

February 19, 2009

CAL 3-08-001

Mitzi Pennington, Site Director
Mallinckrodt, Inc.
2703 Wagner Place
Maryland Heights, MO 63043

SUBJECT: NRC SPECIAL INSPECTION REPORT NO. 030-00001/09-01(DNMS) AND
NOTICE OF VIOLATION – MALLINCKRODT, INC.

Dear Ms. Pennington:

This refers to the ongoing special inspection that began in February 2008 and was initially documented in NRC Inspection Report No. 030-00001/08-01(DNMS) dated May 22, 2008. The ongoing special inspection was continued on January 12 through 15, 2009, at the Maryland Heights, Missouri facility, with continued NRC in office review through January 22, 2009. The in-office review included receipt and review of information that was unavailable during the onsite inspection. The purpose of the inspection was to evaluate the facts, circumstances, and actions taken in response to the increased number of customer complaints that you received regarding the results of molybdenum-99 breakthrough (breakthrough) tests conducted on technetium-99m generators (generators) and to evaluate the actions taken in response to the February 1, 2008, Confirmatory Action Letter (CAL 3-08-001). The enclosed report presents the results of the inspection to date. The special inspection will continue until the NRC has verified that all of the actions described in CAL 3-08-001 have been completed.

Based on your request to withhold proprietary information from public disclosure in accordance with the provisions of 10 CFR 2.390, the inspection report identifies components, equipment, chemicals, and other proprietary-related items in generic terms, such as Component 1 or Chemical 1.

The exit meeting to discuss the preliminary inspection findings was held with you and other members of your staff at the Maryland Heights, Missouri facility on January 15, 2009. On January 27, 2009, Robert Gattone of my staff contacted Jim Schuh of your staff to discuss the inspection findings. On February 13, 2009, Robert Gattone contacted Jim Schuh to discuss an additional inspection finding based on new information that was available on February 12, 2009.

Based on the results of the inspection, the NRC has determined that one Severity Level IV violation of NRC requirements occurred. The violation was evaluated in accordance with the NRC Enforcement Policy. The current Enforcement Policy is included on the NRC's Web site at <http://www.nrc.gov/about-nrc/regulatory/enforcement/enforcement-pol.html>. The violation involves your failure to develop Corrective Action Program procedures in accordance with Condition 20 of your license (see Section 2 of the attached report). The violation of Condition 20 of your license 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 is being cited in the Notice because it was identified by the inspector.

You are required to respond to this letter and should follow the instructions specified in the enclosed Notice when preparing your response. For your consideration and convenience, an excerpt from NRC Information Notice 96-28, "Suggested Guidance Relating to Development and Implementation of Corrective Action," is enclosed. The NRC will use your response, in part, to determine whether further enforcement action is necessary to ensure compliance with regulatory requirements.

As stated in Section 3.2 of NRC Inspection Report No. 030-00001/08-01 (DNMS) dated May 22, 2008, the applicability of NRC notification requirements as they pertain to the breakthrough problem was an Open Item. The NRC completed its review of the applicability of NRC notification requirements as they pertain to increased customer complaints that you received regarding the results of breakthrough tests conducted on generators. As discussed in Section 1.2.c. of the attached report, the NRC determined that you are not required to report the breakthrough events that occurred between January 1, 2008, and January 6, 2009. As such, the Open Item is closed. However, you are required to evaluate future breakthroughs for reportability pursuant to 10 CFR Part 21 on a case-by-case basis.

In addition to the violation, the inspector identified concerns involving: (1) the licensee's method of conducting breakthrough testing on each generator prior to distribution (see Section 1.2.b.5. of the attached report); (2) the effectiveness of the licensee's corrective actions to prevent the breakthrough problem (see Section 1.2.b.8. of the attached report); and (3) licensee procedures that did not contain sufficient detail or adequate information, resulting in an increased potential for misinterpretation and mistakes by individuals who may be responsible for implementing the procedures (see Section 2.2 of the attached report). Therefore, in addition to responding to the violation cited in the Notice, the NRC is requesting that you provide specific actions that have been or will be taken to address the concerns. In addition, provide your perspective on how you are progressing in terms of improving your safety culture in light of the concerns.

The inspector also identified a generic issue associated with the breakthrough problem. Generator users who comply with the NRC regulation for breakthrough testing and do not conduct breakthrough tests on each elution could conduct breakthrough tests on the first eluate with results that do not exceed the regulatory limit and then miss breakthrough problems that may occur on subsequent elutions.

In accordance with 10 CFR 2.390 of the NRC's "Rules of Practice," a copy of this letter, its enclosures, and your response, 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>. To the extent possible, your

M. Pennington

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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/

Steven A. Reynolds, Director
Division of Nuclear Materials Safety

Docket No. 030-00001
License No. 24-04206-01

Enclosures:

- 1. Notice of Violation
- 2. Inspection Report 030-00001/09-01(DNMS)
- 3. Excerpt from NRC Information Notice 96-28

cc: J. Schuh, Radiation Safety Officer
Michele Perry-Williams, Food and Drug Administration
State of Missouri

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NOTICE OF VIOLATION

Mallinckrodt, Inc.
Maryland Heights, Missouri

Docket No. 030-00001
License No. 24-04206-01

During an NRC inspection conducted on January 12 through 15, 2009, a violation of NRC requirements was identified. In accordance with the NRC Enforcement Policy, the violation is listed below:

Condition 20 of License No. 24-04206-01 requires that the licensee maintain a corrective action program (CAP) to identify and correct deficiencies associated with radiation safety, and that:

- A. It develop, implement, and maintain procedures to assure that conditions adverse to radiation safety, such as failures, malfunctions, deficiencies, deviations, defective material and equipment, and non-conformances that could reasonably affect exposures to workers or the public, or releases of radioactive material in effluents or to the sanitary sewer system, are promptly identified and corrected. In the case of significant conditions adverse to radiation safety, the measures shall assure that the cause of the condition is determined and corrective action taken to preclude repetition. The identification of the significant condition adverse to radiation safety, the cause of the condition, and the corrective action taken shall be documented and reported to appropriate levels of management. The procedures shall include appropriate quantitative or qualitative acceptance criteria for determining that the procedures have been satisfactorily accomplished; and
- B. The procedure(s) shall include provisions for: 1) defining conditions that are adverse to radiation safety; 2) identifying conditions that are adverse to radiation safety; 3) reporting the conditions to appropriate management levels; 4) investigating adverse conditions in sufficient detail to identify root causes; 5) developing and implementing corrective actions to address the identified root cause(s) and to prevent recurrence; and 6) establishing time tables (milestones) for each provision, commensurate with the significance of the adverse condition.

Contrary to the above, as of January 12, 2009, the licensee did not develop Product Quality CAP procedures that established time tables (milestones) for: (1) identifying conditions that are adverse to radiation safety; and (2) reporting the conditions to appropriate management levels. Specifically, the licensee's Standard Operating Procedure 33-213, "Performing Complaint Investigations" did not establish time tables (milestones) for: (1) identifying conditions that are adverse to radiation safety; and (2) reporting the conditions to appropriate management levels. In addition, the licensee's Standard Operating Procedure 33-23, "Exception and Deviation Reporting" and the subsequent revision titled, "Exception Reporting," did not establish time tables (milestones) for identifying conditions that are adverse to radiation safety.

This is a Severity Level IV violation (Supplement VI).

Pursuant to the provisions of 10 CFR 2.201, Mallinckrodt Inc. is hereby required to submit a written statement or explanation to the U.S. Nuclear Regulatory Commission, ATTN: Document Control Desk, Washington, DC 20555-0001, with a copy to the Regional Administrator, Region III, within 30 days of the date of the letter transmitting this Notice of Violation (Notice). This reply should be clearly marked as a "Reply to a Notice of Violation" and should include for each violation: (1) the reason for the violation, or, if contested, the basis for disputing the violation or severity level; (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 previous docketed correspondence, if the correspondence adequately addresses the required response. If an adequate reply is not received within the time specified in this Notice, an order or a Demand for Information may be issued as to why the license should not be modified, suspended, or revoked, or why such other action as may be proper should not be taken. Where good cause is shown, consideration will be given to extending the response time.

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.

Because your response 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> to the extent possible, it 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, then 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 material, 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). If safeguards information is necessary to provide an acceptable response, please provide the level of protection described in 10 CFR 73.21.

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

Dated this 19th day of February 2009.

U.S. NUCLEAR REGULATORY COMMISSION

REGION III

Docket No.: 030-00001

License No.: 24-04206-01

Report No.: 030-00001/09-01(DNMS)

Licensee: Mallinckrodt, Inc.

Facility: 2703 Wagner Place
Maryland Heights, Missouri

Inspection Dates: January 12 through 15, 2009
Continued in-office review through
January 22, 2009

Preliminary Exit Meeting: January 15, 2009

Final Exit Meeting: February 13, 2009

Inspector: Robert G. Gattone, Jr.
Senior Health Physicist

Approved By: Patricia J. Pelke, Chief
Materials Licensing Branch
Division of Nuclear Materials Safety

EXECUTIVE SUMMARY

Mallinckrodt, Inc. NRC Inspection Report 030-00001/09-01(DNMS)

On January 12 through 15, 2009, the inspector continued the ongoing special inspection which began in February 2008, at Mallinckrodt, Inc.'s (licensee) Maryland Heights, Missouri facility. The special inspection was initially documented in Nuclear Regulatory Commission (NRC) Inspection Report No. 030-00001/08-01(DNMS) dated May 22, 2008. The purpose of the inspection was to evaluate the facts, circumstances, and the licensee's actions taken in response to the increased number of customer complaints it received associated with technetium-99m generators (generators) that failed the molybdenum-99 breakthrough (breakthrough) test. From approximately October 2006 through February 2007, and particularly in January 2008, the licensee received an increase in the number of customer complaints associated with generators that failed the breakthrough tests. Specifically, an increased number of generators produced elutions that exceeded the 0.15 microcurie of molybdenum-99 per millicurie of technetium-99m regulatory limit in Title 10 Code of Federal Regulations (CFR) 35.204, "Permissible Molybdenum-99 Concentration" at either the first or a subsequent generator elution. The inspector also evaluated the actions associated with Confirmatory Action Letter No. 3-08-001 dated February 1, 2008 (CAL).

The inspector identified a violation of Condition 20 of NRC License No. 24-04206-01 involving failure to develop Product Quality Corrective Action Program (CAP) procedures that established time tables (milestones) for: (1) identifying conditions that are adverse to radiation safety; and (2) reporting the conditions to appropriate management levels.

In addition to the violation, the inspector identified concerns involving: (1) the licensee's method of conducting breakthrough testing on each generator prior to distribution; (2) the effectiveness of the licensee's corrective actions to prevent the breakthrough problem; and (3) licensee procedures that were written without sufficient detail or included inadequate information, resulting in an increased potential for misinterpretation and mistakes by individuals who may be responsible for implementing the procedures. The inspector also identified a generic issue associated with the breakthrough problem. Generator users who comply with the NRC regulation for breakthrough testing and do not conduct breakthrough tests on each elution could conduct breakthrough tests on the first eluate with results that do not exceed the regulatory limit and then miss breakthroughs that may occur on subsequent elutions.

Based on the licensee's request to withhold proprietary information from public disclosure in accordance with the provisions of 10 CFR 2.390, the report identifies components, equipment, chemicals, and other proprietary-related items in generic terms, such as Component 1 or Chemical 1.

The licensee's investigation into the cause(s) of the breakthrough problem is still ongoing. The licensee's actions included: (1) testing to determine the role of Chemical 1 in Component 1 and its relationship to breakthrough; and (2) reviewing instrumentation used to measure breakthrough as part of its investigation of the problem.

The licensee's corrective actions to prevent the breakthrough problem included: (1) acquiring Component 1 with low Chemical 1 content; (2) using a new label affixed to the top of its generators alerting customers to test each generator eluate for molybdenum-99 content before use; (3) conducting breakthrough testing on each generator prior to distribution; (4) standardizing important manufacturing aspects of Component 2; (5) improving methods to identify Component 2 defects; (6) improving training for licensee staff responsible for identifying Component 2 defects; and (7) standardizing the processing of Component 1.

On March 10, 2008, the licensee completed all of the actions described in Item 3 of the CAL regarding its evaluation of 10 CFR Part 21 reportability of the breakthrough problem. The NRC determined that the licensee was not required to report the breakthrough events that occurred between January 1, 2008, and January 6, 2009, to the NRC pursuant to 10 CFR Part 21. As such, the associated Open Item is closed. However, the licensee is required to evaluate future breakthroughs for reportability pursuant to 10 CFR Part 21 on a case-by-case basis. The licensee has initiated but not completed the actions described in Items 1, 2, and 4 of the CAL regarding investigation of the breakthrough problem, corrective actions to prevent the problem, and Important Product Notification distribution, respectively. The licensee estimated that it would complete all of the actions described in Items 1 and 2 of the CAL by March 2009; and it would complete Item 4 of the CAL by May 2009.

Report Details

1 Implementation of Actions Described in CAL 3-08-001

1.1 Inspection Scope

The inspector reviewed Mallinckrodt, Inc.'s (licensee) implementation of actions described in the Confirmatory Action Letter 3-8-001 dated February 1, 2008 (CAL), by interviewing several members of the licensee's staff involved with those actions including, but not limited to, the Radiation Safety Officer (RSO), health physicists, and product quality staff. In addition, the inspector observed production and testing of technetium-99m generators (generators). The inspector also reviewed applicable licensee documents including, but not limited to, Standard Operating Procedures (SOPs), Management of Change records, and Standard Test Method (STM) records. The inspector also evaluated customer complaint information regarding the molybdenum-99 breakthrough (breakthrough) problem.

1.2 Observations and Findings

a. Investigation of the Molybdenum-99 Breakthrough Problem

As stated in Item 1 of the CAL, the licensee committed to provide the following information and take the following actions as soon as possible:

"Conduct an investigation (which has already been initiated) into the problem of elevated concentrations of molybdenum-99 in elutions from generators. The investigation will include how and why the problem occurred, when the problem first occurred, the extent of condition of the problem, the root and supporting causes of the problem, and the safety significance of the elevated concentrations of molybdenum-99 in elutions from generators. The results of the investigation will be provided to the Nuclear Regulatory Commission (NRC), including any interim reports."

The licensee continues to conduct an investigation into the breakthrough problem. The details regarding the licensee's investigation as of May 22, 2008, are discussed in Sections 1 and 2 of NRC Inspection Report No. 030-00001/08-01(DNMS) dated May 22, 2008. The ongoing investigation includes how and why the problem occurred and the root and supporting causes of the problem. The licensee now estimates that it will complete all of the actions stated in Item 1 of the CAL by March 2009.

The licensee provided the NRC with interim reports of its breakthrough investigation dated August 18 and November 26, 2008. The reports included preliminary results of the licensee's investigation.

During the summer of 2008, the licensee conducted testing to determine the role of Chemical 1 in Component 1 and its relationship to breakthrough. The testing involved use of Chemical 1 content in Component 1 that ranged from very high to about the same level as that found in Component 1 lots that were used to produce generators over the last several months and during this inspection. The testing was representative of large

scale generator production because it was conducted in a manner that accurately reproduced current manufacturing procedures for generator component preparation and assembly. The licensee noted that, as the content of Chemical 1 in Component 1 increased, so did the incidence of breakthrough. Based on the licensee's operating experience with the level of Chemical 1 content in Component 1 to produce generators over the last several months, it noted that the incidence of breakthrough complaints exceeded the normal frequency. Therefore, the licensee determined that additional testing was required involving lower levels of Chemical 1 content in Component 1 than those found in Component 1 lots that were used to produce generators over the last several months and during this inspection.

The licensee acquired Component 1 that contained lower levels of Chemical 1 content than that used to produce generators over the last several months and during this inspection. The licensee repeated the testing for breakthrough using Component 1 with a range of very low Chemical 1 content. The licensee noted that, as the Chemical 1 content in Component 1 increased, the incidence of breakthrough did not increase until the Chemical 1 content reached a certain threshold. The licensee determined that, as long as the Chemical 1 content in Component 1 did not exceed that threshold, the incidence of breakthrough did not increase. Therefore, the licensee established that threshold of Chemical 1 content in Component 1 as a proposed specification for Component 1.

Between October and December 2008, the licensee conducted additional testing to evaluate the effect on generator quality if production included use of the Component 1 with Chemical 1 content below the proposed specification level, including, but not limited to, the incidence of breakthrough. On January 19, 2009, the licensee submitted its request to the Food and Drug Administration (FDA) for approval to use Component 1 with Chemical 1 content below the proposed specification for generator production. In addition, the licensee estimated that it would be able to use Component 1 with Chemical 1 content below the proposed specification for generator production in late February 2009. If the FDA does not approve the licensee's request, the licensee planned to continue using Component 1 that is currently used for generator production. If the supply of currently used Component 1 runs out, the licensee planned to acquire more Component 1 with Chemical 1 content similar to that currently used.

The licensee reviewed instrumentation used to measure breakthrough as part of its investigation of the problem. For example, the licensee noted the use of canisters to measure molybdenum-99 radioactivity within a vial of technetium-99m. The canisters essentially functioned to shield lower energy radiation emitted from the technetium-99m and allow a fraction of the higher energy radiation emitted from the molybdenum-99 to be counted by a dose calibrator. The dose calibrators corrected the molybdenum-99 counts using a correction factor, and displayed the results in units of microcuries of molybdenum-99.

The licensee conducted breakthrough tests of a given generator eluate using different canisters from a sample of its clients. The licensee noted that the breakthrough tests of a given eluate varied based on measurements taken with different canisters. The licensee identified that some of its clients used canisters that had bent canister caps that allowed some of the lower energy radiation emitted from the technetium-99m to escape the canister unshielded, resulting in a false failed breakthrough test result. That is,

despite a failed breakthrough test, the actual concentration of molybdenum-99 in the eluate was below the 0.15 microcurie of molybdenum-99 per millicurie of technetium-99m regulatory limit (limit) in 10 CFR 35.204, "Permissible Molybdenum-99 Concentration." The licensee determined that the canister caps can bend if they are dropped, possibly resulting in false failed breakthrough test results.

In response to the findings, the licensee replaced customers' damaged canisters. In addition, it developed a training program to alert its customers about proper breakthrough test procedures and the importance of using undamaged canisters during the tests.

The licensee received a breakthrough complaint in October 2008 from a customer outside of the United States that indicated breakthrough well in excess of the limit. The licensee dispatched two staff members to the customer's facility to follow up on the complaint.

The customer was a hospital for the poor. The physician who conducted the breakthrough test had minimal nuclear medicine training and was not very familiar with nuclear medicine instrumentation and radioactivity measurement calculations. The licensee's staff observed the physician demonstrate how the breakthrough test was conducted. The staff noted that the physician placed the unshielded vial containing the elution into a dose calibrator and pressed the "molybdenum-99" button to measure the molybdenum-99 content. The customer did not possess a canister, nor was the physician aware of the need to use a canister to conduct a proper breakthrough test.

At the customer's facility, the licensee staff measured an eluate in an unshielded vial with the dose calibrator set to measure the radioactivity of molybdenum-99 and then technetium-99m. The resulting radioactivity measurement ratio was 7.2 millicuries of molybdenum-99 to 1 millicurie of technetium-99m. The licensee staff noted that the same ratio of molybdenum-99 radioactivity to technetium-99m radioactivity applied to the breakthrough complaint. Therefore, the licensee concluded that the breakthrough complaint that was received from the customer in October 2008 was based on an improperly performed breakthrough test.

The licensee initially attempted to have the affected generator returned for investigation; however, since the customer was not part of the licensee's "return program," the generator was not shipped with the proper return labelling. From the customer's facility, the licensee staff attempted to ship the affected generator back to the licensee; however, they could not because the shipping box had been disposed of. Therefore, the generator could not be shipped to the proper licensee location for investigation.

The licensee received four breakthrough complaints during a two day period in early January 2009. All four complaints were identified by the licensee as a condition adverse to radiation safety within 24 hours of receipt. The licensee promptly initiated an investigation of the cause of the complaints, and the investigation was ongoing during the inspection.

b. Corrective Actions to Prevent the Breakthrough Problem

(1) Overview

As stated in Item 2 of the CAL, the licensee committed to provide the following information and take the following actions as soon as possible:

“Identify and implement immediate, short-term, and long-term corrective actions to address the causes of the problem and prevent recurrence. Provide the NRC with the corrective actions that have and will be taken, including a timetable for completion. “

The details regarding the licensee's corrective actions to prevent the breakthrough problem as of May 22, 2008, are discussed in Section 1 of NRC Inspection Report No. 030-00001/08-01(DNMS) dated May 22, 2008. The licensee provided the NRC with an interim report of corrective actions it took to prevent the breakthrough problem dated November 26, 2008. The interim corrective actions were completed in the fall of 2008 and they were based on the probable causes of the problem that were identified by the licensee, with the realization that its investigation of the problem was ongoing. The licensee estimated that it would complete all of the actions stated in Item 2 of the CAL by March 2009.

(2) Chemical Treatment of Component 1

The licensee had planned to investigate whether the Component 1 with higher Chemical 1 content could be chemically treated to reduce the Chemical 1 content to a level that would not cause breakthrough. The licensee also planned to conduct testing with treated Component 1 to determine if it would adversely affect generator quality. However, since the licensee acquired Component 1 that contained lower Chemical 1 content, it stopped plans to chemically treat Component 1 with higher Chemical 1 content.

(3) Supplier of Component 1

The licensee took actions to identify a new supplier of Component 1 as a means of acquiring Component 1 with low Chemical 1 content. Although the licensee's attempts to find a new supplier of Component 1 were unsuccessful, the licensee was able to acquire Component 1 that contained lower Chemical 1 content from its original Component 1 supplier.

(4) New Generator Label

In May 2008, the licensee requested FDA approval to use a new label affixed to the top of its generators alerting customers to test each generator eluate for molybdenum-99 content before use. The FDA approved use of the new label on November 17, 2008. The licensee began using the new label on December 3, 2008. During a tour of the facility, the inspector randomly selected a generator packaged for shipment, and noted that the generator had the new label affixed to it.

(5) Pre-Distribution Breakthrough Testing

On September 17, 2008, the licensee began conducting breakthrough testing on each generator prior to distribution. The licensee's process of conducting breakthrough testing on each generator prior to distribution did not involve changes in how the generators were produced. Therefore, the licensee concluded that breakthrough testing on each generator prior to distribution did not adversely affect generator quality.

The inspector identified two concerns regarding the licensee's method of conducting breakthrough testing on each generator prior to distribution. During the breakthrough tests, vials containing between hundreds of millicuries and low curie quantities of technetium-99m within capped lead vial shields were placed into a plastic tray. The lead caps of the vial shields were not fastened to the shields; therefore, the caps would fall off the shields if they were inverted. After about eight shielded vials were placed into the plastic tray, an individual would hand carry the tray several feet to another area for molybdenum-99 measurements. The plastic tray had no handles; therefore individuals usually carried the trays by grasping a rim of plastic at the top of the tray. The trays were relatively heavy, and weighed approximately 15 pounds. The inspector identified a concern that this step of the process had a high potential for a significant radioactive spill and/or injury to an individual. Specifically, if a filled tray was dropped, one or more vials could break on the floor causing significant radioactive contamination and/or a lead vial shield(s) could fall and injure an individual.

The inspector also identified a concern that the licensee made an assumption about its method of assaying the radioactivity of molybdenum-99 without sufficient testing to verify that its assumption was correct. As previously discussed, each vial of technetium-99m was within a capped lead vial shield. The licensee measured the radioactivity of molybdenum-99 while the vial was in the capped lead vial shield. The capped lead vial shields were not designed for conducting molybdenum-99 assays. The licensee assumed that the critical dimension of the vial shields for measuring the radioactivity of molybdenum-99 was consistent.

During testing of its method to conduct molybdenum-99 assays, the licensee randomly selected 5 lead vial shields out of more than 150 (a non-representative sample) to conduct measurements of a calibrated molybdenum-99 standard, in part, to determine if the critical dimension of the vial shields was consistent. In addition, the licensee did not measure the critical dimension of the 5 vial shields to assess potential variations. Therefore, the licensee took insufficient action to verify that its assumption about the critical dimension of the vial shields was correct. If the critical dimension of a vial shield(s) is thicker than the vial shield specification thickness beyond an unknown threshold, the measured molybdenum-99 radioactivity would be erroneously low, such that a vial could contain a molybdenum-99 concentration above the limit and still pass a breakthrough test.

(6) Component 2 Manufacturing and Inspection

In the spring of 2008, the licensee standardized important aspects of Component 2 manufacturing. Specifically, the licensee identified critical dimensions and features needed for proper Component 2 function. The licensee also trained applicable staff on

the dimensions and features, including how to identify defects before they are installed in generators.

The licensee implemented actions to more effectively identify Component 2 defects. For example, the licensee tripled the number of Component 2 defect check criteria to enhance identification of defects. The licensee also began to use color-coded parts to assemble Component 2 items, which allowed the staff to more effectively recognize Component 2 assembly problems. In addition, the licensee implemented dual, independent inspections for defects on all assembled Component 2 items prior to installation in generators.

In April 2008, the licensee implemented revised training for licensee staff responsible for identifying Component 2 defects. The training included, among other things, passing a vision test, studying visual aids of each type of Component 2 defect, studying samples of normal and defective Component 2 items, and passing written and practical examinations.

The inspector observed an engineer demonstrate how Component 2 items were produced. The individual demonstrated actions that were taken to ensure that Component 2 items were produced in accordance with the parameters specified in the applicable procedure. For example, flow of liquid used for processing Component 2 was measured with a calibrated device and a visual aid was used to verify the dimensions of Component 1 that was installed in Component 2.

The inspector observed licensee staff conduct dual, independent inspections for defects associated with Component 2. The inspector observed licensee staff identify Component 2 defects and reject those items. The staff was very knowledgeable regarding the various types of defects they were looking for. In addition, the staff understood the adverse effects associated with installation of defective Component 2 items into generators.

(7) Component 1 Processing

In March 2008, the licensee revised its SOP to standardize processing of Component 1. For example, the procedure was changed to require staff to document start and stop times and flow rates associated with Component 1 processing as a means of ensuring that the start and stop times and flow rates were within the parameters in the procedure.

(8) Concern Regarding Corrective Action Effectiveness

The inspector identified a concern regarding the effectiveness of the licensee's corrective actions discussed above. The inspector noted that the frequency of breakthrough complaints varied widely over the last several months, with a particularly increased frequency in January and February 2009. Considering the licensee's corrective actions taken to date and the fact that the content of Chemical 1 in Component 1 used to produce generators has been very similar over the last several months, it is reasonable to expect that the frequency of breakthrough complaints would be relatively constant. The wide variation of breakthrough complaint frequency indicates that there may be another cause(s) for the breakthrough problem that the licensee is unaware of, thus rendering the licensee's corrective actions taken to date less effective.

c. Evaluation of 10 CFR Part 21 Reportability.

As stated in Item 3 of the CAL, the licensee committed to provide the following information and take the following actions as soon as possible:

“Conduct an evaluation of the reportability of this problem pursuant to Title 10 Code of Federal Regulations (CFR) Part 21 and provide the NRC with the results of this evaluation.”

The licensee conducted its evaluation and, in its letter to the NRC dated March 10, 2008, described why it determined that the breakthrough problem did not require notification pursuant to 10 CFR Part 21.21. Therefore, the licensee completed the actions described in Item 3 of the CAL on March 10, 2008. As stated in Section 3.2 of NRC Inspection Report No. 030-00001/08-01(DNMS) dated May 22, 2008, the applicability of NRC notification requirements as they pertain to the breakthrough problem was an Open Item.

The NRC completed its independent evaluation of the reportability of the molybdenum-99 breakthrough problem pertaining to 10 CFR Part 21. Title 10 CFR Part 21, “Reporting of Defects and Non-Compliance” requires, in part, that the licensee notify the NRC of defects which could create a substantial safety hazard. Title 10 CFR Part 21.3, “Definitions” defines, “Substantial Safety Hazard,” as, “a loss of safety function to the extent that there is a major reduction in the degree of protection provided to public health and safety for any facility or activity licensed or otherwise approved or regulated by the NRC, other than for export...” The NRC determined that the breakthrough events that occurred between January 1, 2008, and January 6, 2009, did not constitute a “substantial safety hazard” as defined in 10 CFR Part 21.3. Therefore, the licensee was not required to report those breakthrough events to the NRC pursuant to 10 CFR Part 21. As such, the Open Item is closed. However, the licensee is required to evaluate future breakthroughs for reportability pursuant to 10 CFR Part 21 on a case-by-case basis.

d. Important Product Notification Distribution

As stated in Item 4 of the CAL, the licensee committed to provide the following information and take the following actions as soon as possible:

“Continue distribution of the “Important Product Notification” (Notification) dated January 26, 2008, to your customers. Prior to discontinuing the distribution of the Notification, you will contact the NRC to discuss: (1) why distribution of the Notification is no longer necessary; (2) your understanding of the Food and Drug Administration’s perspective on whether or not distribution of the Notification is no longer necessary; and (3) whether or not you have completed all of the corrective actions necessary to prevent recurrence.”

As discussed in Section 1.f of NRC Inspection Report No. 030-00001/08-01(DNMS) dated May 22, 2008, the licensee began distributing the Notification with all of its

generators shipped on or after January 27, 2008. In addition, the licensee mailed the Notification to all customers who received generators from the affected lots. The Notification included a summary of the breakthrough problem, including the affected generator lot numbers; a reminder that the eluates expire 12 hours post elution, a reminder that each eluate should not contain more than the 0.15 microcurie of molybdenum-99 per millicurie of technetium-99m limit at the time of administration, and a recommendation to follow the generator package labelling.

The licensee received breakthrough complaints in April and June 2008 that involved molybdenum-99 concentrations that were much higher than previous complaints. Therefore, effective with generator shipments beginning on June 27, 2008, the licensee began distributing a revised Notification that informed generator customers about the recent reports of molybdenum-99 concentrations that were higher than previous complaints, discussed that the higher concentrations of molybdenum-99 could potentially increase the possibility of an adverse health effect, and re-emphasized the need for customers to conduct breakthrough tests on each generator elution. The inspector observed that the licensee continued to distribute the revised Notification with all of its generators.

After the licensee completes the CAL actions described in Sections 1.2.a., 1.2.b.1., and 1.2.c. above, it planned to contact the NRC to discuss: (1) why distribution of the Notification is no longer necessary; (2) its understanding of the FDA's perspective on whether or not distribution of the Notification is no longer necessary; and (3) whether or not it completed all of the corrective actions necessary to prevent recurrence. The licensee estimated that it would complete all of the actions stated in Item 4 of the CAL by May 2009.

1.3 Conclusions

The inspector identified concerns involving the licensee's method of conducting breakthrough testing on each generator prior to distribution, and the effectiveness of the licensee's corrective actions to prevent the breakthrough problem. On March 10, 2008, the licensee completed all of the actions described in Item 3 of the CAL regarding its evaluation of 10 CFR Part 21 reportability of the breakthrough problem. The NRC determined that the licensee was not required to report the breakthrough events to the NRC pursuant to 10 CFR Part 21. As such, the associated Open Item is closed. The licensee has initiated but not completed the actions described in Items 1, 2, and 4 of the CAL regarding investigation of the breakthrough problem, corrective actions to prevent the problem, and Notification distribution, respectively. The licensee estimated that it would complete all of the actions described in Items 1 and 2 of the CAL by March 2009; and it would complete Item 4 of the CAL by May 2009.

2 Corrective Actions to Prevent the Previously Identified Violation

2.1 Inspection Scope

The inspector interviewed selected licensee management representatives and staff, reviewed SOPs, and reviewed selected training records in order to evaluate the licensee's implementation of the corrective actions it took to prevent the violation that

was previously identified during the special inspection and documented in the Notice of Violation and NRC Inspection Report No. 030-00001/08-01(DNMS) dated May 22, 2008.

2.2 Observations and Findings

Condition 20 of License No. 24-04206-01 required that the licensee maintain a Corrective Action Program (CAP) to identify and correct deficiencies associated with radiation safety, and that:

- It develop, implement and maintain procedures to assure that conditions adverse to radiation safety, such as failures, malfunctions, deficiencies, deviations, defective material and equipment, and non-conformances that could reasonably affect exposures to workers or the public, or releases of radioactive material in effluents or to the sanitary sewer system, are promptly identified and corrected. In the case of significant conditions adverse to radiation safety, the measures shall assure that the cause of the condition is determined and corrective action taken to preclude repetition. The identification of the significant condition adverse to radiation safety, the cause of the condition, and the corrective action taken shall be documented and reported to appropriate levels of management. The procedures shall include appropriate quantitative or qualitative acceptance criteria for determining that the procedures have been satisfactorily accomplished; and
- The procedure(s) shall include provisions for: 1) defining conditions that are adverse to radiation safety; 2) identifying conditions that are adverse to radiation safety; 3) reporting the conditions to appropriate management levels; 4) investigating adverse conditions in sufficient detail to identify root causes; 5) developing and implementing corrective actions to address the identified root cause(s) and to prevent recurrence; and 6) establishing time tables (milestones) for each provision, commensurate with the significance of the adverse condition.

The NRC previously identified a violation of Condition 20 of License No. 24-04206-01 and issued a Notice of Violation (NOV) to the licensee on May 22, 2008. The violation involved the licensee's failure to develop, implement, and maintain CAP procedures that included actions to assure that conditions adverse to radiation safety were promptly identified and corrected. In addition, the licensee's CAP procedures did not include measures to be taken to assure that the cause of significant conditions adverse to radiation safety were determined and corrective action was taken to preclude repetition, and that the cause of the condition and the corrective action taken was documented and reported to appropriate levels of management. Specifically, the licensee developed, implemented, and maintained separate CAP procedures for Environmental Health and Safety issues and Product Quality issues, and the Product Quality CAP procedures did not include provisions for: 1) defining conditions that are adverse to radiation safety; 2) identifying conditions that are adverse to radiation safety; 3) reporting the conditions to appropriate management levels; 4) investigating adverse conditions, in sufficient detail to identify root causes; and 5) establishing time tables (milestones) for each provision, commensurate with the significance of the adverse condition.

The licensee responded to the NOV by letter to the NRC dated June 20, 2008. The letter states that the licensee planned to complete modifications to SOP 33-201, "Corrective Action Program," SOP 33-23, "Exception and Deviation Reporting," and SOP

33-213, "Performing Complaint Investigations" to comply with the provisions in Condition 20 of its NRC license by July 25, 2008. In addition, the letter states that the licensee: (1) specifically identified the required information in the applicable Product Quality SOPs as an NRC regulatory requirement in order to facilitate approval and ensure that required information is not modified contrary to Condition 20 of its NRC license; and (2) trained key staff members in the Quality and Health Physics Organizations to assure familiarity with the required elements of the CAP as described in Condition 20 of its NRC license.

The inspector noted that the RSO approved all new or revised SOPs. The licensee's "Management of Change" record dated July 30, 2008, documented approval by the RSO, a Quality Manager, and a Training Manager of revisions of SOPs 33-201, 33-23, and 33-213 to comply with Condition 20 of the NRC license. The inspector noted that the revised SOPs included changes to comply with Condition 20 of the NRC license. For example, SOP 33-213 included the definition of, "Conditions Adverse to Radiation Safety" with examples and it required that all customer complaints associated with radioactive products be provided to the Radiation Safety Officer.

However, the inspector identified that, as of January 12, 2009, the licensee did not develop Product Quality CAP procedures that established time tables (milestones) for: (1) identifying conditions that are adverse to radiation safety; and (2) reporting the conditions to appropriate management levels. Specifically, SOP 33-213 did not establish time tables (milestones) for: (1) identifying conditions that are adverse to radiation safety; and (2) reporting the conditions to appropriate management levels. In addition, the inspector identified that SOP 33-23 and the subsequent revision titled, "Exception Reporting," did not establish time tables (milestones) for identifying conditions that are adverse to radiation safety. The licensee's failure to develop Product Quality CAP procedures that established time tables (milestones) for: (1) identifying conditions that are adverse to radiation safety; and (2) reporting the conditions to appropriate management levels is a violation of Condition 20 of License No. 24-04206-01.

The licensee staff believed that it had revised its Product Quality procedures to comply with Condition 20 of the NRC license. However, licensee staff interpreted that provision 6 in Condition 20 of the NRC license (establishing time tables (milestones) for each provision, commensurate with the significance of the adverse condition) did not apply to provision 2 in Condition 20 of the NRC license (identifying conditions that are adverse to radiation safety). Therefore, the licensee did not revise SOPs 33-213 and 33-23 to establish time tables (milestones) for identifying conditions that are adverse to radiation safety. In addition, the licensee failed to revise Standard Operating Procedure 33-213 to establish time tables (milestones) for reporting the conditions to appropriate management levels due to an oversight.

The inspector identified a concern that some licensee procedures were written without sufficient detail or adequate information, resulting in an increased potential for misinterpretation and mistakes by individuals who may be responsible for implementing the procedures. For example, SOP 33-213 defines, "Conditions Adverse to Radiation Safety," and it includes examples. One example is "elevated breakthrough reports." The key individual responsible for identifying conditions adverse to radiation safety knew the threshold for elevated breakthrough reports in the context of the SOP. However, other less experienced individuals who may fill in for the key individual and implement

the procedure may interpret the word “elevated” incorrectly because it is not described in the SOP.

In addition, SOP 33-213 describes actions to identify conditions adverse to radiation safety, including, but not limited to, notifying a manager about all customer complaints associated with radioactive products. Although the manager knew he was responsible for evaluating each customer complaint associated with radioactive products to determine whether or not they are conditions adverse to radiation safety, the SOP did not state that the manager is responsible for doing so. Also, the manager stated that more significant conditions adverse to radiation safety would be reported to higher levels of licensee management at his discretion. However, the SOP was silent about reporting more significant conditions adverse to radiation safety to higher levels of licensee management.

Other examples of the concern were identified in the licensee’s STM Code 240-018, “Ultra Technekow Generator Testing.” The section that included steps for calculating the results of in-house breakthrough tests was difficult to follow and contained inadequate information. Specifically, a step in the calculation called for entering the times that radioactivity measurements were made; however, the step did not indicate what units of time should be used. In the same section of the STM, the term, “Decay Correction” was erroneously used instead of, “Decay Factor” such that an individual following the calculation steps would be confused by different terms that meant the same thing.

The inspector noted that STM 240-018 was reviewed and approved by licensee management. The inspector determined that the cause of the concern was the licensee’s assumption that individuals responsible for implementing the procedures would have sufficient experience and training before being responsible for implementing the procedures; therefore, the procedures were written with less detail. Nonetheless, the concern with lack of detail and inadequate information in the procedures increased the potential for misinterpretation and mistakes by individuals who may be responsible for implementing the procedures.

The licensee trained key staff members in the Quality and Health Physics Organizations to assure familiarity with the required elements of the CAP as described in Condition 20 of the NRC licensee. For example, the licensee used a computer system to remind applicable staff of the need to review applicable procedures at a specified frequency and electronically certify that they read and understand the procedures. The computer system also assisted the licensee with documenting completion and status of the training for all applicable individuals. Based on staff interviews, the inspector determined that the staff understood the training and they noted procedure revisions to ensure that the changes were implemented.

The inspector observed that SOP 33-201 dated July 30, 2008, included a list of SOPs that had requirements commensurate with the regulatory requirements in Condition 20 of the NRC license. The licensee did this to facilitate approval and ensure that required information is not modified contrary to Condition 20 of its NRC license. In addition, the licensee planned to revise SOPs 33-201, 33-23, and 33-213 to consolidate all of the regulatory requirements in Condition 20 of the NRC license into a single section of the procedures instead of having them dispersed throughout the procedures.

The inspector noted that the licensee revised SOP 33-213 to require that all customer complaints be acknowledged by the Site Quality Manager, and that all radioactive hot product complaints be acknowledged by the RSO. The revision was done to ensure that hot product complaints are promptly evaluated by the RSO to determine if they are "conditions adverse to radiation safety."

The licensee took actions to ensure that conditions adverse to radiation safety related to product quality, such as breakthrough complaints, are promptly corrected in accordance with Condition 20 of the license. Specifically, licensee management met with licensee staff biweekly to discuss near due action items involving review of product quality issues to ensure that the action items are completed timely.

2.3 Conclusions

The inspector identified a violation of Condition 20 of License No. 24-04206-01 involving failure to develop Product Quality CAP procedures that established time tables (milestones) for: (1) identifying conditions that are adverse to radiation safety; and (2) reporting the conditions to appropriate management levels. In addition, the inspector identified concerns involving licensee procedures that were written without sufficient detail or adequate information, resulting in an increased potential for misinterpretation and mistakes by individuals who may be responsible for implementing the procedures.

3.0 Potential Generic Issues Relative to the Breakthrough Problem

3.1 Inspection Scope

The inspector interviewed selected licensee staff, including the RSO and licensee management; reviewed selected records, including SOPs and licensee correspondence with the NRC; and observed selected generator parts as means of identifying potential generic issues associated with the breakthrough problem.

3.2 Observations and Findings

The inspector identified a generic issue associated with the breakthrough problem. Specifically, a number of generators were reported to have produced elutions that exceeded the limit at either the first or a subsequent elution test. Several breakthrough complaints involved breakthrough tests results that did not exceed the limit for the first eluate of a given generator, and then exceeded the limit based on a breakthrough test on a subsequent elution of that generator.

10 CFR Part 35, Section 35.204(b) requires that molybdenum-99 concentrations be checked at the time of the first elution. Therefore, generator users who comply with 10 CFR 35.204 and do not conduct breakthrough tests on each elution could conduct breakthrough tests on the first eluate with results that do not exceed the limit and then miss breakthrough problems that may occur on subsequent elutions. The administration of higher levels of molybdenum-99 could possibly result in a safety issue, as well as have an impact on nuclear medicine image quality and medical diagnosis.

The inspector will continue to review potential generic issues relative to the breakthrough problem. Future identified generic issues relative to the molybdenum-99 problem,

including actions taken to address the generic issues, will be documented in a future inspection report.

3.3 Conclusions

The inspector identified a generic issue associated with the breakthrough problem. Generator users who comply with 10 CFR 35.204 and do not conduct breakthrough tests on each elution could conduct breakthrough tests on the first eluate with results that do not exceed the limit and then miss breakthrough problems that may occur on subsequent elutions.

4.0 **Exit Meeting**

The inspector discussed the preliminary conclusions described in this report with licensee management during an exit meeting conducted at the licensee's facility on January 15, 2009. The inspector discussed the inspection findings described in this report with the RSO during a teleconference conducted on January 27, 2009. On February 13, 2009, the inspector contacted the RSO to discuss an additional inspection finding based on new information that was available on February 12, 2009.

ATTACHMENT: SUPPLEMENTAL INFORMATION

SUPPLEMENTAL INFORMATION

PARTIAL LIST OF PERSONS CONTACTED

- # Julia Balliet, Quality Assurance Manager
- # Erik Blake, Manager, Operational Excellence
- Branda Breaden, Quality Engineer
- # April Chance, Manager of Radiological Affairs/Radiation Safety Committee Chair
- Scan Clay, Manufacturing Technician
- Terry Cornell, Laboratory Technician
- # Steven Duffy, Site Quality Director
- Sarah Griem, Manufacturing Technician II
- # Dan Hoffman, Radiation Safety Officer
- Margaret Hoff, Technician
- # Melissa Kirkpatrick, Director, Quality
- Brian Lasher, Director, Quality Systems
- John Lehnhoff, Quality Control Supervisor
- # Bryan Lowery, RHP Superintendent
- # Russell Maschek, Quality Assurance Engineer
- Tom McCormack, Distribution Superintendent
- # Craig Miller, Manager, Plant Engineering
- # Mitzi Pennington, Site Director
- Sheree Pineda, DTE Quality Engineer
- Madeline Roche, Validation Supervisor
- #* Jim Schuh, Manager of Environmental Health and Safety/Radiation Safety Officer
(Note: Mr. Schuh serves as the Radiation Safety Officer for NRC License No. 24-04206-01)
- # Richard Sparks, Plant Controller
- # Dirk Stevens, Vice President of Quality
- Athena Tanner, Manufacturing Technician
- Rich Williams, Technician/Chemist

- # participated in onsite exit meeting on January 12, 2009
- * contacted by telephone on January 27, 2009, for final exit meeting

LIST OF ACRONYMS USED

CAL	Confirmatory Action Letter
CAP	Corrective Action Program
CFR	Code of Federal Regulations
FDA	Food and Drug Administration
NRC	Nuclear Regulatory Commission
RSO	Radiation Safety Officer
SOPs	Standard Operating Procedures