October 16, 2007

NMED No. 070574

J. Froehlich, Ph.D.
Acting Chancellor for Research
IUPUI Research and Sponsored Programs (AO 122)
IUPUI /Indiana University Medical Center
355 Lansing Street
Indianapolis, IN 46202

SUBJECT: NRC SPECIAL INSPECTION REPORT NO. 030-01609/07-02(DNMS) - IUPUI/INDIANA UNIVERSITY MEDICAL CENTER

Dear Dr. Froehlich:

This refers to the special inspection conducted on September 19, 2007, with continued in-office review through October 11, 2007, of a medical event involving an underdose from an investigational/experimental therapy treatment with yttrium-90 microspheres (TheraSphere®) that occurred on September 10, 2007, at IUPUI/Indiana University Medical Center. The purpose of the inspection was to review the circumstances, causes, and corrective actions related to this event. The in-office review consisted of a review of the potential generic issues surrounding this medical event. At the conclusion of the on-site inspection, the preliminary 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 by Kenneth G. O'Brien acting for/

Steven A. Reynolds, Director
Division of Nuclear Materials Safety

Docket No. 030-01609
License No. 13002762-03

Enclosure:
Inspection Report No. 030-01609/07-02(DNMS)

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.:	030-01609/07-02(DNMS)
Licensee:	IUPUI/Indiana University Medical Center
Location:	Indianapolis, Indiana
Date:	September 19, 2007
Inspectors:	Darrel G. Wiedeman, Senior Health Physicist Edward Kulzer, Radiation Specialist Johari Moore, Environmental Project Manager
Approved by:	John R. Madera, Chief Materials Inspection Branch Division of Nuclear Materials Safety

NMED No. 070574

Enclosure

EXECUTIVE SUMMARY

IUPUI/Indiana University Medical Center
Indianapolis, Indiana
NRC Inspection Report 030-1609/07-02(DNMS)

This was a special, 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 September 10, 2007, and was reported to the NRC by the licensee on September 11, 2007. The reported medical event involved a 27 percent underdose to the patient utilizing yttrium-90 microspheres (TheraSphere®). The licensee did not anticipate any adverse effects to the patient as a result of the reported medical event.

The root cause of the medical event was an isolated failure of the microcatheter when a kink in the catheter occurred during the surgical procedure. During the process of administering the dosage, each step of the licensee's procedures was followed. At the end of the treatment the licensee implemented the last and final step of their procedures that included a direct radiation measurement of the dose vial, outlet line, stopcocks and waste vial. It was at this time the licensee realized that the entire dose of yttrium-90 microspheres was not completely administered. Subsequent calculations by the licensee indicated that only 47.7 millicuries of the prescribed 64.3 millicuries of yttrium-90 was actually administered.

On September 19, 2007, a representative from MDS Nordion (manufacturer of the TheraSphere® device) did an exhaustive examination of the tubing and catheters and concluded that the cause of the failure to deliver the entire dose was due to a kink in the microcatheter. According to the Nordion representative this was the first time he had seen this type of problem with the microcatheter. The Nordion representative indicated that they were considering sending an "Advisory Letter" to all of their customers to warn them of a potential problem with the microcatheter in that if excessive pressure is exerted during the insertion of the microcatheter, a kink could develop and cause the microspheres to stop flowing along the catheter.

In an attempt to avoid a similar event in the future, the licensee revised their TheraSphere® administration procedures and added an additional step that requires the physician to visually inspect the microcatheter prior to injection of the yttrium-90 to ensure that there are no obvious kinks in the microcatheter.

Report Details

1 Program Scope and Inspection History

Nuclear Regulatory Commission (NRC) License No. 13-02752-03 authorizes IUPUI/Indiana University Medical Center (licensee) to use a variety of byproduct materials for diagnostic and therapeutic medical purposes. Typically, the licensee administers approximately twelve yttrium-90 microsphere treatments (TheraSphere®) per year.

A decommissioning inspection conducted on June 1, 2007, identified one Severity Level IV violation. The last routine inspection was on October 10 through 16, 2006. No violations of NRC regulatory requirements were identified during that inspection.

2 Sequence of Events

2.1. Inspection Scope

The inspectors interviewed the physician user, the Radiation Safety Officer (RSO), and a representative from MDS Nordion (manufacturer of the TheraSphere® device) that were involved with the administration of the yttrium-90 microspheres (TheraSphere®). In addition, the inspectors 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 70 year-old male patient was diagnosed with liver cancer at the licensee's hospital and was referred to the licensee's Oncology Department for radiopharmaceutical therapy to treat any remaining cancerous liver tissue. On September 10, 2007, during the process of administering the dosage, each step of the licensee's TheraSphere® administration procedure was followed. At the end of the treatment the licensee implemented the last and final step of the procedure which included a direct radiation measurement of the dose vial, outlet line, stopcocks and waste vial. It was at this time the licensee realized that the entire dose of yttrium-90 microspheres was not completely administered. Subsequent calculations indicated that only 47.7 millicuries of the prescribed 64.3 millicuries of yttrium-90 was actually administered. According to the licensee, typically 2 to 5 percent of the microspheres will remain in the tubing and catheters; however, in this case the licensee estimated that 25.8 percent of the microspheres remained in the tubing and catheters.

On September 19, 2007, a representative from MDS Nordion did an exhaustive examination of the tubing and catheters and concluded that the cause of the failure to deliver the entire dose was due to a kink in the microcatheter. According to the Nordion representative this was the first time he had seen this type of problem with the microcatheter and indicated that the manufacturer of the microcatheter (Boston Catheter) understood that these catheters are extremely delicate and Boston Catheter is currently developing a more flexible catheter that

will be less likely to kink. The Nordion representative indicated that Nordion is considering sending an “Advisory letter” to all of their TheraSphere® customers to advise them of a potential problem with kinking of the microcatheter.

2.3. Conclusions

The inspectors concluded that the licensee took reasonable precautions during the administration of the yttrium-90 microspheres. The licensee followed their procedures and the manufacturer’s recommendations for the administration of the yttrium-90 microspheres. The inspectors concluded that the failure to deliver the entire prescribed dosage was due to an isolated failure of the microcatheter.

3 Licensee Investigation

3.1 Inspection Scope

The inspectors reviewed the licensee’s investigation of the event, including a root cause assessment. The inspectors also interviewed the RSO and the physician user. In addition, the inspectors observed the examination of the catheters and tubes associated with the TheraSphere® device and reviewed medical records associated with the treatment.

3.2 Observations and Findings

The licensee indicated that at the time of the administration of the dosage they considered the entire procedure a success until the last step of the process when they conducted a direct radiation measurement of the catheters and tubing. It was at this time they realized that the entire dosage was not completely administered. It was estimated that the patient received approximately 47.7 millicuries of the 64.3 millicuries that was prescribed by the authorized user physician. The licensee estimated that this was a 25.8 percent underdose and a reportable medical event.

Nine days after the procedure (September 19, 2007) a representative from MDS Nordion conducted an examination of the catheters and tubing and concluded that the cause of the underdose was due to a kink in the microcatheter and not a malfunction of the TheraSphere® system.

3.3 Conclusions

The inspectors determined that the licensee conducted a thorough investigation of the event, including root cause determination. The root cause was attributed to a kink in the microcatheter that was not readily visible at the time of the procedure. The inspectors agreed with the licensee’s root cause determination.

4 Notifications and Reports

4.1 Inspection Scope

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

4.2 Observations and Findings

On September 10, 2007, the licensee determined that an event requiring notification of the NRC per 10 Code of Federal Regulations (CFR) 35.3047(a) had occurred. The RSO notified the NRC Operations Center of the event at 16:03 EDT on September 11, 2007. The patient and the referring physician were notified of the event on September 10, 2007 in accordance with 10 CFR 35.3045(e). The licensee's 15-day report, dated September 24, 2007, contained the information required by 10 CFR 35.3047(d).

4.3 Conclusions

The inspectors 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 Corrective Actions

5.1 Inspection Scope

The inspectors interviewed the RSO, and selected members of the radiation safety staff, regarding any corrective actions they proposed to prevent a similar event.

5.2 Observations and Findings

The RSO stated that the root cause of the event was an isolated failure of the microcatheter when the microcatheter developed a kink. The licensee determined that the root cause was beyond their control. As a precautionary measure, the licensee revised their procedures and added an additional step that requires the physician to visually inspect the microcatheter prior to injection of the yttrium-90 to ensure that there are no obvious kinks in the microcatheter.

5.3 Conclusions

The inspectors determined that, because the root cause of the event may be beyond the control of the licensee, the licensee's decision to add an additional step to their procedure may not always identify a kink in the microcatheter and prevent a similar event.

6 Exit Meeting Summary

The inspectors discussed the conclusions described in this report with the licensee during a preliminary exit meeting conducted at the licensee's facility on September 19 , 2007. The licensee did not identify any information reviewed during this inspection as proprietary in nature.

LIST OF PERSONS CONTACTED

David Agarwal, M.D., Physician, Interventional Radiologist
Mack Richard, MS, Radiation Safety Officer
John Talbott, Interim Assistant Vice President for Research Administration
Thomas Simpson, Technical Authority, MDS Nordion Company
Jeff Mason, Assistant Radiation Safety Officer

Participated in preliminary exit meeting