licensee as documented on the written directive, determined that 16.2 millicuries of yttrium-90 remained in the dose vial and only 43.9 millicuries of the prescribed 61.3 millicuries was actually administered to the patient.

MDS Nordion (manufacturer of the TheraSphere® device) was contacted after the procedure. A Nordion representative stated that the reason for the microspheres sticking to the dose vial septum was likely caused by the package containing the dose vial being inverted during shipment to the licensee. To prevent the recurrence of another under dosage, Nordion recommended the following enhancements to the procedure: (a) upon receipt, shake the shielded dose vial, then tap the vial on a firm surface to facilitate the movement of any microspheres that may have adhered to the dose vial septum back into the liquid suspension; (b) in addition to the agitation that may occur during the transport of the dosage from nuclear medicine to the treatment room, gently rock the dose vial back and forth prior to placement in the delivery box; and (c) after flushing the delivery system and a direct radiation measurement indicates microspheres still remain in the delivery box, open the delivery box and gently agitate the shielded dose vial using a side-to-side motion and tap the vial on the cart, again, to facilitate the movement of any microspheres that may have adhered to the dose vial septum back into the liquid suspension and flush again.

To avoid a similar event in the future, the licensee revised its TheraSphere® administration procedures to include the additional steps recommended by Nordion.

Report Details

1 Program Scope and Inspection History

IUPUI/Indiana University Medical Center (licensee), a medical broadscope licensee, is authorized by Nuclear Regulatory Commission (NRC) License No. 13-02752-03 to use a variety of byproduct materials for medical diagnosis, therapy, and research in humans. The licensee routinely performs therapeutic treatments for liver carcinoma using the MDS Nordion TheraSphere® device which contains insoluble glass microspheres where the isotope, yttrium-90 is an integral constituent of the glass. Yttrium-90 is a high energy beta emitter with a radioactive half-life of 64 hours. The microspheres are supplied in 0.6 milliliters of sterile water contained in a 1.0 millliter vee-bottom dose vial secured within a clear acrylic vial shield. The microspheres are delivered to the treatment site in the patient via infusion through a catheter. The licensee administers an average of 1-2 TheraSphere® treatments per month.

A decommissioning inspection conducted on June 1, 2007, identified one Severity Level IV violation. The last routine inspection was on April 20 through 24, 2009, which identified one Severity Level IV violation involving two examples of the licensee transporting nitrogen-13 without a shipping paper. The inspection included observation of a TheraSphere® procedure and no concerns or issues were identified with the procedure.

2 Sequence of Events

2.1. Inspection Scope

The inspector interviewed the authorized user physician (AU) and the Radiation Safety Officer (RSO), involved with the administration of the yttrium-90 microspheres. In addition, the inspector reviewed records, a selective number of procedures, and compliance with regulatory requirements relevant to the administration of the yttrium-90 microspheres.

2.2. Observations and Findings

A patient diagnosed with liver cancer was undergoing a TheraSphere® infusion procedure at the licensee's hospital on April 29, 2009. For each TheraSphere® procedure, the licensee's staff follows a written TheraSphere® checklist that includes detailed step-by-step instructions, as provided by Nordion, for the procedure to ensure that the infusion of yttrium-90 microspheres is in accordance with the authorized user's written directive. Each step of the checklist to administer the microspheres was followed in the specified order. To complete the patient treatment, one of the final steps of the procedure was a direct radiation measurement of the delivery box containing the shielded dose vial to verify that all of the microspheres were infused into the patient. The direct radiation measurement result was greater than expected which indicated that microspheres remained in the dose vial. Per procedure, the licensee attempted to clear the microspheres from the dose vial by flushing the vial with sterile flushing solution. Three subsequent flushings of the dose vial did not change the radiation measurement. The licensee completed the remaining steps of the procedure and initiated an

investigation to determine why the microspheres remained in the dose vial after the flushings. The Radiation Safety Office staff attempted to perform some radiation measurements of the delivery system to determine location of the remaining microspheres. However, due to the relatively high radiation exposure rates from the residual microspheres and the potential for contamination, a more thorough review of the delivery system could not be performed until the yttrium-90 exposure rates had been reduced by radioactive decay.

2.3. Conclusions

The inspector concluded that the licensee had followed precisely each step of the TheraSphere® checklist. The licensee did not deviate from the standard procedures nor experience anything unusual until the flushings did not reduce the radiation measurements.

3 Licensee Investigation and Corrective Actions

3.1 Inspection Scope

The inspector reviewed the licensee's investigation of the event, including a root cause assessment. The inspector also interviewed the RSO and the AU. In addition, the inspector reviewed written procedures and medical records associated with the treatment.

3.2 Observations and Findings

After the licensee had completed the procedure, follow up radiation measurements and calculations by the licensee as documented on the written directive, determined that 16.2 millicuries of yttrium-90 remained in the dose vial and only 43.9 millicuries of the prescribed 61.3 millicuries in the written directive was actually administered to the patient.

The licensee estimated that the patient received 26.4 percent less than what was prescribed in the written directive. Although the patient was administered 26.4 percent less than the prescribed dosage, the calculated dose the patient actually received was 86.6 Gy, which is within the desired treatment range. The licensee did not anticipate any negative effects to the patient as a result of the reported medical event.

The licensee contacted a technical adviser at MDS Nordion, (manufacturer of the TheraSphere® device) to notify MDS Nordion of the event and obtain information as what may have been the cause. According to the Nordion technical adviser, the remaining microspheres had adhered to the dose vial septum which was likely caused by the package containing the dose vial being inverted during shipment to the licensee.

To ensure that the microspheres not stuck to the dose vial septum, the Nordion technical adviser recommended adding, as enhancements, three additional steps to the licensee's TheraSphere® procedures: (a) upon receipt of each shipment, shake the shielded dose vial, then tap the vial on a firm surface to facilitate the movement of any microspheres that may have adhered to the dose vial septum back into the liquid suspension; (b) in addition to the agitation that may occur during the transport of the dose vial from nuclear medicine to the treatment room, gently rock the dose vial back and forth prior to

placement in the delivery box; and (c) after flushing the delivery system and a direct radiation measurement indicates microspheres still remain in the delivery box, open the delivery box and gently agitate the shielded dose vial using a side-to-side motion and tap the vial on the cart, once again, to facilitate the movement of any microspheres that may have adhered to the dose vial septum back into the liquid suspension and flush again.

To avoid a similar event in the future, the licensee revised its TheraSphere® Checklist procedures to include the additional steps recommended by Nordion.

3.3 Conclusions

The inspector determined that the licensee conducted a thorough investigation of the event, including root cause determination. The root cause was attributed to the dose vial being inverted during shipment to the licensee causing the microspheres to collect and stick to the dose vial septum. The licensee modified its procedures to ensure that each infusion of yttrium-90 microspheres was in accordance with the written directive as required by 10 CFR 35.41(a)(2). The inspector agreed with the licensee's root cause determination.

4 Notifications and Reports

4.1 Inspection Scope

The inspector interviewed the RSO, AU, and selected radiation safety staff to determine what event notifications and reports had been made.

4.2 Observations and Findings

On April 29, 2009, the licensee determined that the patient had received 26.4 percent less than the prescribed dosage of yttrium-90 microspheres specified in the written directive. 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 50 rem to an organ and the total dosage delivered differs from the prescribed dosage by 20 percent or more. 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 RSO notified the NRC Operations Center of the event at 14:51 EDT on April 30, 2009. The patient's spouse and the referring physician were notified of the event on April 29, 2009, by the AU in accordance with 10 CFR 35.3045(e). The licensee's 15-day report, dated May 11, 2009, contained the information required by 10 CFR 35.3047(d).

4.3 Conclusions

The inspector determined that the licensee made the required event notification and report to the NRC. The telephonic notification to the NRC was made the next calendar day after discovery of the event. The licensee provided a timely 15-day report, and the report included all required information.

5 Exit Meeting Summary

The inspector discussed the conclusions described in this report with the licensee during an exit meeting conducted at the licensee's facility on May 14, 2009. The licensee did not identify any information reviewed during this inspection as proprietary in nature.

LIST OF PERSONS CONTACTED

Matthew Johnson, M.D., Authorized User Physician, Interventional Radiologist
Mack Richard, MS, Radiation Safety Officer
Jeff Mason, Assistant Radiation Safety Officer
* Marcia Gonzales, Executive Director Research Compliance

Participated in exit meeting
* Participated in telephonic exit meeting on June 9, 2009