

November 17, 2006

U.S. Nuclear Regulatory Commission  
Region III  
Materials Licensing Section  
2443 Warrenville Road, Suite 210  
Lisle, Illinois 60532-4352

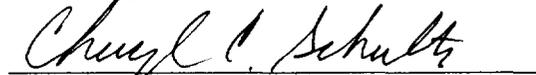
RE: Possible Medical Event

Attached is the report of a possible medical event and two printed photographs. IMG-2279 shows the clumping of the Y-90 SIRSheres from the patient's delivery set that was photographed 48 hours after the treatment. Both the medical physicist and Dr. Savin agreed that the clumping was very similar; however, the clumping was distributed throughout the line and not confined to the area of the stopcock as shown in the photo.

IMG-2289 shows our experimental set up. After we prepared the dose for the patient done on Nov. 8, the same amount of dose was prepared in a spare "V" vial with sterile water from what was left of the Y-90 SIRSpheeres in the original shipping vial. A spare delivery set was set up behind appropriate shielding, primed with sterile water and a similar amount of Y-90 microspheres infused by the medical physicist in a simulated injection. This photo was taken 24 hours after the experiment.

Please contact the Corporate Radiation Safety Officer if you have any questions or require additional information (248-551-0548).

Sincerely,



Cheryl Culver Schultz, M.S.  
Corporate Radiation Safety Officer

William Beaumont Hospital  
3601 West Thirteen Mile Road  
Royal Oak, Michigan 48073  
NRC License No. 21-01333-01

**Notice of Medical Misadministration**

Licensee: William Beaumont Hospital, 3601 West Thirteen Mile Road, Royal Oak, MI  
Date/Time of Discovery: November 7, 2006 at 1:45 p.m.  
Referring and Attending Physician: Michael Savin, M.D.  
Authorized User: Michael Savin, M.D.

Date of Report: November 13, 2006

**A. Description of Event**

A possible medical event occurred on Tuesday, November 7, 2006 at 1:10 p.m. A patient prescribed a dose of 0.36 GBq (9.8 mCi) received 0.24 GBq (6.5 mCi) Y-90 microspheres (Sirtex SIRSpheres) for the treatment of liver cancer. The Y-90 microspheres were prescribed for treatment of colon metastases to the left lobe of the liver. The right lobe of the liver was successfully treated on September 26, 2006 with 1.35 GBq (36.8 mCi). The prescribed dose was 1.34 GBq (36.5 mCi).

The radiopharmacist in Nuclear Medicine prepared the dose prior to administration by withdrawing the required volume from the shipping vial, transferring it to the administration or "V" vial that was prepared with about 2.5 cc of sterile water, and assaying it in the dose calibrator, while the radiopharmacy technician observed the whole process. The authorized user and radiopharmacist confirmed the dose activity in the dose calibrator (0.399 GBq or 10.78 mCi at 1:00 p.m. on November 7, 2006) and both initialed the dose label.

The authorized medical physicist assembled the delivery device in accordance with the manufacturer's instructions and documented this on the Check List and Data Form for SIRSphere Treatment, with the angiography technologist's assistance. The authorized physician checked the set up with the documentation on the Check List and proceeded with the therapy administration. He carefully observed the Y-90 microspheres in the "V" vial as he injected the sterile water from the injection syringe. He watched to ensure that the Y-90 microspheres did not rise too close to the septum of the "V" vial, which has caused minor leakage to occur on a previous occasion. When approximately half of the dose volume was administered, the physician stopped because he planned to flush the "A" line (between the delivery device three way stop cock connection and the intra-arterial catheter) and inject contrast to perform angiography. Up to this time neither he nor the medical physicist noted any problem with the injection. When he stopped the Y-90 injection, he noticed that some of the Y-90 microspheres in the injection tubing ("C" line between the "V" vial and the three way stopcock) appeared to be clumped together, in non-spherical configuration, noticeably visible, and non-uniformly distributed in the tubing. He then noted similar yet a much less amount of clumping in the "A" line. After discussion with the authorized medical physicist, the authorized physician decided to

infuse the Y-90 microspheres that were in the intra-arterial catheter into the patient by flushing with sterile water, so that he could then proceed with the contrast injection and angiography. During the contrast injection and angiography, the physician encountered slow flow in the left hepatic artery. The physician decided to terminate the therapy administration at this time (1:15 p.m.) because of the slow flow which would prevent further microspheres from being administered.

The medical physicist measured 41% residual activity in accordance with the post administration protocol and notified the authorized user. The authorized physician modified the written directive to a prescribed dose of 0.24 GBq (6.5 mCi) of Y-90. The reason for the modification was documented by the authorized physician on the Quality Management Form as follows: "1) slow flow in the left hepatic artery, 2) clumping of SIR-Spheres identified in tubing." The medical physicist notified the Radiation Safety Officer (RSO) on November 7, 2006 at 3:45 p.m.

## **B. Why the Event Occurred**

The patient received 41 percent less than the prescribed dose. The authorized physician terminated the dose administration because of low flow in the left hepatic artery, which was probably caused by the patient's vasculature. Once the vessels are embolized, flow is decreased, preventing further infusion of the microspheres. A contributing factor was that authorized physician, through his careful observation, noted that some of the Y-90 microspheres were clumped in an unusual, non-spherical, and non-uniform configuration, which could compromise the dose distribution. The clumping could have contributed to or possibly caused the low flow to occur; however, there is no way to prove whether it had any effect at all.

The manufacturer recommends the use of sterile water rather than saline in the preparation of the "V" vial and priming of the tubing in the delivery device. The radiopharmacist who prepared the "V" vial remembers selecting the sterile water vial. The sterile water is stored separate from the saline vials. The radiopharmacy technician who observed the dose preparation confirmed that there was nothing unusual in the preparation. After terminating the treatment, both the authorized user and medical physicist confirmed that sterile water was used to prime the delivery device by checking the labels on the empty vials used to fill the syringes and actually taste testing the remaining contents of the syringe used to prime the delivery device. According to both the Sirtex representative and medical director, clumping was reported one time previously from exposure of the Y-90 microspheres to contrast media. The contrast media was kept separate from the delivery device. Syringes for contrast media have a different color, size, and label. Only the authorized physician withdrew the contrast media into the syringe prior to injection. Contrast media cannot be introduced into the delivery device tubing ("C" line) from the intra-hepatic tubing because the three way stopcock prevents backflow. It was confirmed that sterile water was used to prime the delivery device tubing. The clumping was observed in the "C" line prior to the injection of contrast for the angiography and after the termination of the Y-90 dose administration. We concluded that only sterile water was used in the dose preparation and delivery in

conformance with the manufacturer's instructions. The final cause to be ruled out for the clumping was whether this was a flawed batch of Y-90 SIRSpheres from the manufacturer (lot no. 110986-008).

### **C. The Effect on the Patient**

Based on the residual activity measured, the patient received 59 percent of the prescribed dose. The intended left lobe of the liver dose was 100 Gy and the actual dose delivered was 59 Gy. The Y-90 microsphere clumps that were injected into the patient may have embolized in a more proximal vessel and may not have distributed in as homogenous pattern as intended. This may result in less than the expected therapeutic outcome; however, no dose compensation is planned at this time due to slow flow. No adverse effects are expected.

### **D. What Improvements are Needed to Prevent Recurrence**

A complete investigation was conducted to determine the root cause of the possible medical event. The authorized physician, medical physicist and RSO discussed the following with the manufacturer's medical director on November 7, 2006 at 6:00 p.m. EST: causes and appearance of Y-90 microsphere aggregation, initial results of our investigation indicating that only sterile water was used, effects of clumping on dose distribution, and proposed corrective actions. An incident report was filed by Sirtex, the Y-90 microsphere manufacturer, on November 8, 2006. The delivery set and shipping vial with residual Y-90 microspheres will be stored for decay on site for 30 days then sent to the manufacturer for analysis of the cause for the clumping. The results of the Sirtex analysis will take about 2 weeks.

### **E. Actions Taken to Prevent Recurrence**

The contents of the delivery set including the "V" vial, delivery set, tubing, and intra-hepatic catheter were examined using appropriate shielding on November 8, 2006. While the specific gravity of the microsphere resin (1.6) will cause it to separate out, the clumped microspheres were also clearly visible in the "C" line. Both the authorized physician and medical physicist confirmed that the appearance was similar to what was observed at the time they were administering the dose.

The authorized user, medical physicist and RSO were concerned that a bad batch of Y-90 SIRSpheres from the manufacturer might cause clumping for the therapy patient scheduled on November 8, 2006. When questioned about this the previous evening, the Sirtex medical director assured us that it was very unlikely that clumping would occur since we were receiving a different lot number. The Y-90 dose was received at 9:00 a.m. on November 8, 2006. As a precaution, we ran the following experiment before we administered the Y-90 treatment on November 8, 2006. After the prescribed dose was prepared and assayed, the same amount of dose was prepared in a spare "V" vial with sterile water from what was left of the Y-90 SIRSpheres in the original shipping vial. A spare delivery set was set up behind appropriate shielding, primed with sterile water

and a similar amount of Y-90 microspheres infused by the medical physicist in a simulated injection, while the RSO and radiopharmacist observed the appearance of the microspheres in the plastic tubing. The injection was stopped and the microspheres were observed for several minutes. No clumping occurred and the authorized physician proceeded with the patient's therapy administration.

Once adequate decay in storage has occurred, the Y-90 delivery set and shipping vial used in this medical event will be returned to the manufacturer to determine the possible cause of the clumping. Once we receive the results of the Sirtex analysis, additional corrective actions will be taken as recommended by the manufacturer.

#### **F. Notification of the Patient and Referring Physician**

The referring physician was notified at 1:15 p.m. on November 7, 2006. He notified the patient on 11/9/06 at 1:20 p.m. The patient will receive written notification within 15 days of the event's occurrence.

#### **G. Conclusion**

1. A possible medical event occurred on Tuesday, November 7, 2006 at 1:10 p.m. A patient prescribed a dose of 0.36 GBq (9.8 mCi) received 0.24 GBq (6.5 mCi) Y-90 microspheres (Sirtex SIRSpheres) for the treatment of liver cancer. Based on the residual activity measured after completion of the treatment, the patient received 59 percent of the initially prescribed dose. (59 Gy to the left lobe of the liver instead of 100 Gy).
2. The authorized physician terminated the dose administration because of low flow in the left hepatic artery which was probably caused by the patient's microsphere embolization blocking many of the distal arteries. A contributing factor was that some of the Y-90 microspheres were clumped in an unusual, non-spherical, and non-uniform configuration, which could compromise the dose distribution. The clumping could have contributed to or possibly caused the low flow to occur; however, there is no way to prove whether it had any effect at all.
3. William Beaumont Hospital conducted a complete investigation and took the following actions. We confirmed that only sterile water was used in the dose preparation and delivery in conformance with the manufacturer's instructions. We discussed the following with the manufacturer's medical director on November 7, 2006 at 6:00 p.m. EST: causes and appearance of Y-90 microsphere aggregation, effects of clumping on dose distribution, and proposed corrective actions.
4. The manufacturer, Sirtex, filed an incident report on November 8, 2006. The delivery set and shipping vial with residual Y-90 microspheres will be stored for decay on site for 30 days then sent to the manufacturer for analysis of the cause for the clumping. The results of the Sirtex analysis will take about 2 weeks. Once we

receive the results of the Sirtex analysis, additional corrective actions will be taken as recommended by the manufacturer.

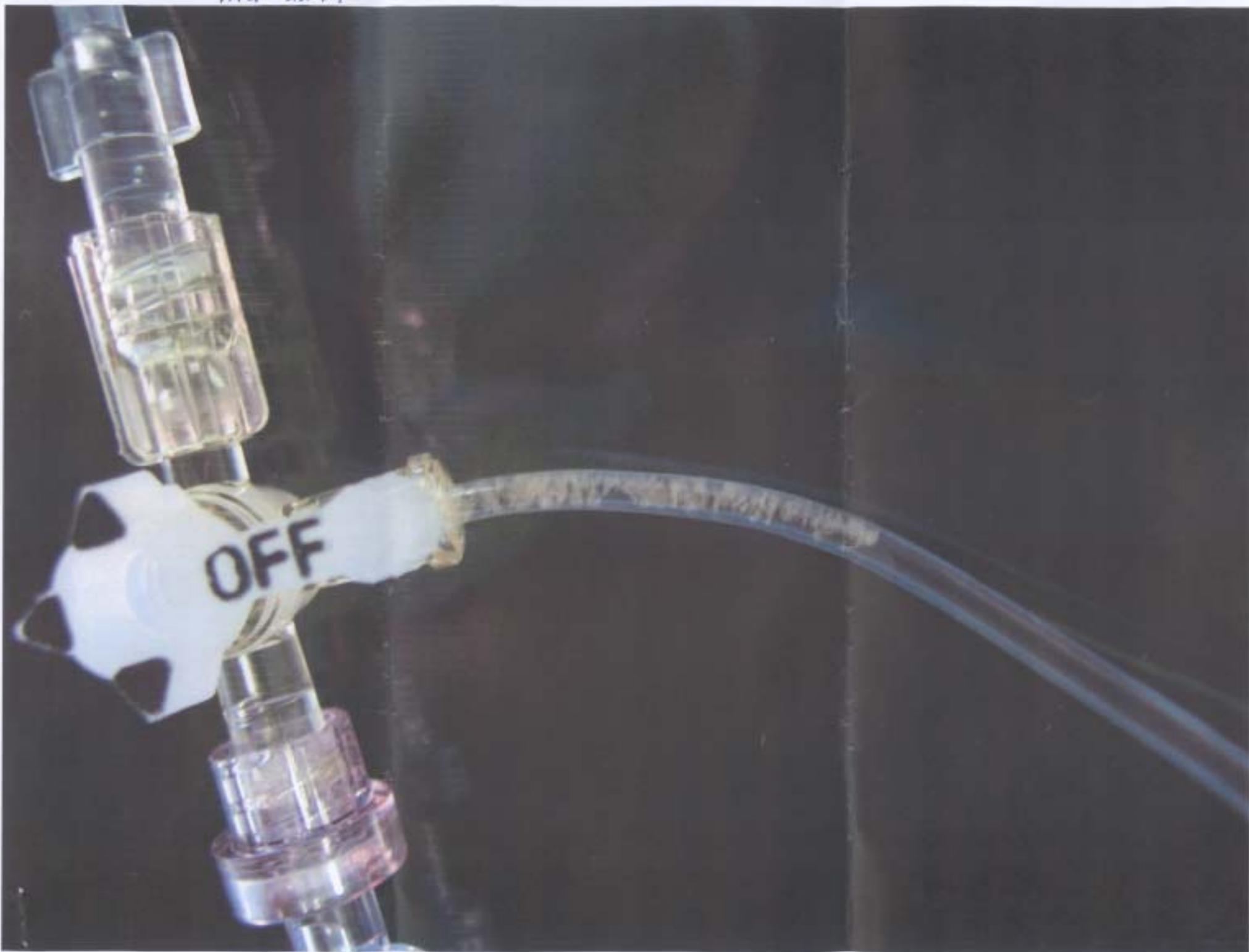
5. This event was reported to the U.S. NRC Operations Center at 10:10 a.m. on November 8, 2006 as a possible medical event. After the RSO explained the event, the NRC staffer did not think that it was a reportable medical event and referred the RSO to Region III. The RSO explained the possible medical event to an inspector in Region III who discussed the event with the acting regional director and with NRC Headquarters. At 4:15 p.m. on November 8, 2006, the Region III inspector instructed the RSO to report this as a possible medical event to the NRC Operations. The RSO reported a possible medical event to NRC Operations at 5:15 p.m. on November 8, 2006 (#42975). The written report will be submitted to NRC within 15 days of the discovery of the medical event as required.
6. This event was reported to the referring physician within 24 hours after the discovery of the misadministration. The patient was notified by the authorized physician on November 9, 2006. The patient will receive a written report within 15 days of the discovery of the medical event as required.
7. No violations of NRC regulations or our Quality Management Program were identified.

Report Prepared By:

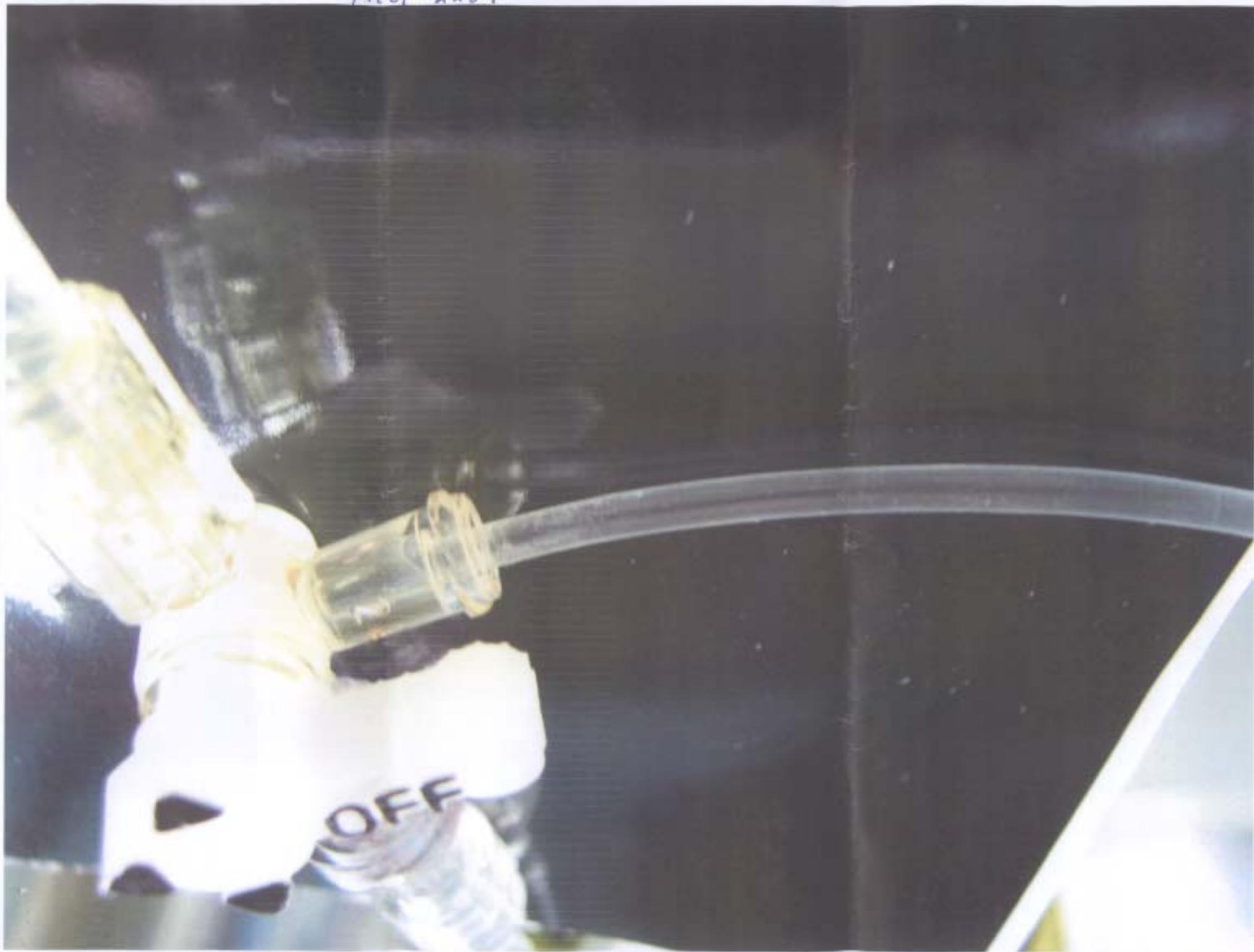


Cheryl Culver Schultz, M.S.  
Corporate Radiation Safety Officer  
November 13, 2006

IMG-2219



1MG-2289



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