UNITED STATES
NUCLEAR REGULATORY COMMISSION
REGION I
475 ALLENDALE ROAD
KING OF PRUSSIA, PENNSYLVANIA 19406-1415

December 21, 2001

Docket No. 03002939 License No. 37-00118-07

Neal Nathanson, M.D.
Vice Provost
University of Pennsylvania
Radiation Safety Office
1412 Blockley Hall
Philadelphia, PA 19104-6021

SUBJECT: INSPECTION 03002939/2001001, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PENNSYLVANIA SITE

Dear Dr. Nathanson:

On May 7, 2001, Penny Lanzisera of this office conducted a safety inspection at the above address and at the Medical Center of activities authorized by the above listed NRC license. The inspection was limited to a review of a reported misadministration. Additional information provided in your correspondence dated May 9, May 16, and June 4, 2001, and information provided by the medical consultant in a report dated November 30, 2001, was also examined as part of the inspection. The findings of the inspection were discussed with Mr. Robert Forrest of your organization at the conclusion of the inspection. The enclosed report presents the results of this inspection.

Within the scope of this inspection, no violations were identified. In addition, the medical consultant concluded that "At this dose level in an adult male there is no significant risk for a secondary malignancy."

In accordance with 10 CFR 2.790, a copy of this letter will be placed in the NRC Public Document Room and will be accessible from the NRC Web site at http://www.nrc.gov/NRC/ADAMS/index.html. No reply to this letter is required.

Your cooperation with us is appreciated.

Sincerely,

Original signed by William H. Ruland

William H. Ruland, Chief
Nuclear Materials Safety Branch 1
Division of Nuclear Materials Safety

Enclosure:
Inspection Report No. 03002939/2001001

cc:

Robert D. Forrest, Radiation Safety Officer
Commonwealth of Pennsylvania

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REGION I

INSPECTION REPORT

Inspection No.	03002939/2001001
Docket No.	03002939
License No.	37-00118-07
NMED Tracking No.	010413
Licensee:	University of Pennsylvania
Address:	Radiation Safety Office 1412 Blockley Hall Philadelphia, PA 19104-6021
Other Locations Inspected:	University of Pennsylvania Medical Center
Inspection Date:	May 7, 2001
Date Followup Information Received:	May 9, May 16, June 4, and November 30, 2001

Inspector: **Original signed by:** **December 21, 2001**

Penny Lanzisera (date)
Senior Health Physicist

Approved By: ***Original signed by William H. Ruland*** ***December 21, 2001***

William H. Ruland, Chief (date)
Nuclear Materials Safety Branch 1
Division of Nuclear Materials Safety

EXECUTIVE SUMMARY

University of Pennsylvania
NRC Inspection Report No. 03002939/2001001

An announced special inspection was performed on May 7, 2001, to review the circumstances surrounding a misadministration that was reported to the NRC by the licensee on May 5, 2001. The misadministration involved a leaking iodine-125 (I-125) source that was implanted into the prostate of a patient on May 4, 2001. Following the completion of an implant involving 94 I-125 sources of approximately 0.5 millicuries each, the licensee's radiation safety staff noted that an applicator needle used during the implant was contaminated. After further measurements of the operating room, the patient's thyroid, and the applicator needle, the licensee determined that the leaking source was implanted within the patient. The licensee further concluded that since only one needle was found contaminated, the leaking sources involved a maximum of 4 sources, with the most probable scenario of 1 leaking source. The licensee's review of the root causes concluded that the most likely cause of the incident, was that the cold-cup forceps had cut into a source during removal of the source from the bladder by the urologist for re-implantation by the radiation oncologist. (Section I)

The licensee submitted a written report dated May 16, 2001, as required by 10 CFR 35.33, and described corrective and preventive actions taken to prevent similar incidents in the future. (Section I)

The NRC contracted a medical consultant to review the incident, its effect on the patient, and the licensee's corrective actions taken to prevent recurrence of similar incidents. The medical consultant's report was received via e-mail on November 30, 2001, and concluded that "at this dose level in an adult male there is no significant risk for a secondary malignancy (Section I). In addition, the medical consultant concluded that the licensee's corrective actions were appropriate for the case.

Within the scope of this inspection, no violations were identified.

REPORT DETAILS

I. Event Description

a. Inspection Scope

The inspection focused on a review of the prostate implant program and the circumstances surrounding the reported misadministration, in accordance with 10 CFR 35.33, involving a leaking I-125 source. The inspection of the event consisted of observations by the inspector, interviews with involved personnel, and a selected examination of records describing the event and followup actions. A chronology of the event is described below.

b. Observations and Findings

Prostate Implant Program

The licensee performs approximately 50 permanent implants for prostate cancer annually. I-125 is currently used for all prostate implants.

Incident Chronology

May 2 — 180 I-125 seeds for two prostate implants were received by the medical physicist in the source storage room. The package was surveyed for exposure rates by the medical physicist and registered 0.2 milliRoentgen/hour measured on contact to the package and no measurable readings at 3 feet from the package. A wipe test of the package indicated no detectable activity. Two patients were scheduled for prostate implants on May 4, 2001.

May 3 — The medical physicist selected 10 seeds from the first batch of 94 seeds and 8 seeds from the second batch of 86 seeds for calibration. The seeds were reported from the manufacturer with activities of between 0.507 and 0.533 millicuries per seed. The seeds were calibrated in a well ion chamber, corrected for temperature and pressure. The seeds were within 1.3% of the manufacturer's calibration, and deemed acceptable for use. The medical physicist visually inspected the needles to be used for implants for any bends or breaks. No bends or breaks were noted. The medical physicist loaded the seeds into applicator needles for the implants, in the source storage room, with the use of tweezers. The tray used for the source preparation was surveyed and found at background dose levels.

May 4
10:00 a.m. — Prior to the implant, the written directive was reviewed and signed by the authorized user. The written directive noted that 94 seeds, with a total activity of 48.88 millicuries, were to be implanted into the patient to deliver a dose of 160 Gray to the treatment site. The loaded needles were

brought to the operating room and the radiation oncologist implanted the 94 sources into the patient's prostate. The urologist performed a cystoscopy on the patient after the implant, and noted that 4 seeds were located in the bladder. The urologist removed the 4 seeds from the bladder with cold-cup forceps, which are designed with sharp jaws to cut into soft tissue to remove tumors, and the seeds were loaded into a clean needle and re-inserted by the radiation oncologist into the prostate. The patient was catheterized and a urine bag was secured to the side of the patient's leg. During the cystoscopy, the operating nurse called the radiation safety staff to perform radiation surveys of the patient, equipment used during the implant, and the operating room. According to the radiation oncologist, the implant appeared routine and no difficulty was encountered when loading the 4 sources into the clean needle. The radiation surveys were performed by the radiation safety staff and a measurable exposure rate on the needles used during the implant was identified. The radiation safety staff conducted further radiation surveys and narrowed the item down to one needle. Discussions with the radiation safety staff indicated that the staff believed that the needle contained a stuck I-125 source. The needle was placed in a plastic bag and secured in the radiation safety instrument calibration room. The radiation safety staff indicated that gloves were worn during all surveys and subsequent handling of the needle. All other surgical equipment was found to be at approximately background dose rates and released.

4:30 p.m. The needle was investigated further by the radiation safety staff, and the staff noted that a seed was not lodged in the needle. The entire length of the needle plunger and the sheath were then wiped by the staff, with measurable results, as indicated in the table below.

7:00 p.m. Once removable contamination was identified on the plunger, the staff immediately re-surveyed all areas where the I-125 seeds had been stored and handled. The areas included the source storage room, template storage area, surgery clean room, operating room, and operating room autoclave. Additionally, the tweezers used to load the seeds into the needles, the package used for shipping the sources, and the source vial were surveyed. All contamination surveys and ambient dose rate surveys were found to be at approximately background levels. Discussions with the medical physicist confirmed that the ion chamber used to measure the activity of the I-125 seeds was free of contamination, i.e., the background measurement prior to seed measurement was zero and after seed measurement was zero.

8:30 p.m. A bioassay of the patient's urine was taken and found to be positive. The bioassay results are provided in the table below.

9:00 p.m. Potassium iodide was administered to the patient to block the uptake of I-125 by the thyroid. The original prescription was written for 3 days by the radiation oncologist.

May 5
10:30 a.m. The radiation safety staff conducted direct measurements of the patient's thyroid, which were positive. The survey results are provided in the table below.

11:30 a.m. The patient was released from the hospital.

12:00 p.m. A survey of patient's room was performed by the radiation safety staff. All results were approximately background.

May 7 The radiation oncologist extended the potassium iodide prescription for 1 month.

May 8 The licensee decided to continue thyroid bioassay measurements to ascertain the effectiveness of the potassium iodide on blocking the thyroid. The patient returned to the hospital for follow-up. During the follow-up, the radiation safety staff collected thyroid and urine bioassay samples. The results of the analysis are provided in the table below. The licensee noted that the activity in the urine was decreasing and the activity in the thyroid had increased. The licensee also measured the dose rate from the urine bag and noted a contact dose rate of 0.2 milliRoentgen/hour. The urine bag was removed from the patient.

May 16 The patient returned to the hospital for follow-up. During the follow-up, the radiation safety staff performed a thyroid bioassay. The results of the analysis are provided in the table below.

May 31 The patient returned to the hospital for follow-up. During the follow-up, the radiation safety staff performed a thyroid bioassay. The results of the analysis are provided in the table below.

DATE AND TIME	TYPE OF MEASUREMENT	GROSS COUNTS PER MINUTE	BACKGROUND (CPM)	NANOCURIES
May 4 7:00 p.m.	Needle Plunger Swipe	81154	27	47.4
May 4 7:00 p.m.	Needle Sheath Swipe	580	27	0.32
May 4 8:30 pm	Urine Aliquot	202576	20	23.7/milliliter
May 4 8:30 pm	Urine Aliquot	202432	20	23.7/milliliter
May 4 8:30 pm	Urine Aliquot	205859	20	24.1/milliliter

DATE AND TIME	TYPE OF MEASUREMENT	GROSS COUNTS PER MINUTE	BACKGROUND (CPM)	NANOCURIES
May 5 10:30 am	Thyroid	1292	10	318
May 8 10:00 am	Thyroid	3668	10	907
May 8 10:00 am	Urine Aliquot	109649	30	12.8/milliliter
May 8 10:00 am	Urine Aliquot	113273	30	13.2/milliliter
May 8 10:00 am	Urine Aliquot	109687	30	12.8/milliliter
May 16 10:00 am	Thyroid	not reported	not reported	1030
May 31 2:30 pm	Thyroid	not reported	not reported	2590

Based on the above data, the licensee concluded that the patient would not encounter complications from the misadministration and that no clinically observable effects were expected as a result of the thyroid dose. The licensee also determined during their investigation that: i) only 1 source was damaged during the implant; ii) the source was damaged when using the cold-cup forceps; iii) the implant needles are not re-used for treatments so contamination was not spread; iv) only one needle was contaminated, since the needle was manufactured by a manufacturer different from the needles originally loaded for the treatment; v) the source was damaged during removal of the source from the bladder and prior to placing in the new needle; and vi) the contamination was limited to the needle, since no other areas were found contaminated.

Notification of the Incident

On May 5, 2001, the licensee notified the NRC Operations Center of the misadministration involving a leaking I-125 source, as required by 10 CFR 35.33. During the inspection on May 7, 2001, the authorized user stated that the patient was notified of the incident on May 4, 2001 and that the referring physician was notified as soon as possible, on May 7, 2001. A written report of the incident was submitted to the NRC on May 16, 2001, as required by 10 CFR 35.33. According to the radiation safety officer and the authorized user, a copy of the report was also provided to the referring physician and the patient.

No violations of 10 CFR 35.33 requirements were identified.

Medical Consultant's Evaluation of the Incident

In accordance with the NRC's Medical Event Assessment Program, NRC contracted a medical consultant to review the misadministration and assess the probable deterministic effects of the leaking source on the patient.

In their letter dated May 16, 2001, the licensee stated that " the effect on the individual who received the misadministration was an unintended thyroid dose of approximately 4.1 rads" and that "no clinically observable effects are expected as a result of this thyroid dose." Based on thyroid bioassay measurements made on May 31, 2001, the licensee revised their dose estimate to the thyroid to 13.3 rads. Subsequent discussions with the radiation safety officer confirmed that the licensee continued to support their previous statements about the effect on the patient.

The medical consultant, in her report dated November 30, 2001, stated that "the case appears to be handled appropriately." Therefore, the medical consultant concluded that "at this dose level in an adult male there is no significant risk for a secondary malignancy."

Licensee's Corrective and Preventive Actions

During the inspection conducted on May 7, 2001, and in a letter dated May 16, 2001, the licensee provided the following corrective and preventive actions:

1. Prior to re-implanting sources removed from the bladder back into the patient's prostate, the sources will be placed on a gauze pad, which will be analyzed for radioactive contamination. Additionally, the forceps used for removal of the sources will be surveyed for contamination. If contamination is found, the sources will not be re-implanted.
2. The use of vacuum type tweezers for source loading will be investigated, instead of the use of sharp tipped tweezers.
3. The use of cold-cup forceps for source retrieval will be reviewed along with possible alternatives for source retrieval.
4. Contamination surveys of previous shipments and vials from the source manufacturer were reviewed and indicated no contamination concerns or leaking sources.
5. The administration of potassium iodide, to limit uptake to the thyroid, was administered immediately once contamination was verified.

c. Conclusions

Due to a leaking source being implanted into the prostate of a patient, the I-125 was taken up in the patient's thyroid and resulted in an unplanned dose to the thyroid. According to the medical consultant and the authorized radiation oncologist, during any prostate implant, the dose to the bladder from the implant is significant, and therefore any additional dose from a 0.5 millicurie leaking I-125 source would be minor.

The licensee's implemented corrective actions appear to be comprehensive and include steps that will minimize re-implantation of leaking sources in the future.

No violations of 10 CFR Part 35 or 10 CFR Part 20 requirements were identified.

II. Quality Management Program

a. Inspection Scope

The licensee's submitted quality management program was reviewed during the inspection. In particular the quality management program implementation and adequacy for prostate implants was reviewed. The inspection of the quality management program developed in accordance with 10 CFR 35.32 consisted of a selected examination of records documenting the quality management program and its implementation in this case and interviews of licensee personnel.

b. Observations and Findings

10 CFR 35.32(a) requires, in part, that the licensee establish and maintain a written quality management program to provide high confidence that byproduct material or radiation from byproduct material will be administered as directed by the authorized user.

To meet the objectives of 10 CFR 35.32(a), the licensee's quality management program requires: i) an authorized user will sign and date a written directive prior to implantation of brachytherapy sources; ii) prior to implantation, the patient will be identified by at least two methods and the items in the written directive will be verified; iii) a treatment plan will developed which shall contain the number of sources, the source strength, and, if applicable, the loading sequence; iv) an authorized user or the physicist will review the treatment plan to assure the final plans of treatment and related calculations are in accordance with the written directive; and v) the individual who administers the dose shall date and sign or initial a record of the treatment after the brachytherapy procedure is completed.

The inspector confirmed that an appropriate written directive was prepared and signed and the patient was verified prior to implantation. The inspector also confirmed that the authorized user verified the plan of treatment with the physicist prior to the implantation. A written record of the treatment was appropriately prepared and signed and dated by the authorized user who was involved in the implantation.

While the licensee's quality management program does not require leak testing of all sealed sources prior to implanting in a patient, the licensee does perform a measurement of the empty source vial to ensure no contamination remains on the vial prior to disposal. The vials containing the sources used in this implant were found to be free of contamination.

c. Conclusions

The licensee's implementation of their quality management program specific to prostate implants is adequate and meets the requirements in 10 CFR 35.32. No violations of 10 CFR 35.32 requirements were identified.

III. Facilities and Equipment

a. Inspection Scope

The inspection reviewed the licensee's equipment used for surveys in this incident. Surveys conducted by the licensee included area radiation level surveys, radioactive contamination surveys, and bioassay measurements. The calibration of the equipment used for each survey and the adequacy of the instrumentation for the survey were reviewed.

b. Observations and Findings

The inspector collected the following information with regards to surveys conducted in this event:

i. A Wallac Wizard Automatic Gamma Counter was used for analyzing wipes and urine. The background on this instrument was approximately 20 counts per minute (cpm) with a 77% efficiency for I-125. The minimal detectable activity for I-125 was 0.02 nanocuries and the instrument's calibration factor was approximately 6E-4 nanocuries/cpm. The licensee used a mock I-125 source and a cesium-137 source for calibration of the counter.

Ii. A Ludlum Model 3 with a Ludlum Model 44-3 Sodium Iodide (NaI) low energy probe was used for surveys of the equipment and operating room. The instrument was calibrated in-house with a cesium-137 source on February 19, 2001.

Iii. A Ludlum Model 44-3 NaI low energy probe connected to a Ludlum Model 2221 scaler was used for thyroid bioassay measurements of the patient. The scaler was calibrated on July 19, 1995 by Ludlum. The detection system was calibrated for measuring the patient's thyroid using the swipe of the contaminated needle and using the patient's urine collected the night of the incident. According to the licensee's facsimile dated May 9, 2001, the urine activity was determined using the Wallac Wizard Gamma Counter, placed in a lucite thyroid phantom, and the remainder of the phantom source holder filled with water. Measurements of the activity in the thyroid phantom were made with the probe on contact and at 10 centimeters from the phantom. Surveys of the patient were taken at 10 cm. The minimal detectable activity of the instrument for I-125 was 4.88 nanocuries in the laboratory and 4.3 nanocuries in the field, with an efficiency of 4.03 counts per minute/nanocurie. The background of the detector was 10 counts per minute.

In addition, confirmatory measurements of the equipment room and the contaminated needle were performed by the inspector with a Ludlum Model 44-21 probe connected to a Ludlum Model 16 analyzer that was calibrated on January 15, 2001. The background in the area varied from 50-100 counts per minute. Measurements on the needle were approximately 50 counts per minute above background. Measurements of the equipment room were at background.

c. Conclusions

The licensee's instrumentation used for surveys conducted of their facility, the contaminated needle and the patient were appropriate for the use and were appropriately calibrated. No violations of 10 CFR Part 20 or 10 CFR Part 35 requirements were identified.

IV. Exit Meeting

An exit meeting was conducted with the staff identified in the next section at the conclusion of the inspection on May 7, 2001. On May 8, 2001, the inspector informed the licensee that a medical consultant had been contracted to review the reported incident. On November 30, 2001, the inspector informed the licensee of the medical consultant's conclusions.

PARTIAL LIST OF PERSONS CONTACTED

Licensee
*Robert Forrest, Radiation Safety Officer
*William Davidson, Radiation Safety Staff
Richard Whittington, M.D., Radiation Oncology
Indra Das, Ph.D., Chief of Clinical Physics
Gregory Desobry, Medical Physicist

*indicates presence at exit meeting

NRC Medical Consultant
Nora Janjan, M.D.