



**UNITED STATES
NUCLEAR REGULATORY COMMISSION**

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

September 21, 2017

EA-17-082
NMED No. 170074 (Closed)

Mr. Bruce Backus
Assistant Vice Chancellor, Environmental
Health & Safety
Washington University in St. Louis
Campus Box 8053, 660 S. Euclid Avenue
St. Louis, MO 63110-1093

SUBJECT: NOTICE OF VIOLATION - NRC SPECIAL INSPECTION REPORT
NO. 03002271/2017001(DNMS) - WASHINGTON UNIVERSITY IN ST. LOUIS

Dear Mr. Backus:

This refers to the U.S. Nuclear Regulatory Commission (NRC) inspection conducted on February 1 and 2, 2017, at your St. Louis, Missouri campus, with continued in-office review through May 25, 2017. The purpose of this inspection was to review the circumstances, root and contributing causes, and proposed corrective actions for a medical event that occurred on April 8, 2016, where your staff had sufficient information on April 16, 2016, to discover the event and make the appropriate notification to the NRC; however the notification was not made until January 31, 2017. The significance of the issue and the need for lasting and effective corrective actions were discussed with you during the exit meeting held on May 25, 2017. Details regarding the apparent violation were provided in NRC Inspection Report No. 03002271/2017001(DNMS), dated June 21, 2017. The inspection report is available electronically in the NRC's Agencywide Documents Access and Management System (ADAMS) at Accession Number ML17173A070.

In the letter transmitting the inspection report, we provided you with the opportunity to address the apparent violation identified in the report by either attending a predecisional enforcement conference or by providing a written response before we made our final enforcement decision. In a July 20, 2017 (ML17202U846), letter you provided a response to the apparent violation. In the response, Washington University noted the corrective actions taken and requested that the NRC reduce the severity level of the violation to severity level IV. The NRC's response is provided in Enclosure 2.

Based on the information developed during the inspection and the information that you provided in your response to the inspection report, dated July 20, 2017, the NRC has determined that a violation of NRC requirements occurred. The violation is cited in the enclosed Notice of Violation (Notice) and the circumstances surrounding it are described in detail in the subject inspection report. The violation involved the failure to notify the NRC Operations Center the next calendar day after the discovery of a medical event as required by Title 10 of the *Code of Federal Regulations* (CFR) 35.3045(c). The root cause of the violation was the licensee's: (1) misunderstanding of "shunting" in context with the Microspheres Guidance; and (2) determining that the cause of the incident was unintentional patient intervention that shifted the catheter tip due to breathing, coughing, or other movement, when there was no indication of patient intervention.

The NRC considers the failure to promptly notify the NRC of a medical event to be a significant violation that affects the NRC's ability to perform its regulatory oversight function. Although there were no adverse patient consequences resulting from this failure to identify the medical event and comply with the requirements in 10 CFR 35.3045(c), there was a potential that additional medical events could go unrecognized. Therefore, this violation has been categorized in accordance with the NRC Enforcement Policy at Severity Level III. In accordance with the NRC Enforcement Policy, a base civil penalty in the amount of \$7,000 is considered for a Severity Level III violation.

Because your facility has not been the subject of escalated enforcement actions within the last two inspections, the NRC considered whether credit was warranted for *Corrective Action* in accordance with the civil penalty assessment process in Section 2.3.4 of the Enforcement Policy. Specifically, your corrective actions included: (1) reporting the medical event to the NRC and providing a written report; (2) committing to report yttrium-90 microsphere medical events as described in the NRC guidance; (3) implementing improved communications between team members if someone were to have a concern about catheter placement; (4) reminding the team about stopping the procedure and speaking up if there are any concerns; and (5) requiring that all participating team members confirm that it is okay to proceed with administering the microspheres prior to the administration. Based on these corrective actions, the NRC determined credit was warranted.

Therefore, to encourage prompt and comprehensive correction of violations, and in recognition of the absence of previous escalated enforcement action, I have been authorized, after consultation with the Director, Office of Enforcement, not to propose a civil penalty in this case. However, significant violations in the future could result in a civil penalty. In addition, issuance of this Severity Level III violation constitutes escalated enforcement action that may subject you to increased inspection effort.

The NRC has concluded that information regarding: (1) the reason for the violation; (2) the corrective actions that have been taken and the results achieved; and (3) the date when full compliance was achieved is already adequately addressed on the docket in Inspection Report No. 03002271/2017001(DNMS), and your letter, dated July 20, 2017. Therefore, you are not required to respond to this letter unless the description therein does not accurately reflect your corrective actions or your position. In that case, or if you choose to provide additional information, you should follow the instructions specified in the enclosed Notice.

In accordance with 10 CFR 2.390 of the NRC's "Rules of Practice," a copy of this letter, its enclosures, and your response, should you provide one, will be made available electronically for public inspection in the NRC Public Document Room and in the NRC's Agencywide Documents Access and Management System (ADAMS), accessible from the NRC Web site at <http://www.nrc.gov/reading-rm/adams.html>. 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. If personal privacy or proprietary information is necessary to provide an acceptable response, please provide a bracketed copy of your response that identifies the information that should be protected and a redacted copy of your response that deletes such information. If you request withholding of such information, you must specifically identify the portions of your response that you seek to have withheld and provide in detail the bases for your claim of withholding (e.g., explain why the disclosure of information will

create an unwarranted invasion of personal privacy or provide the information required by 10 CFR 2.390(b) to support a request for withholding confidential commercial or financial information). The NRC also includes significant enforcement actions on its Web site at (<http://www.nrc.gov/reading-rm/doc-collections/enforcement/actions/>).

Sincerely,

/RA by James M. Trapp acting for/

Cynthia D. Pederson
Regional Administrator

Docket No. 030-02271
License No. 24-00167-11

Enclosure:

1. Notice of Violation
2. NRC Response

cc w/encls: Susan Langhorst, Ph.D., RSO
State of Missouri

Letter to Mr. Bruce Backus from Cynthia D. Pederson dated September 21, 2017

SUBJECT: NOTICE OF VIOLATION - NRC SPECIAL INSPECTION REPORT
NO. 03002271/2017001(DNMS) - WASHINGTON UNIVERSITY IN ST. LOUIS

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NOTICE OF VIOLATION

Washington University in St. Louis
St. Louis, Missouri
EA-17-082

Docket No. 030-02271
License No. 24-00167-11

During a U.S. Nuclear Regulatory Commission (NRC) inspection conducted on February 1 and 2, 2017, with continue in-office review through May 25, 2017, a violation of NRC requirements was identified. In accordance with the NRC Enforcement Policy, the violation is listed below:

Title 10 of the *Code of Federal Regulations* (CFR) 35.3045(c) requires the licensee to notify the NRC Operations Center, by telephone, no later than the next calendar day after discovery of the medical event.

Contrary to the above, on April 16, 2016, the licensee had sufficient patient treatment data to determine that a medical event occurred and did not notify the NRC until January 31, 2017, which was later than the next calendar day. Specifically, the administration of radiation from a yttrium-90 microspheres treatment resulted in a dose that exceeded 0.5 Sv (50 rem) to tissue and 50 percent or more of the dose expected from the administration defined in the written directive to tissue other than the treatment site. This is a medical event as defined in 10 CFR 35.3045(a)(3).

This is a Severity Level III violation (Section 6.3).

The NRC has concluded that information regarding the reason for the violation, the corrective actions taken and planned to correct the violation and prevent recurrence, and the date when full compliance was achieved, is already adequately addressed on the docket in Inspection Report No. 03002271/2017001, and the license's letter, dated July 20, 2017. However, you are required to submit a written statement or explanation pursuant to 10 CFR 2.201 if the description therein does not accurately reflect your corrective actions or your position. In that case, or if you choose to respond, clearly mark your response as a "Reply to a Notice of Violation, (EA-17-082)," and send it to the U.S. Nuclear Regulatory Commission, ATTN: Document Control Desk, Washington, DC 20555-0001 with a copy to the Regional Administrator, Region III, 2443 Warrenville Road, Suite 210, Lisle, IL 60532 within 30 days of the date of the letter transmitting this Notice of Violation.

If you contest this enforcement action, you should also provide a copy of your response, with the basis for your denial, to the Director, Office of Enforcement, United States Nuclear Regulatory Commission, Washington, DC 20555-0001.

If you choose to respond, your response will be made available electronically for public inspection in the NRC Public Document Room or in the NRC's Agencywide Documents Access and Management System (ADAMS), accessible from the NRC Web site at <http://www.nrc.gov/reading-rm/adams.html>. Therefore, to the extent possible, the response should not include any personal privacy, proprietary, or safeguards information so that it can be made available to the Public without redaction.

In accordance with 10 CFR 19.11, you may be required to post this Notice within two working days of receipt.

Dated this 21st day of September 2017

NRC RESPONSE TO INFORMATION
PROVIDED BY WASHINGTON UNIVERSITY IN ST. LOUIS
IN LETTER, DATED JULY 20, 2017

On July 20, 2017, Washington University in St. Louis provided its response to the apparent violation discussed in U. S. Nuclear Regulatory Commission (NRC) Inspection Report No. 03002271/2017001(DNMS). In its response, Washington University maintains its position that there was not a reportable event; however, it does not believe it is productive to dispute further NRC's different determination. Washington University's response also provided information that it believes should be considered in reducing the severity level of the violation. In addition, Washington University's response indicated that it did not agree that it had the necessary information to discover the medical event on April 16, 2016, and is concerned with the statements in Section 3.2 of the inspection report that imply post-administration imaging of yttrium-90 microspheres patients should be done in all cases to identify whether a medical event occurred. The following details Washington University's position as described in its response letter as well as the NRC response.

1. Washington University Position: Washington University performed the medical procedures without error.

NRC Position: Section 6.9.c.2.d. of the NRC Enforcement Policy provides a very clear example of a Severity Level III violation pertinent to the apparent violation, where a licensee fails to make an immediate report that if it had been made would likely have caused the NRC to undertake a substantial further inquiry. The fact that the licensee implemented its procedures without error for the treatment that resulted in a medical event is not a factor in the assessment of the apparent violation for a reporting requirement. In the instance where the licensee incorrectly implements its procedures, the NRC potentially would have identified an additional apparent violation that would be assessed separately and independently from this apparent violation of a reporting requirement. There have been numerous instances where licensees implemented their procedures without error for treatments that still resulted in a medical event. However, this does not relieve licensees of its requirement to report these instances to the NRC as medical events. The failure to notify the NRC of a medical event is a significant issue as it affects the NRC's ability to perform its regulatory oversight function.

2. Washington University Position: The patient suffered no ill effects.

NRC Position: The fact that the patient suffered no ill effects is not a factor in the assessment of the severity level for an apparent violation of a reporting requirement. The failure to notify the NRC of a medical event, including when there are no ill effects to the patient, is a significant issue as it affects the NRC's ability to perform its regulatory oversight function.

3. Washington University Position: The wrong-site delivery was identified only because of our use of a cutting-edge imaging machine to develop a post-treatment imaging protocol designed to improve patient outcomes.

NRC Position: The fact that the wrong-site delivery was identified only because of the licensee's use of a cutting-edge imaging machine to develop a post-treatment imaging protocol designed to improve patient outcomes is not a basis for reducing the severity level of the apparent violation. The NRC currently does not require licensees to conduct

post-treatment patient imaging for microspheres. However, if images are taken or information is obtained that indicate a medical event has occurred, that event must be reported.

4. Washington University Position: There is no evidence of any cause for the wrong-site delivery other than patient intervention.

NRC Position: As documented in the NRC inspection report, there was no indication of patient intervention during the applicable treatment. The licensee's speculation that patient intervention occurred without indication of it is not in accordance with the definition of "patient intervention" in Title 10 of the *Code of Federal Regulations* (10 CFR) 35.2, which states, "actions by the patient or human research subject, whether intentional or unintentional, such as dislodging or removing treatment devices or prematurely terminating the administration." Therefore, the licensee's speculation that patient intervention occurred, without indication of it, is not a basis for reducing the severity level of the apparent violation.

5. Washington University Position: Washington University exercised due diligence and good faith in interpreting NRC's medical event reporting requirements.

NRC Position: The licensee was familiar with the NRC's definitions of "medical event" and "patient intervention" in 10 CFR 35.2, and the NRC's current and previous microspheres guidance documents. Nonetheless, the licensee misinterpreted "medical event" and "patient intervention" by determining that patient intervention occurred without indication of it, and concluded that the incident was not a medical event.

In addition, the licensee misinterpreted "shunt" in the context of the applicable microspheres guidance document. Specifically, the licensee misinterpreted "shunt" as when the licensee's procedure for administering Therasphere® is complied with and the Therasphere® go to the wrong location in the patient's body. Although "shunting" is not defined in the microspheres guidance document, it states, in part, "The licensee shall commit to report any event, except for an event that results from intervention of a patient or human research subject, in which the administration of byproduct material results in dose or activity to an organ or tissue other than the treatment site, as documented in the written directive, except for shunting when shunting was evaluated prior to the treatment in accordance with the manufacturer's procedures." The licensee conducted shunting evaluation prior to Therasphere® treatments, which included conducting a single photon emission computed tomography scan, and anterior and posterior planar images acquired by a gamma camera to determine the percent of liver to lung shunting in accordance with the medical definition of "shunt." Previous versions of the microspheres guidance also included verbiage consistent with the medical definition of "shunt." Finally, at least two applicable licensee physicians interpreted "shunting" in the context of the Microspheres Guidance as per the medical dictionary, rather than, when the licensee's procedure for administering Therasphere® is complied with and the Therasphere® go to the wrong location in the patient's body. Therefore, the licensee demonstrated an incorrect interpretation of the NRC's medical event reporting requirements despite applicable information that was known by the licensee when the incident that resulted in the medical event was identified by the licensee. The licensee's misinterpretation of NRC requirements is not a basis for reducing the severity level of the apparent violation.

6. Washington University Position: Washington University voluntarily disclosed this incident upon a general inquiry from Region III.

NRC Position: While the NRC appreciates that the licensee "voluntarily" disclosed the incident upon a general inquiry from a Region III inspector, 10 CFR 30.9 requires, in part, that information provided to the Commission by a licensee be complete and accurate in all material respects. As such, the licensee voluntarily disclosed this incident in accordance with 10 CFR 30.9. Compliance with 10 CFR 30.9 is not a basis for reducing the severity level of the apparent violation.

7. Washington University Position: Washington University took prompt and appropriate comprehensive corrective action once notified by Region III of NRC's medical event determination.

NRC Position: The fact that the licensee took prompt and appropriate comprehensive corrective action once notified by Region III of NRC's medical event determination is not a basis for reducing the severity level of the apparent violation. The NRC assesses the licensee's corrective actions for promptness and comprehensiveness, and uses corrective actions as part of the civil penalty assessment process in accordance with Section 2.3.4 of the NRC Enforcement Manual.

8. Washington University Position: Washington University commits to making medical event notifications to NRC of future similar incidents if we have not observed a patient action, which led to movement of the catheter tip.

NRC Position: The fact that the licensee committed to making medical event notifications to NRC of future similar incidents if it does not observe a patient action, which led to movement of the catheter tip, should not be a basis for reducing the severity level of the apparent violation. The commitment to making medical event notification to the NRC in future similar incidents is considered corrective actions by the licensee and would be used in the civil penalty assessment process.

9. Washington University Position: We do not agree with the NRC conclusion that we had the "necessary information to discover the medical event" on April 16, 2016.

NRC Position: On April 8, 2016, the licensee conducted a PET-MRI scan on the patient. On April 16, 2016, the results of the PET-MRI scan were assessed by the licensee, where it was determined that approximately 95 percent of the microspheres were delivered to the right lobe of the patient's liver, rather than the left lobe as prescribed in the written directive. After identifying that the treatment was not performed as planned, the licensee notified the interventional radiologist, who was also the referring physician. Therefore, the NRC determined that on April 16, 2016, the licensee had the necessary information to discover that the incident was a medical event per 10 CFR 35.3045(a)(3), and the information in the NRC's current yttrium-90 microspheres guidance, dated February 12, 2016.

10. Washington University Position: We are concerned that the NRC statement in Section 3.2 of the inspection report implies that post-administration imaging of yttrium-90 microsphere patients should be done in all cases to identify whether a medical event occurred.

NRC Position: Section 3.2 is stating facts involving the use of microspheres at Washington University. The report is stating that 40 of the 150 patients treated with microspheres have had post-treatment PET-MRI scans, and that the procedure used for microsphere treatments was silent on conducting post-treatment imaging of microsphere patients. The NRC's regulations or guidance do not require post-treatment imaging of microsphere patients.