UNITED STATES
NUCLEAR REGULATORY COMMISSION
REGION I
2100 RENAISSANCE BLVD.
KING OF PRUSSIA, PA 19406-2713

June 25, 2019

Michael M. Gottesman, M.D.
Deputy Director for Intramural Research
Department of Health & Human Services
National Institutes of Health
Building 1, Room 103
1 Center Drive, MSC0140
Bethesda, MD 20892-0140

SUBJECT: NRC INSPECTION REPORT NOS. 03001786/2019001 AND 03037773/2019001, DEPARTMENT OF HEALTH & HUMAN SERVICES, NATIONAL INSTITUTES OF HEALTH, AND NOTICE OF VIOLATION

Dear Dr. Gottesman:

This letter refers to the inspection conducted on May 13-17, 2019, at your Bethesda, Frederick, Poolesville, and Baltimore, Maryland facilities. This inspection examined activities conducted under your license as they relate to public health and safety, and to confirm compliance with the Commission's rules and regulations and with the conditions of your license. Within these areas, the inspection consisted of selected examination of procedures and representative records, observations of activities, and interviews with personnel.

Based on the results of this inspection, the NRC has determined that a Severity Level IV violation of NRC requirements occurred. Specifically, in 2015 and 2017, two physicians were approved as authorized users for parenteral administrations of any radioactive drug requiring a written directive and neither physician had documented training and experience with parenteral radioactive drugs requiring a written directive in accordance with 10 CFR 35.390(b)(1). The violation was evaluated in accordance with the NRC Enforcement Policy. The current Enforcement Policy is included on the NRC's Web site at https://www.nrc.gov/about-nrc/regulatory/enforcement/enforce-pol.html. The violation is cited in the enclosed Notice of Violation (Notice) because the violation was identified by the NRC.

The NRC has concluded that information regarding: (1) the reason for the violation; (2) the corrective actions that have been taken and the results achieved; and (3) the date when full compliance will be achieved is already adequately addressed on the docket and include: immediately rescinding authorization for administration of parenteral radioactive drugs requiring a written directive by both physicians and confirming that the physicians had not performed the activities; a commitment to have multiple reviews of authorizations by the Radiation Safety Committee to ensure that all required training and experience has been completed; and a cursory review of current authorizations and refresher training which resulted in a memo to a third physician suspending his status as an authorized user for your high-dose rate remote afterloader pending his completion of annual refresher training. Therefore, you are not required to respond to this letter unless the description herein does not accurately reflect your corrective actions or your position. In that case, or if you choose to provide additional information, you

should follow the instructions specified in the enclosed Notice.

In accordance with 10 CFR 2.390 of the NRC's "Rules of Practice," a copy of this letter and your response, if you choose to provide one, will be made available electronically for public inspection in the NRC Public Document Room or from the NRC document system (ADAMS), accessible from the NRC Web site at http://www.nrc.gov/reading-rm/adams.html. To the extent possible, your response should not include any personal privacy, proprietary, or safeguards information so that it can be made available to the Public without redaction.

If you have any questions regarding this matter, please contact Penny Lanzisera of my staff at 610-337-5169 or via electronic mail at penny.lanzisera@nrc.gov.

Thank you for your cooperation.

Sincerely,

/RA/

Donna M. Janda, Chief
Medical and Licensing Assistance Branch
Division of Nuclear Materials Safety
Region I

Docket Nos. 03001786 and 03037773
License No. 19-00296-10 and 19-00296-21

Enclosures:
1. Notice of Violation
2. Inspection Report

cc w/ Enclosures:
Catherine Ribaudo, RSO
State of Maryland

NRC INSPECTION REPORT NOS. 03001786/2019001 AND 03037773/2019001,
DEPARTMENT OF HEALTH & HUMAN SERVICES, NATIONAL INSTITUTES OF HEALTH,
AND NOTICE OF VIOLATION DATED JUNE 25, 2019

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NOTICE OF VIOLATION

National Institutes of Health
Bethesda, MD

Docket No. 03001786
License No. 19-00296-10

During an NRC inspection conducted on May 13-17, 2019, one violation of NRC requirements was identified. In accordance with the NRC Enforcement Policy, the violation is listed below:

> License Condition 22 of License No. 19-00296-10 requires, in part, that the licensee conduct its program in accordance with the statements, representations, and procedures contained in the letter dated July 3, 2012.
>
> Item 7 of the letter dated July 3, 2012, requires, in part, that clinical authorized users (CAUs) meet the training and experience requirements in 10 CFR 35 and are approved by the Radiation Safety Committee (RSC).
>
> Contrary to the above, in 2015 and 2017, two CAUs did not meet the training and experience requirements in 10 CFR 35 and both were approved by the RSC. Specifically, the RSC approved the two CAUs for activities described in 10 CFR 35.390(b)(1) and neither physician had training and experience with parenteral radioactive drugs requiring a written directive. The licensee confirmed that neither physician was involved with the use of parenteral administations requiring a written directive even though incorrectly authorized.
>
> This is a Severity Level IV violation (Enforcement Policy Section 6.3).

The NRC has concluded that information regarding the reason for the violation(s), the corrective actions taken and planned to correct the violation(s) and prevent recurrence and the date when full compliance will be achieved is already adequately addressed on the docket. However, you are required to submit a written statement or explanation pursuant to 10 CFR 2.201 if the description therein does not accurately reflect your corrective actions or your position. In that case, or if you choose to respond, clearly mark your response as a "Reply to a Notice of Violation," and send it to the U.S. Nuclear Regulatory Commission, ATTN: Document Control Desk, Washington, D.C. 20555 with a copy to the Regional Administrator, Region I, within 30 days of the date of the letter transmitting this Notice of Violation (Notice).

If you contest this enforcement action, you should also provide a copy of your response to the Director, Office of Enforcement, United States Nuclear Regulatory Commission, Washington, DC 20555-0001. Under the authority of Section 182 of the Act, 42 U.S.C. 2232, any response which contests an enforcement action shall be submitted under oath or affirmation.

Your response will be placed in the NRC Public Document Room (PDR) and on the NRC Web site. To the extent possible, it should, therefore, not include any personal privacy, proprietary, or safeguards information so that it can be made publically available without redaction. However, if you find it necessary to include such information, you should clearly indicate the specific information that you desire not to be placed in the PDR, and provide the legal basis to support your request for withholding the information from the public.

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

Dated This _25th_ day of June 2019

U.S. NUCLEAR REGULATORY COMMISSION
REGION I

INSPECTION REPORT

Inspection No.	03001786/2019001 03037773/2019001
Docket No.	03001786 03037773
License No.	19-00296-10 19-00296-21
Licensee:	Department of Health and Human Services National Institutes of Health
Location:	Bethesda, Frederick, Poolesville, and Baltimore, Maryland
Inspection Dates:	May 13-17, 2019

Inspectors:

/RA/ ***06/04/19***
Penny Lanzisera date
Senior Health Physicist
Medical and Licensing Assistance Branch
Division of Nuclear Materials Safety

/RA/ ***06/04/19***
Robin Elliott date
Health Physicist
Medical and Licensing Assistance Branch
Division of Nuclear Materials Safety

/RA/ ***06/07/19***
Shawn Seeley date
Health Physicist
Medical and Licensing Assistance Branch
Division of Nuclear Materials Safety

/RA/ ***06/05/19***
Elizabeth Ullrich date
Senior Health Physicist
Commercial, Industrial, R&D, and Academic Branch
Division of Nuclear Materials Safety

Approved By:

/RA/ ***06/25/19***
Donna Janda, Chief date
Medical and Licensing Assistance Branch
Division of Nuclear Materials Safety

EXECUTIVE SUMMARY

Department of Health and Human Services
National Institutes of Health
NRC Inspection Report Nos. 03001786/2019001 and 03037773/2019001

A routine, unannounced team inspection was conducted at the National Institutes of Health (NIH) facilities located in Bethesda, Frederick, Poolesville, and Baltimore, Maryland on May 13-17, 2019. The inspection was performed in accordance with NRC Inspection Procedures 87125, 87126, 87127, and 87134 and reviewed activities associated with the use of licensed materials authorized by License Numbers 19-00296-10 (medical broad scope) and 19-00296-21 (cyclotron production).

The inspectors conducted interviews with NIH personnel, observed day-to-day operations, toured NIH's facilities, and reviewed documents and procedures. Based on the results of this inspection, one apparent violation of NRC requirements was identified. Specifically, in 2015 and 2017, two physicians were approved as authorized users for parenteral administrations of any radioactive drug requiring a written directive and neither physician had documented training and experience with parenteral radioactive drugs requiring a written directive in accordance with 10 CFR 35.390(b)(1). The licensee confirmed that neither physician had used the material in question and issued revised authorizations rescinding this use immediately. Both physicians were appropriately qualified for diagnostic uses of radiopharmaceuticals and iodine-131. License Condition 22 of License No. 19-00296-10 requires, in part, that the licensee conduct its program in accordance with the statements, representations, and procedures contained in the letter dated July 3, 2012. Item 7 of the letter dated July 3, 2012, requires, in part, that clinical authorized users (CAUs) meet the training and experience requirements in 10 CFR 35.

REPORT DETAILS

1. Organization, Oversight, and Scope of the Program

a. Inspection Scope

A routine, unannounced team inspection was conducted on May 13-17, 2019; at the NIH main campus in Bethesda, Maryland; the Integrated Research Facility in Frederick, Maryland; the NIH Animal Center in Poolesville, Maryland; and the Baltimore Research Center (BRC) in Baltimore, Maryland. A temporary jobsite inspection was also conducted on May 13, 2019, at the Montgomery County Fire and Rescue Training Academy in Gaithersburg, Maryland. The inspection was performed in accordance with NRC Inspection Procedures 87125, 87126, 87127, and 87134, and reviewed activities associated with the use of licensed materials authorized by License Numbers 19-00296-10 (medical broad scope) and 19-00296-21 (cyclotron production). The following focus areas were reviewed: (i) security and control of licensed material; (ii) shielding of licensed material; (iii) comprehensive safety measures; (iv) radiation dosimetry program; (v) radiation instrumentation and surveys; (vi) radiation safety training and practices; and (vii) management oversight. In addition, decommissioning activities, releases to the environment, and financial assurance were reviewed.

The inspectors conducted interviews with NIH personnel, observed day-to-day operations, toured NIH's facilities, and reviewed documents and procedures.

b. Observations and Findings

Program Scope and Management Oversight

NIH's radiation safety staff oversees the radiation safety program and is located within the Division of Radiation Safety (DRS) on the main campus of NIH. The staff consists of a Division Director/Radiation Safety Officer (RSO), a Division Director/Deputy RSO/Manager for the cyclotron/PET activities, an Irradiator Manager, two Branch Chiefs, an Executive Secretary, a Radiation Safety Committee (RSC), and a total of 27 support staff (with three vacancies) to carry out the functions of DRS. In addition, approximately 15 contract staff assist DRS in the conduct of routine surveys, package delivery, instrument calibrations, and waste processing.

Several thousand regulatory compliance surveys were conducted by NIH staff and contractors since the last inspection. In 2018, there were approximately 663 posted laboratory modules where 461 authorized users and 3,616 individual users conducted research activities. Most of the laboratory space and clinical facilities are on the main campus in Bethesda, Maryland; however, the licensee has several satellite facilities in Rockville, Baltimore, Poolesville, Gaithersburg, and Frederick, Maryland.

Approximately 24 laboratory protocols, 93 animal study proposals, and 104 clinical research protocols per year are reviewed by the RSC. DRS also performs triennial renewals of protocols previously approved. Approximately 75 percent of all protocols use Positron Emission Tomography (PET) radioisotopes. Clinical protocols are reviewed by one of the 12 Institutional Review Boards and the RSC, as well as the

Radioactive Drug Research Committee (RDRC), as needed. The RSC is actively involved in the licensed program and meets monthly to discuss: (i) NRC licensing and regulatory matters; (ii) RDRC activities; (iii) triennial reviews of permit renewals; (iv) laboratory use of radionuclides; (v) new license permit applications and users; (vi) new clinical protocol applications and users; (vii) personnel exposure monitoring; (viii) annual audit findings; (ix) any events; and (x) any corrective actions for items identified by DRS.

The inspectors reviewed the training and experience approvals of six clinical authorized users (CAUs) and 15 research authorized users performed by the RSC, with most of them found to be appropriately documented. The inspectors also confirmed that the RSC completed approvals of all authorized users to close out the previous violation of License Condition 11.B. of License No. 19-00296-10 for failure to complete one review of an authorized user during/after the government shutdown. For two physicians reviewed during this review period, the inspectors noted that clinical protocols had recently been approved for parenteral administrations requiring a written directive and the physicians approved did not have documented training for these uses. Upon further evaluation, the inspectors noted that in 2015 and 2017, these two physicians were approved as authorized users for parenteral administrations of any radioactive drug requiring a written directive and neither physician had documented training and experience with parenteral radioactive drugs requiring a written directive in accordance with 10 CFR 35.390(b)(1). Both physicians were appropriately qualified for diagnostic uses of radiopharmaceuticals and Iodine-131 (I-131). NIH immediately rescinded authorization for administration of parenteral radioactive drugs requiring a written directive for both physicians and confirmed that neither physician had performed the activities. NIH also performed a cursory review of current authorizations and refresher training which resulted in a memo to a third physician suspending his status as an authorized user for the high-dose rate remote afterloader pending his completion of annual refresher training. At the exit meeting, NIH management committed to have multiple reviews of authorizations by the Radiation Safety Committee to ensure that all required training and experience had been completed.

NIH DRS staff responded to approximately 50 incidents since the last inspection, most of them minor. The inspectors reviewed the following incidents: (i) fluorine-18 (F-18) skin contamination during hot cell work due to line disconnect; (ii) F-18 floor contamination in several areas of a lab due to inadequate surveys when staff worked with zirconium-89 which created a higher than usual background; (iii) exhaust failure that could have resulted in positive airflow into unfinished lab space; iv) spill of germanium/gallium-68 (Ge-68/Ga-68) and Ga-68 dotatate; (v) contamination in cyclotron bathroom and of several personnel's' shoes after inadequate surveys post F-18 production earlier in the day; (vi) leaking bag containing I-131 patient waste identified at the loading dock; (vii) exposure from I-131 patient's emesis; and (viii) phosphorus-32 spill with no personnel contamination. Corrective and preventative actions were reviewed for the above events with no concerns noted. Re-training of involved staff was conducted, as necessary. In addition, the events were confirmed to be below the regulatory reporting requirements and to have met the criteria in the NRC Enforcement Policy (Section 2.3) for a minor violation, when applicable.

Medical Activities Conducted under License Number 19-00296-10

Currently there are approximately 20 staff in Nuclear Medicine including 5 technologists, 32 staff in PET including 7 technologists, and 25 staff supporting the inpatient care of I-131 patients. The nuclear medicine facility currently includes a temporary radiopharmacy, two injection rooms, two quiet rooms, and five cameras. Patients treated with greater than 33 millicuries of I-131 are housed in one of two shielded rooms. All I-131 patients are issued written instructions on methods for controlling exposures to members of the public. The PET research facility includes: a radiopharmacy, quiet rooms, one PET camera, and one PET/CT (computed tomography) unit. The high dose-rate remote afterloader (HDR) is located in the radiation oncology department.

The nuclear medicine department is still in the process of relocating its hot lab, so only unit and bulk doses are being used while the hot lab is in its smaller, interim location. The authorized nuclear pharmacist (ANP) is responsible for assaying all doses prior to administration by the nuclear medicine technologists (NMT). NMTs cover for the ANP when needed. Unit doses of short-lived radiopharmaceuticals are delivered directly to the radiopharmacy by various vendors. All other doses go to DRS, are checked in, and then delivered to nuclear medicine. Technetium-99m (Tc-99m) and F-18 are the primary radioisotopes used in the nuclear medicine department. Currently, NIH performs six to ten nuclear medicine studies per day. In addition approximately five I-131 therapies (inpatients) and 15-20 diagnostic I-131 studies (mostly outpatients) are performed per year. The inspectors reviewed written directives (WDs), room surveys, patient release criteria, and patient release instructions and found them to be acceptable. The inspectors also interviewed nursing staff and fount their training acceptable.

The PET research facility uses F-18, C-11, nitrogen-13 (N-13), and oxygen-15 (O-15) for human and animal research protocols. Other PET radionuclides are also used on rare occasion. F-18, C-11, and N-13 are delivered from the cyclotron to the radiopharmacy via a “rabbit system.” The ANP uses a robotic system for drawing up the dosages and assays them prior to injection by the NMT. Because of the short half-life of O-15, it is delivered directly from the cyclotron to the scan room via a “water on the wall system.” The O-15 system uses isolation valves to contain the activity to be measured and administered. All excess activity in the system that is not located between the isolation valves is pumped back to waste. Since the protocols are all research studies, a signed informed consent form is on file for each patient prior to the dose administration. Surveys of the waste during the inspection noted background dose rates.

During a tour of the PET area, the inspector visited room 1C488A, which contained sealed sources in boxes ready for shipment. The gallium-68 sources were less than 10 times the quantity listed in 10 CFR 20, Appendix C, and therefore considered a minor violation per NRC’s Enforcement Policy. A memo was immediately sent by DRS staff to the authorized user on the permit informing them of the violation of NIH policy and the sources were immediately moved to a secure room.

Since the last inspection, the use of Ga-68 and lutetium-177 (Lu-177) under two separate investigation new drug applications (INDs) has continued for imaging and treatment of neuroendocrine tumors. The patient rooms used for I-131 are also used for Lu-177. Occasionally, due to the patient’s health, administrations of Lu-177 are also

performed in the intensive care unit (ICU). DHS staff conduct training with ICU nurses immediately prior to administrations. In addition, the RSC has approved investigational protocols for Thorium-227, Radium-223, and Lu-177 (Prostate-Specific Membrane Antigen-PMSA), however clinical use has not yet commenced. Release calculations for patients to be administered up to 540 millicuries of Lu-177-PMSA is under review by the RSC to ensure that public dose limits in 10 CFR 35.75 will be met.

The HDR was used to treat 7 patients in 2018 and has been in storage since November 5, 2018 due to construction in the room. The HDR is locked in a closet with keys controlled by the licensee. Full calibrations, spot-checks, WDs, maintenance activities performed by the manufacturer, and treatment plans were reviewed with no concerns noted.

An authorized medical physicist does an internal review of records and procedures every year for the HDR program. An audit by DRS was also conducted in 2017 with all findings addressed by the radiation oncology staff. The audit included WDs, spot-checks, full calibrations, instrument calibrations, and administration of the WD. The inspectors reviewed the audit results and found the audit comprehensive. The next audit is scheduled in 2019.

Research Activities Conducted under License Number 19-00296-10

Research activities typically involve microcurie to millicurie quantities of radioactive material used on the bench top, in a fume hood, plexiglass enclosure, or hot cell involving 47 different isotopes including: Hydrogen-3 (H-3), Carbon 11, Carbon-14, Oxygen-15, Nitrogen-15, F-18, Sodium-22, Phosphorus-32, Phosphorus-33, Sulfur-35, Calcium-45, Chromium-51, Manganese-54, Colbalt-57, Colbalt-58, Cobalt-60, Copper-64, Zinc-65, Gallium-67, Ga-68, Ge-68, Yttrium-86, Yttrium-88, Zirconium-89, Strontium-90, Tc-99m, Cadmium-109, Indium-111, Iodine-123, Iodine-125 (I-125), Iodine-129, I-131, Barium-133, Xenon-133, Cesium-137, Europium-152, Gadolinium-153, Lu-177, Iridium-192, Mercury-203, Bismuth-207, Radium-223, Actinium-225, Thorium-227 and Americium-241.

Active research using radioactive materials has remained steady over the past four years. The inspector visited the only operational iodination facility, which typically uses two millicuries of I-125 approximately 4 times per year. Iodinations were performed in a vented plexiglass enclosure (through a charcoal filter) inside a fume hood whose linear flow rate is evaluated by maintenance yearly. Bioassays performed post iodination have not revealed any uptake. The authorized user was knowledgeable of radiation safety practices and requirements.

The inspectors visited a sampling of research laboratories in buildings 6, 8, 10, CRC, 21, 35, 37, and 50 on the main campus; the Integrated Research Facility at Fort Detrick in Frederick, Maryland; Poolesville Animal Center in Poolesville, Maryland; and the BRC in Baltimore, Maryland. Security is restricted to the campus via the main gate which screens visitors. Once on the campus, some buildings have general access areas; however, access to laboratory areas requires additional measures such as card access, security guard clearance, or key control. Access to radioactive material use areas is limited to only those who are authorized to be in that area. Additionally, not all DRS staff have access to all radioactive material use areas. Within laboratory modules on the main campus, radioactive material stock vials are secured within locked refrigerators or freezers, and waste is consistently secured in locked

containers to prevent unauthorized access or removal. Security at the Integrated Research Facility, the Poolesville Animal Center and the BRC all included security guard access to the facility followed by secured laboratory areas.

Overall, the scientists were found to be exercising good practices for radiation safety and ALARA. NIH facilities for conducting research include graded safety systems; i.e. work generating airborne radioactive materials or aerosols is done in a fume hood or glove box, operations generating radiation fields are performed in hot cells, etc. Laboratory doors, freezers, and refrigerators are posted with the appropriate warning labels. Current copies of the NRC Form 3 are prominent in the lab areas. Radioactive use areas on the bench are clearly demarcated and absorbent paper is consistently used in an effort to prevent fixed contamination. The laboratories are consistently equipped with more survey meters than needed due to the reduced level of research from past years and are functional and calibrated. Workers were observed using survey meters and demonstrated proper technique. Scientists used appropriate shielding for radioisotopes. In these cases, shielding is employed for benchtop use, as well as for waste and storage locations. Typically laboratories where work is performed are surveyed and wiped monthly by either lab personnel or a contractor (CLYM). Most lab workers interviewed perform daily Geiger counter surveys and proactively clean work areas at the conclusion of licensed material use. All researchers were observed using personal protective equipment such as gloves and lab coats. Personnel also utilized shielding where applicable and had survey equipment readily available to check their areas.

Laboratory facilities are protected from other hazards associated with the research involving licensed materials. Sprinkler systems and fire extinguishers are present for protection from fire; eye wash units and safety showers are present to address splash or spill hazards; biosafety cabinets, infectious waste containers and biohazard labels are in use for biosafety concerns; etc. Laboratory personnel were questioned regarding hazards in the workplace and all indicated they were aware and had been trained regarding these hazards. No one indicated they would be unwilling to raise concerns if they arose. Safety appeared to be at the forefront of their activities indicating a healthy safety culture existed.

The Integrated Research Facility primarily utilizes bulk (100 mCi) and unit doses (2 mCi) of F-18 for animal studies involving PET/CT and occasionally bulk Tc-99m (40 mCi) for instrument linearity checks. The licensee reported that a microPET would be obtained for small animals. Very little benchtop use occurred. The material is delivered directly to the facility. The inspector toured the cook tank area and the areas outside the BSL-IV containment. Remote handling devices were obtained to decrease the NMT's extremity dose during injection and handling. Only two health physicists have the requisite training required to enter the biosafety level IV containment. Radioactive material is stored for decay within containment, surveyed for release, and then disposed. Liquid waste disposal is normally though the cook tanks. A review of the records including exposure and waste records did not raise any concerns.

Research activities at the Poolesville Animal Center mainly involves AIDS research using non-human primates. There are two protocols in place that were approved by both the Animal Care and Use Committee as well as the Radiation Safety Committee which involved the use of Tc-99m and Indium-111. A new protocol is undergoing the approval process which will require the use of F-18 FDG. All workers are required to obtain animal handling and radiation safety training. Typically 4-5 people are present when the primates are injected and scanned. Surveys are performed each day of radioisotope use; personal

protective equipment (PPE) is worn to address both the radioisotope and animal hazards. Waste is decayed and disposed of as infectious waste after reaching background levels. Dosimeters are mounted in the hallways outside scan rooms to assure exposure levels do not exceed public dose limits.

Benchtop and animal studies are also conducted at the BRC using a variety of radioisotopes including but not limited to phosphorus-32, phosphorus-33, I-125, and F-18. Materials are received in Bethesda and shipped to Baltimore after being entered into the inventory system. Researchers were observed using appropriate radiation safety techniques including PPE, survey meters, dosimeters, labels, and shielding when needed. Researchers interviewed were knowledgeable about the hazards of the material they are working with and the precautions to take to reduce their exposure. Material was secured in locked storage locations inside laboratories. Dosimeters were used to monitor public doses outside PET scan rooms.

Cyclotron Activities Conducted under License Number 19-00296-21

NIH operates three cyclotrons to produce various radioisotopes (F-18, Carbon-11, Zirconium-89, Oxygen-15 (O-15), Manganese-51, Copper-64, etc.) for research and clinical use with Fluorine-18 and Carbon-11 the predominate radioisotopes produced. The cyclotrons are located within two vaults which are located behind two heavily shielded doors. Access to the area is controlled and appropriate warning signs are posted. Radioactive material that is produced in the cyclotrons is either piped directly to hot cells or transferred manually using heavily shielded and labeled containers. Lines that are used to transfer the radioisotope from the cyclotrons to the hot cells are marked with the appropriate warning labels as well as a phone number to be contacted in the event of an emergency. The cyclotron facility utilizes a dumb waiter for transporting radioactive material between floors to minimize handling time and personnel exposure. Material production is managed by schedule and orders. Material production was compared to the license limits with no concerns noted. Material transfer to the broad scope license is done by a Form 88-1. Normally the researcher that intends to receive the material completes the form and electronically submits it to DRS. DRS uses the information on the Form 88-1 to update the inventory.

The cyclotron vaults and the hot cells are equipped with collection bags to trap volatile radioactive material and minimize the concentrations of radioisotopes in air effluent. In addition, exhaust ducts are equipped with a HEPA filter and a charcoal filter. When there is an unexpected release in the cyclotron vault or a hot cell, the charcoal filters are effective at trapping the activity and minimizing the release to the environment. However, the filters themselves can become a significant source of radiation for a limited period of time. Therefore, the charcoal filter areas are normally posted as a radiation area. If a large amount of volatile material is released within a hot cell, DRS is prepared to post the affected area as a high radiation area and control it in accordance with 10 CFR 20.1601(b).

One of the transfer lines from the cyclotron is used to transfer O-15 and travels through a parking garage. The transfer line is clearly labeled and the junction boxes are closed and secured with padlocks to prevent tampering. The licensee posts dosimeters in the area to monitor long term doses to ensure public dose limits are not exceeded.

The cyclotron vaults and the hot cells are maintained under negative pressure. The ventilation system has a redundant back-up exhaust motor in the event that the primary motor were to fail to provide the proper exhaust. There is an electronic readout of the pressure differential and ventilation performance is tied into the Siemens monitoring system to assure that the cyclotron engineer would be alerted of a ventilation problem or malfunction.

Contamination at the cyclotron is controlled several ways. Individuals that enter the cyclotron vault don bootie shoe covers that are removed upon exiting. The licensee has deployed a "sticky" step-off pad in an effort to control the potential spread of contamination. Portable survey meters are available at the vault exit for personnel to survey themselves and their shoes. All the meters present were checked and were operational, and had been calibrated within the last twelve months. All employees are required to use the Berthold hand and foot monitor prior to leaving the cyclotron restricted area and the inspectors observed this practice.

The cyclotron facility and associated hot cells are also equipped with a hold-up tank to capture any radioisotopes prior to release to the sanitary sewer. Radioisotopes are held in the tank and allowed to decay. The hold-up tank has not been released to the sanitary sewer for several years and not since the last inspection. The licensee is in the process of determining the feasibility of removing and decommissioning the tank and sink in the cyclotron area as it has not been used for several years. Most liquid waste is placed into a container and transferred to Building 21.

The inspectors toured the cGMP hot cell facility which has direct transfer capability from the cyclotron. The facility was commissioned and considered operational by DRS. The licensee installed a portal monitor for exiting the facility. These hot cells utilize a small carbon filter in each hot cell prior to exhausting through the exhaust line. The inspectors reviewed records for the activities noted above with no concerns noted.

Radiation Safety Training

DRS requires all personnel to obtain training prior to working with radioactive material. Individual users and authorized users take on-line training that includes verification by exam. Refresher training is also required and is available via on-line sessions. DRS offers several on-line radiation safety courses on a variety of topics tailored to each individuals need, such as irradiator use, PET use, etc.

In addition to on-line training, DRS continues to conduct face-to-face training. The sessions are typically conducted by health physicists to targeted groups including: hot cell users and I-131 therapy nurses, etc., and auxiliary groups such as police, fire fighters and housekeepers. Approximately 100 of these sessions are conducted annually. The DRS staff and researchers involved in shipping radioactive materials off-site obtain Department of Transportation (DOT) and International Air Transport Association (IATA) training, where applicable, every three years. The inspector evaluated a sample of training records of laboratory and medical personnel and found all training up to date.

Material Receipt, Use, Transfer, Control and Transportation

The inspector reviewed the material ordering, receipt, and control of radioactive materials at NIH. All materials used on the NIH campus are ordered and received through DRS, with the exception of F-18 and Tc-99m, which is received directly in nuclear medicine and at Fort Detrick. DRS contracts with CLYM Environmental for package receipt and delivery. In 2018, 7,366 packages were received by DRS, roughly half of which were used for patient use and the other half for non-patient use. The number of packages received per year has held steady at an average of about 7,500/year. Approximately 95% of the packages received are used on the Bethesda campus with the remaining 5% used at the various remote locations.

Requests for purchase of radioactive material are completed by the researcher and submitted to the purchasing department and DRS simultaneously. Purchasing agents place the orders, and the vendor ships the material to DRS. Prior to placing the order, the request is checked to assure it is within the researcher's authorization for the specific isotope and quantity. Upon arrival, packages are surveyed for radiation levels and contamination and the contents are verified against the packaging list and the order. Vials are wipe tested to confirm there is no contamination present, and then re-packaged for transport to the authorized user by contract personnel.

The inventory system is also checked to assure that the researcher does not exceed the quantity of material they are authorized for. If that occurs, then the contractor holds the material until either it decays or the researcher reconciles their current inventory to remove disposed items. Contract personnel verify the electronic inventory annually. The researchers provide updates to their inventories as they use the material. The inspectors spot checked physical inventories against what was present in the laboratories. The inspectors found that, in many cases, the inventory was not updated to remove materials that were no longer present. The reason for this was generally that the researcher was faxing their updates to DRS who did not receive them consistently. Researchers who used the DRS portal to provide updates consistently had inventories that matched what was in the laboratory. The concern of inventory reconciliation when the portal is not used was relayed to the RSO for follow-up.

Transfers to/from other licensees are managed by health physicists within DRS. All the individuals that are involved with preparing radioactive material shipments are trained and tested in accordance with the DOT requirements. A copy of the license from the institution receiving material is obtained prior to the shipment and reviewed to verify the recipient is authorized. Packaging, labeling, and preparing shipping papers for these shipments is performed by the health physics staff. The inspectors spot checked records of transfers, and found no concerns. With regard to shipment of blood samples from patients administered licensed material, the licensee is in the process of evaluating the exempt quantities allowed per shipment pursuant to 10 CFR Part 30 and whether international shipments are authorized. For instance, blood samples from patients treated with radium-223, thorium-227, or astatine-211 will be taken and sent to various labs domestically and internationally. However, since these radionuclides are not in the exempt quantity/concentration tables in 10 CFR Part 30; NIH is preparing a petition for re-evaluation of the table contents to include alpha emitters. For the international shipment of blood, urine, and fecal samples from patients treated with thorium-227, the manufacturer, Bayer, has provided instructions for preparing shipments to Germany. NIH is in the process of contacting NRC's Office of International Programs to discuss export requirements.

Radiation Surveys

The inspectors reviewed NIH's radiation and contamination survey process and performed confirmatory surveys. The inspectors noted the following:

(i) Technologists and ANPs, in both the nuclear medicine area and the PET areas, performed end of day surveys and weekly contamination surveys. NIH personnel were able to adequately demonstrate these surveys to the inspectors.

(ii) Researchers performed adequate surveys. Some researchers utilized a contractor to perform their required surveys while others perform the surveys themselves which are then reviewed by one of the area health physicists. The inspectors reviewed records of surveys performed in the labs by researchers as well as comprehensive surveys performed by NIH's contractor and noted that when removable contamination was detected, the areas were appropriately cleaned and re-monitored, with follow up surveys adequately documented.

(iii) In radiation oncology, surveys of the patient and remote afterloader unit were performed, as required, prior to patient release.

(iv) Surveys in the cyclotron area and the waste management areas were performed weekly. In addition, the O-15 transfer line through the parking garage was monitored by area dosimeters. The inspectors reviewed records maintained of these surveys, with no concerns noted.

(v) Clearance surveys were performed prior to release of licensed facilities. The inspectors reviewed records maintained to support the release of facilities, with no concerns noted.

NIH uses a contractor to perform comprehensive compliance audits in all labs twice a year. As part of this survey, the contractor performs a contamination wipe and dose rate survey, as well as interviews with the authorized users. The contractor collects information about material usage, training qualifications, and reviews the authorized user's survey records. The contractor also reviews postings, calibrations of survey equipment, the flow on ventilation hoods, shielding in use, and confirms that there is no eating, drinking or smoking in the restricted area. The inspectors reviewed the contractor's audits, with no concerns noted. The laboratories and departments are also audited by a member of the radiation safety staff at least every two years. This authorized user audit is more comprehensive, and reviews protocols, inventory, and use. Audit records were reviewed, with no concerns noted.

Calibration of instrumentation is performed onsite, as well as offsite. The contractor performs the onsite calibrations for count rate meters. Dose rate meters are sent offsite to AM Calibrations and Ludlum. The inspectors also reviewed the process for maintaining calibration schedules for instruments. Authorized users are accountable for calibrating their own liquid scintillation counters. The inspectors reviewed calibration and counting statistics performed on survey instruments and liquid scintillation counters, and noted that they appeared satisfactory and in accordance with the manufacturer's recommendations.

Occupational Exposure

External exposure is monitored by personnel dosimeters and the dosimetry issuance policy is based on a millicurie per hour nuclide specific schema that is documented in the license application. Cyclotron engineers and radiochemists are issued whole body dosimeters and extremity dosimeters for each hand. The extremity dosimeters are exchanged weekly. When personnel have incidents that result in skin contamination, the Varskin software is used by a member of DRS to calculate the skin dose.

Internal dose is assessed by bioassay. The bioassays that are performed are thyroid scans, body scans, and urine sample analysis. The thyroid monitoring equipment used is the Canberra Accuscan II system which has a dual calibration to allow monitoring of I-125 and I-131 uptakes. The Canberra Fastscan system is used for whole body counting. Based on the records reviewed and information provided by the health physicist from DRS, there were no personnel doses in excess of the regulatory limits specified in 10 CFR 20.1201.

In addition, the licensee has developed a comprehensive procedure for addressing fetal and nursing child protection for occupationally exposed workers. The procedure is reviewed during initial radiation safety training. A review of the records for declared pregnant workers indicated that none of the women had received a fetal dose greater than 500 millirem during the gestation period, in accordance with 10 CFR 20.1208.

Effluent Monitoring

In the cyclotron area, effluent is sampled and analyzed by the licensee. Each line also has a plastic scintillator coincidence detector to continuously monitor for radiation levels.

The licensee also performs air sampling in the ducts of the laboratories to quantify releases during iodinations. The air sampling data is corrected based on the total effluent volume and wind rose data and converted to dose utilizing the data in 10 CFR Part 20, Appendix B. This data provides the basis for estimating the releases of radionuclides in effluents for comparison to the regulatory limits. The remaining site inventory is combined to establish the source term for the EPA's COMPLY computer program to determine the dose to the maximally exposed member of the public.

The results were as follows:

- 2017 – 2.158 mrem
- 2018 – 2.177 mrem

Therefore, the results indicated full compliance with the constraint rule in 10 CFR 20.1101(d).

Radioactive Waste Management

The radioactive waste program is managed by a member of DRS and supported by contractors who are employees of Clym Environmental. Radioactive waste streams are segregated. Radioactive waste containers are well labeled, bar coded to note contents, and tracked in a database. Laboratory researchers track the activity per container and call for a

pick up when they are full. Waste is collected from laboratories daily. A three-ply waste tag is used per container. One copy of the tag is kept in the laboratory, one stays on the waste and one is used to enter the material into the waste database. Solid wastes are placed in cubic yard boxes and then barcoded to track the boxes. The compactors for radioactive waste have not been used regularly and only used to compact glass when needed. The ultraviolet processing system that was used to treat aqueous mixed waste had not been used since the last inspection and there are no plans to use this system in the future. Liquid scintillation vial wastes are segregated based on regulated and non-regulated constituents as per 10 CFR 20.2005(a)(1). Regulated vials are disposed via Duratek. Non-regulated vials are shredded by a vyleater on site. The scintillation fluid is bulked in a drum and shipped to DSSI in Houston, TX as waste flammable liquid. The shredded vials are discarded as dry active radioactive waste and shipped to Energy Solutions in Oak Ridge, TN. Medical/pathological waste (MPW), mixed organic liquids and animal carcasses with a half-life less than 120 days are held for decay-in-storage. The waste is surveyed using a portable gamma spectrometer to identify any waste that has not reached background levels. In those cases, the waste is identified and decayed longer if appropriate. A resurvey is performed to demonstrate that the waste is indistinguishable from background before disposing as either MPW or hazardous waste. Any waste identified with half-life greater than 120 days, such as waste contaminated with Lu-177m, is transferred to the radioactive waste stream. All radioactive dry active waste is shipped as low specific activity (LSA) material. Waste manifests are signed by a DRS health physicist.

Instructions pertinent to the exclusive use shipment are provided to the driver. All of the workers involved with packaging and labeling radioactive waste or transporting the radioactive waste between sites receive hazardous material training and are tested in accordance with DOT requirements. The health physicist over the waste program receives IATA training for air shipments as necessary.

The waste facility is equipped with nine 2,250 gallon fiberglass tanks that hold aqueous non-RCRA radioactive waste. The licensee made one batch release from the tanks to the sanitary sewer on October 16, 2018. The combined total activity was approximately 105 millicuries, mostly of tritium. The licensee was in compliance with 10 CFR 20.2003.

The inspectors made independent measurements of the waste area and did not identify contamination on the floors or surfaces. The licensee performs surveys on a daily basis and a more extensive weekly survey in the waste areas. A hand and foot monitor was located in the area and personnel were observed using it. The facility is well designed with sloped floors and dykes to contain leaks and prevent the spread of contamination. The 2014 waste disposal guide that was in use during the inspection is being revised and expected to be issued in the near future.

Posting and Labeling

The inspectors toured the nuclear medicine department, PET areas of use, the radiation oncology department, research facilities, cyclotron facilities, and Building 21 (DRS). All areas of use and storage were properly posted and radioactive materials were properly labelled.

Financial Assurance and Decommissioning

The inspectors reviewed the financial assurance submittals prior to the site visit and determined that adequate instruments and certificates were on file for the materials currently licensed. However, a slight change to accommodate the alpha program was made in Amendment Number 129 with the addition of byproduct material with atomic numbers 93-96 and reductions in the plutonium radionuclide quantities. The licensee is in the process of reviewing their submittals and will submit a new Certification of Financial Assurance.

Decommissioning activities of laboratories and modules at the Bethesda Campus had been performed since the last inspection. Buildings 18, 32 and 10 E-wing underwent decommissioning using the MARSSIM technique with oversight by CLYM Environmental. These projects are not routinely submitted to the Region I office and are reviewed during inspection. The inspectors reviewed the process NIH uses to release laboratories and buildings, and no concerns were noted. Inquiries from the licensee about decommissioning of buildings on the Bethesda Campus and possible release of two 10,000 gallon abandoned waste storage tanks located under Building 21 were referred to the Region I Decommissioning Branch.

The inspectors reviewed records of active laboratories that demonstrate the licensee is maintaining information important to decommissioning.

c. Conclusions

Based on the results of this inspection, one apparent violation of NRC requirements was identified for License No. 19-00296-10. Specifically, in 2015 and 2017, two physicians were approved as authorized users for parenteral administrations of any radioactive drug requiring a written directive and neither physician had documented training and experience with parenteral radioactive drugs requiring a written directive in accordance with 10 CFR 35.390(b)(1) and the license. Corrective actions were taken by NIH as documented above.

2. Exit Meeting

At the conclusion of the onsite inspection on May 17, 2019, the inspection findings were discussed with NIH’s senior management.

PARTIAL LIST OF PERSONS CONTACTED

Licensee

*Alfred Johnson, Ph.D., Deputy Director for Management
*Lisa Coronado, Deputy Chair, RSC
*Ronald Neumann, M.D., Deputy Chief, Nuclear Medicine
+*Cathy Ribaudo, RSO and Director, Division of Radiation Safety (DRS)
*Peter Herscovitch, M.D., Chief, PET Department
*Colleen McGowan, Director, Office of Research Services
+*Michael Roberson, Deputy RSO and Division Director, Cyclotron and PET, DRS
+*Laurenti Ngutter, Chief, Radiation Safety Operations, DRS
+*Victor Voegtli, Chief, Materials Control and Analysis, DRS
*Kenneth Chang, Pharm.D., Radiopharmacist, Manager PET Department
* Cheryl Ann Beegle, Supervisor, Nuclear Medicine
+ Wendy Rubin, Manager, Irradiator Security
* Kris Kim, Cyclotron Section Chief
* Mark Ahlman, M.D., Nuclear Medicine Physician
* Frank Lin, M.D., Clinical Investigator
Eric Munger, Health Physicist, DRS
Neena Patel, Health Physicist, DRS
Allen Anthony, Health Physicist, DRS
* Newbegin Devaraj, Health Physicist, DRS
* Olumide Owoade, Health Physicist, DRS
* Joseph Cross, Health Physicist, DRS
* Keith Ball, Health Physicist, DRS
* Alan Boudreau, Health Physicist, DRS
* Teresa Fisher, RSC Executive Secretary, Health Physicist, DRS
* Andrew Cabot, Health Physicist, DRS
* Korressa Williams, Health Physicist

Various medical staff, researchers, contractors, and support staff

+Present at entrance meeting
*Present at exit meeting