UNITED STATES
NUCLEAR REGULATORY COMMISSION
REGION II
101 MARIETTA ST., N.W.
ATLANTA, GEORGIA 30323

Report No: 52-01946-07/89-01

Licensee: University of Puerto Rico
San Juan, Puerto Rico

Docket No: 030-13584 License No: 52-01946-07

Facility Name: University of Puerto Rico
Medical Science Campus

Inspection Conducted: March 16, 17, and 20, 1989

Inspector: _____ 5/12/89
E. B. Kline, Radiation Specialist Date Signed
Nuclear Materials Safety Section
Nuclear Materials Safety and Safeguards Branch

Approved by: _____ 5/24/89
Charles M. Hosey, Chief Date Signed
Nuclear Materials Safety Section
Nuclear Materials Safety and and Safeguards Branch
Division of Radiation Safety and Safeguards

SUMMARY

Scope: This special, announced inspection was performed to review the circumstances and events surrounding a phosphorus-32 (P-32) therapeutic misadministration and included a review of the organization and administration of the radiopharmaceutical therapy program; operation and quality control of the dose calibrator; procedures and protocols for administering P-32; training and experience of authorized users and technologists; quality assurance program to mitigate therapeutic misadministrations; management's involvement in the radiation safety program; and auditing of the radiation safety program by the Radiation Safety Officer.

Results: No violations or deviations were identified. A Confirmation of Action (COA) letter dated March 27, 1989, was issued by the NRC to confirm actions taken or to be taken to assure accurate determinations of P-32 therapy dosages prior to administration, proper training of all authorized users and technologists who handle P-32 for therapeutic applications, and an evaluation of the cause of the dose calibrator inaccuracies.

REPORT DETAILS

1. Persons Contacted

*I. Guzman, Acting Dean of Administration
*N. Ildefonso, Director of Occupational Safety Office
*F. Silva, M.D., Director of Nuclear Medicine Laboratory
S. Gracia, M.D., Staff Nuclear Medicine Physician
J. Negron, M.D., Staff Nuclear Medicine Physician
W. Ruiz, M.D., Staff Nuclear Medicine Physician
*S. Gomez, Radiation Safety Officer
J. Negron, Nuclear Medicine Technologist
J. Veliazquuz, Nuclear Medicine Technologist
I. Martin, Nuclear Medicine Technologist
S. Torres, Nuclear Medicine Technologist

*Attended Exit Interview

2. Scope of Program (87100)

The Nuclear Medicine Laboratory uses primarily technetium-99m (Tc-99m) radiopharmaceuticals for diagnostic studies. The laboratory performs approximately 475 diagnostic studies using Tc-99m per month. The licensee also performs approximately 10 diagnostic studies per month using xenon-133 (Xe-133). In addition, liquid iodine-131 (I-131) and phosphorus-32 (P-32) are used for therapeutic applications. The laboratory performs approximately between 15 and 20 therapeutic studies per month using I-131, and approximately between 2 and 4 therapeutic studies per month using P-32.

3. Organization (87100)

The inspector reviewed the licensee's organization and management controls in the Nuclear Medicine Laboratory. The inspector also reviewed the licensee's program for controlling and administering therapeutic quantities of radiopharmaceuticals. The Nuclear Medicine Laboratory is staffed by five (5) physicians and four (4) technologists. The hospital employs a Radiation Safety Officer who is responsible for all uses of radioactive material at the university under a broad scope license (NRC License No. 52-01946-07).

4. Circumstances Relative to Misadministration (92700)

On March 10, 1989, during a routine review of patient charts, the Director of the Nuclear Medicine Laboratory and a staff Nuclear Medicine Physician discovered that on March 7, 1989, another staff Nuclear Medicine Physician delivered 24 millicures of a colloidal suspension of chromic phosphate P-32 via instillation into the peritoneal cavity of a patient in the Nuclear Medicine Laboratory. The licensee's procedure called for the administration of 15 millicuries of P-32. The individual who discovered

the misadministration usually administers all therapeutic quantities of P-32. The Director of the Nuclear Medicine Laboratory immediately notified the Radiation Safety Officer of the therapeutic misadministration.

The Radiation Safety Officer (RSO) immediately notified NRC Region II on March 10, 1989, of the therapeutic misadministration. The (RSO) conducted an investigation and determined that the staff Nuclear Medicine Physician who administered the therapeutic dose of P-32 did not follow current established procedures. Licensee procedure (Protocol for Instillation of P-32 for Ovarian Cancer) requires the instillation of 15 millicuries of P-32. Therefore, the misadministration was determined to be in error by +60 percent.

5. Inspection Results (92700)

a. Accuracy of Dose Calibrator

The inspector determined that the alleged 24 millicurie P-32 therapeutic dose administered on March 7, 1989, should have been calculated to be 17.3 millicuries on March 7, 1989, and not 24 millicuries. The 17.3 millicurie dose calculation was based on the assay data supplied by the radiopharmaceutical company which stated that the vial of P-32 would contain 15 millicuries as of March 10, 1989. A review was initiated to determine whether the radiopharmaceutical supplier had mislabeled the P-32 vial or the licensee had incorrectly measured the P-32 in the dose calibrator.

The inspector contacted the radiopharmaceutical supplier to determine if the supplier had erroneously assayed or mislabeled the P-32 vial used by the University of Puerto Rico on March 7, 1989. The supplier's technical representatives appeared confident that the assay data was correct as indicated on the P-32 vial. The representative described their current nuclear pharmacy QA program and their mechanisms for assaying P-32 therapy doses.

The inspector reviewed the licensee's dose calibrator quality assurance testing performed between March 3, 1988, and March 20, 1989. License Condition 12 requires the accuracy, linearity, constancy, and geometry of the dose calibrator measurements to be within ±5 percent of calculated values. All testing of the dose calibrator was performed as required and determined to be within acceptable tolerances.

No major repairs had been performed on the dose calibrator over the past seven (7) years. The dose calibrator was in-line with other high voltage equipment and did not incorporate a high voltage regulator. Consideration was given to the effects of high voltage "spikes" in the same line and their influence on the operation of the dose calibrator. Subsequent dose calibrator measurements indicated consistently similar measurements (precision) but questionable

correct values (accuracy) when measuring P-32. Therefore, it appeared unlikely that the dose calibrator was significantly influenced by high voltage disturbances in the same electrical circuit.

The inspector observed the RSO perform multiple measurements of 15 mCi vials in the licensee's dose calibrator (specific activity of each vial was 3.3 mCi/mg). Each vial contained three milliliters of chromic phosphate P-32 suspension prepared by the supplier. The contents of each vial were then transferred to 5cc disposable syringes. Identical measurements were performed with the syringes. The appropriate correction factors for geometry, volume configurations, and material density differences were applied as described in the dose calibrator operating instructions. As has been established in literature, the material density differences of glass versus plastic, when measuring vials versus syringes, can dramatically change the dose calibrator readout for P-32. If correction factors are not used, the readout for the syringe will be definitely higher. This is predictable because geometries and the absorptions are different. The glass vial contains silicon and its density is relatively high (2.5 gm/cc); the syringe is polypropylene, a carbon-based material, and its density is much lower (0.9 gm/cc). Using the appropriate correction factors supplied by dose calibrator manufacturers, the dose calibrator readout for syringes varied by approximately +33-44% when compared to the radiopharmaceutical supplier's assay data for the P-32. The radiopharmaceutical supplier stated a tolerance of ±10% in prescribed radiopharmaceutical dose versus actual dose. The radiopharmaceutical supplier technical personnel stated that the error is usually ±5%. Also, background measurements made on the dose calibrator's P-32 channels indicated "out of range" readouts for approximately 75 percent of the background measurements. Background in the Nuclear Medicine Laboratory was measured by the licensee and found to be within normal values.

The RSO performed identical measurements using P-32 at a local Veterans Administration Medical Center - Nuclear Medicine Department. The measurements were performed on two (2) calibrated dose calibrators manufactured by a different company than the one used by the licensee. Comparable readings were obtained using the V.A.'s dose calibrators under identical experimental conditions when measuring P-32 in plastic syringes. The syringe measurements in both V.A. dose calibrators varied by approximately -11% when compared to the supplier's assay data for P-32. The differences in the V.A. Medical Center's dose calibrators and the University of Puerto Rico's dose calibrator when measuring in syringes was approximately +62%.

Based on these apparent errors in the licensee's dose calibrator measuring system, correction factors were used by the inspector and RSO in order to reconstruct what true P-32 dose was delivered to the therapy patient on March 7, 1989. The University of Puerto personnel who measured the P-32 doses in syringes used a correction factor which produced an apparent error of +44%. Therefore, the actual,

calculated dose delivered appears to have been approximately 13.44 mCi instead of 24 mCi as originally reported to the NRC. Therefore, the error in the administration of the prescribed dose versus the actual dose appears to be approximately -10.4% instead of +60%.

b. Other Possible Misadministrations (92700)

The inspector interviewed each Nuclear Medicine Physician and technologist who had prepared, handled, or administered P-32 in the licensee's Nuclear Medicine Laboratory. All individuals, except for the Nuclear Medicine Physician who assayed the P-32 involved in the misadministration, measured current and past P-32 therapy doses in the original manufacturer's 10cc glass vials in the dose calibrator. Dose calibrator errors in measuring the glass vials were approximately +12.7% when using appropriate calibration factors. Therefore, of greatest concern were the patients who had been administered P-32 that was measured in the plastic syringe where errors may have approximated +44%.

Two (2) other patients were administered P-32 therapy doses on March 7, 1989, by the same Nuclear Medicine Physician who administered the P-32 dose discussed above. These patients' doses were measured in the plastic syringe configuration in the dose calibrator. It appears these 2 patients received approximately 10.64 and 12.32 mCi doses of P-32 instead of the prescribed 15 mCi doses. The errors were calculated to be approximately -29.1% and -17.9%, respectively.

The inspector reviewed medical records for therapies performed between August 31, 1984 and March 20, 1989. No other patients appeared to receive a therapeutic dose of P-32 which differed from the prescribed dose by more than ±10%. Also, all prior patients appeared to have been administered P-32 which was measured in the dose calibrator using the manufacturer's glass vial and not the plastic syringe.

6. Exit Interview

The inspection findings were discussed in an exit interview with those indicated in Paragraph 1. The inspector reviewed the areas inspected and discussed the following weaknesses identified in the licensee's program for the therapeutic misadministration of P-32:

(1) Clear and detailed procedures for determining the activity of P-32 have not been established.

(2) Nuclear Medicine Physicians are not required, in writing, to follow the established department protocol for patient therapy using P-32.

(3) A QA program or "double check" mechanism to mitigate therapeutic misadministrations has not been established.

(4) A program to ensure correct and accurate operation of the dose calibrator for P-32 has not been established.

(5) Training for all authorized users and technologists in procedures regarding the determination of P-32 dose, and clinical protocol for P-32 therapeutic applications has been inadequate.

The licensee acknowledged the NRC concerns and provided no dissenting comments. A CAL was issued by the NRC on March 27, 1989, to document actions to be taken by the licensee to insure the accuracy of doses of P-32 used for therapeutic applications.