Department of Veterans Affairs
Office of Inspector General

Healthcare Inspection

Research Practices at Carl T. Hayden VA Medical Center Phoenix, Arizona

Report No. 07-00589-118 **April 20, 2007**

VA Office of Inspector General
Washington, DC 20420

To Report Suspected Wrongdoing in VA Programs and Operations
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Executive Summary

The Office of Inspector General received allegations of research improprieties at the Carl T. Hayden VA Medical Center in Phoenix, AZ. We substantiated that one unlicensed physician performed muscle biopsies, conducted history and physical examinations, and changed medications in accordance with research protocols. We identified a second unlicensed physician who had a scope of practice that allowed similar activities. ("Scope of practice" is a term used to describe activities that may be performed by health care workers, whether they are licensed independent health care providers or not.) Additionally, a nurse involved in the same protocol performed functions that were not included in her scope of practice. Laboratory data for a study involving non-veterans had not been reviewed in a timely manner. We substantiated that the facility did not maintain accurate inventories of tritium, a substance that emits low levels of radiation, in a manner consistent with VA policies and procedures. The facility failed to maintain an accurate inventory of tritium contaminated solid wastes. We could neither substantiate nor refute that a research official voted on his own grant as a result of the facility's failure to maintain voting records; however, his position on the Board of Directors of the VA-affiliated nonprofit corporation could be an appearance of a conflict of interest.

Based upon the issues in our review, we made the following recommendations: (1) prevent unlicensed physicians working in VA research from engaging in activities that constitute the practice of medicine; (2) establish procedures for ensuring that the storage, use, and disposal of radioactive wastes are managed in compliance with all applicable VA and Federal regulations and policies; (3) ensure that researchers have the requisite skills, training, and experience to conduct the research in accordance with the requirements of VA policy; (4) clearly delineate the responsibilities of VA laboratories for patient notification of abnormalities in certain situations; and (5) define conflict of interest in terms applicable to research activities of VA medical centers and VA-affiliated nonprofit corporations.

Managers concurred with the findings and recommendations of this inspection. We believe that their comments, along with their corrective action plans, meet the intent of our recommendations. We will follow up on all planned actions until they are completed.

DEPARTMENT OF VETERANS AFFAIRS
Office of Inspector General
Washington, DC 20420

TO: Director, Veterans Integrated Service Network (10N18)

SUBJECT: Healthcare Inspection – Research Practices at Carl T. Hayden VA Medical Center, Phoenix, Arizona

Purpose

The VA Office of Inspector General (OIG), Office of Healthcare Inspections (OHI) conducted an inspection to determine the validity of allegations concerning research improprieties at Carl T. Hayden VA Medical Center (hereafter the facility) and its VA-affiliated nonprofit corporation, Carl T. Hayden Medical Research Foundation (hereafter CTHMRF).

Background

OHI received a complaint concerning potential violations of Veterans Health Administration (VHA) policy in four areas: (1) the facility's program for the protection of human subjects engaged in research, (2) credentialing and privileging of research personnel, (3) the use and storage of radioactive materials, and (4) conflict of interest in the setting of a VA-affiliated nonprofit corporation (NPC)[1].

Specifically, the complainant alleged:

- Researchers violated human subject protection and research safety policies, procedures, and regulations by: (1) allowing unlicensed personnel to perform muscle biopsies (Protocols A, B, and C), (2) utilizing radioactive materials in a manner not consistent with VHA policies and procedures (Protocol C), and (3) publishing research not previously approved by the facility's Institutional Review Board (IRB) (Protocol D).

[1] VA-affiliated nonprofit corporations (NPCs) are also called nonprofit research corporations.

- The facility's IRB inconsistently applied available penalties for these violations, barring one principal investigator (PI)[2] from research for publication of an unapproved abstract (Protocol E), while not penalizing the researchers involved in Protocols A through D. This is alleged to have resulted in delayed implementation of Protocol E, contributing to two patient deaths because they were unable to enroll in the study.

- A research official used his position as a member of the Board of Directors of CTHMRF to vote on matters in which he had a financial interest in violation of VHA's conflict of interest policies and procedures.

- The same research official (1) attempted to rewrite minutes of the NPC's Board meetings and (2) wrote correspondence for the Chairperson of the IRB and directed a research employee to sign it for the Chairperson without the Chairperson's approval, in violation of documentation policies and procedures.

The complainant also alleged financial mismanagement of CTHMRF. These allegations were referred to OIG's Office of Audit and are not discussed further here. The following is a general discussion of VHA policies pertaining to the issues identified in this report.

VA adheres to the Federal Policy for Protection of Human Subjects (often referred to as the "Common Rule"). This policy requires all research involving human subjects be approved by both the IRB and the Research and Development Committee (R&D Committee) at the facility conducting the research. When a research protocol involving human subjects is proposed, it first goes to the IRB for approval; the IRB is a subcommittee of the R&D Committee. If approved by this subcommittee, the protocol then goes to the R&D Committee for approval.

Relevant IRB and R&D Committee Policies

IRBs bear the primary responsibility for implementing the protections for and policies pertaining to human subjects. VHA Handbook 1200.5 defines IRB duties and responsibilities, including the initial approval of a protocol and its continuing review. The IRB must ensure that the benefits of the research outweigh the risks and that every effort is made to minimize any risk to participants. The IRB can require modifications to a protocol or disapprove a protocol altogether. Furthermore, protocols are reviewed on a continuing basis by the IRB to ensure adequate protection of human subjects at a frequency dependent on the degree of risk, but not less than once per year. IRBs must implement standard operating procedures locally that describe how the facility will

[2] VHA Handbook 1200.5, *Requirements for the Protection of Human Subjects in Research*, July 15, 2003, defines a PI as "an individual who conducts a research investigation, i.e., under whose immediate direction research is conducted, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team."

ensure compliance with VHA Handbook 1200.5, including termination or suspension of a protocol for investigator noncompliance.

The facility's local policy in effect during the events described in the complaint was the R&D Committee and IRB *Standard Operating Procedures Manual*, 2004 edition. We note these procedures were revised on October 30, 2006. Both the 2004 and 2006 policies describe the general scope of IRB authority, specifically stating that the IRB can "restrict, suspend or terminate an investigator's privilege to conduct human studies." The 2006 version describes the degree of investigator noncompliance, defining "minor non-compliance" as the unintentional violation by an investigator of any IRB requirement, while "serious non-compliance" is defined to include "any actions which place a subject at increased risk of injury or which compromise the integrity of the data or study."

The facility also maintains a local policy on research performance improvement.[3] This policy requires assessment and improvement in compliance with certain provisions of VHA Handbook 1200.5, as well as in responsiveness to complaints or questions from human research participants. It does not, however, address performance improvement in such areas as the credentialing and privileging of research personnel; radioactive materials safety, storage, and disposal methods; fiscal accountability; VA-affiliated nonprofit corporation activities; or conflict of interest.

Credentialing and Privileging of Research Personnel

VHA and facility policies do not identify specific requirements for the credentialing and privileging of research personnel. Credentials generally include the formal education, training, and licensure of an individual, while privileges commonly refer to the activities that a licensed independent health care provider can perform at a given facility. "Scope of practice" is a term that can be used to describe activities that may be performed by health care workers, regardless of whether they are licensed independent health care providers. While not specifying a means of credentialing and privileging research personnel, VHA Handbook 1200.5 does require the Medical Center Director to ensure "that IRB members and investigators are appropriately knowledgeable to conduct research in accordance with ethical standards and all applicable regulations."

VHA also has a handbook[4] for the credentialing and privileging of health care providers, but it applies only to those individuals "permitted by law and the facility to provide patient care services independently." Only licensed personnel are permitted by law to provide patient care services independently. A second policy, VHA Directive 2006-067,[5] applies to those individuals who are licensed, certified, or registered. There are, however, no research positions listed in the attachment describing applicable occupations. VHA

[3] Carl T. Hayden VA Medical Center Phoenix, AZ, Policy Memorandum No. ERS/151-8, *Research Performance Improvement*, June 3, 2002.
[4] VHA Handbook 1100.19, *Credentialing and Privileging*, March 6, 2001.
[5] VHA Directive 2006-067, *Credentialing of Health Care Professionals*, December 22, 2006.

currently has no formal policy for verifying the credentials or appropriate scope of practice for employees without a license, certification, or registration who are engaged in research activities, such as unlicensed graduates of foreign medical schools.[6] The Office of Research and Development (ORD) does offer credentialing guidance on its website. This guidance states that licensed independent practitioners are credentialed through VetPro[7] or its paper equivalent. ORD's guidance also states that other staff not covered by VetPro (in effect, individuals not licensed to function as independent practitioners) should have their credentials verified and should provide the research service with an education verification form. It does not address what procedures a facility should use to verify appropriate scopes of practice for unlicensed research personnel.

Policies Pertaining to the Use of Radioactive Compounds in Research

Unique requirements and compliance issues apply to research protocols involving the use of radioactive compounds. The Nuclear Regulatory Commission (NRC) is the agency with authority to regulate the use and storage of radioactive compounds. On March 17, 2003, the NRC issued a Master Materials License (MML) to VA, consolidating multiple NRC facility licenses into a single master license. Under the MML, VA oversees 115 facilities with permits to use radioactive materials, while the NRC maintains oversight of the MML. VHA Handbook 1105.1[8] describes VHA policies and procedures for performing licensure and oversight of activities involving ionizing radiation or radioactive materials. VA's National Radiation Safety Committee (NRSC) is responsible for regulating the acquisition, receipt, storage, distribution, use, transfer, and disposal of radioactive materials within VA facilities.

At the facility level, VHA policy places primary responsibility for these activities with the facility's Radiation Safety Committee (RSC) and Radiation Safety Officer (RSO). The RSO is defined as someone "with specific education and professional experience in radiation protection practice appointed by a VHA facility director and approved by the VHA RSC to manage radiation safety programs."

VHA Handbook 1105.1 also describes procedures for the management of radioactive wastes. It specifically requires that all radioactive materials or items contaminated with radioactive materials must be accounted for by inventory pending disposal. The facility RSO is responsible for preparing procedures for waste management in consideration of local factors such as available storage and type of waste.

Two years after implementation of VHA Handbook 1105.1, in response to a request from the Secretary of Veterans Affairs, OHI conducted a review of security and inventory controls over radioactive agents on March 14, 2002. While concluding inventory

[6] VHA Directive 2003-036, *Credentials and Training of Employees Involved in Human Subjects Research*, dated July 7, 2003, was rescinded on July 29, 2003.
[7] A computerized system guiding facilities through verification of a provider's credentials and practice history.
[8] *Procedures for Management of Radioactive Materials*, March 13, 2000.

controls for radioactive materials "were more effective than those for managing biological agents and chemicals," the report recommended that managers "reevaluate the extent of compliance with radiation safety and handling/delivery procedures…."[9]

Policies Governing Conflict of Interest in VA-Affiliated Nonprofit Corporations

To provide a more flexible funding mechanism, Congress enacted legislation in 1988 allowing VA medical centers to create VA-affiliated NPCs to administer research funds. VHA policy governs the operations of NPCs, including VHA Handbook 1200.17[10] which states that NPCs "are subject to dissolution should they not serve the best interest of VA." The policy further requires that any VA employee involved "in any fashion" in the operations of the NPCs ensure that these institutions operate in the best interests of VA. VHA currently has no financial conflict of interest policy specific to research.[11] All NPC board members, officers, and employees are subject to Federal rules and regulations regarding conflicts of interest and conduct of Federal employees. At the time NPC duties are assumed, all individuals must sign a statement "certifying awareness of and compliance with Federal conduct and conflicts of interest laws and regulations."

Scope and Methodology

To investigate the complainant's allegations in the areas of credentialing and privileging of research personnel; use, storage, and disposal of radioactive materials; human subject protection violations; conflict of interest; and documentation irregularities in CTHMRF, we conducted a site visit from December 4, 2006, through December 7, 2006. We interviewed the Associate Chief of Staff for Research and Development (ACOS/R&D), R&D Committee members, IRB members, PIs, the research compliance officer, the research safety and RSOs, officers of the NPC, financial personnel, and the administrative officer (AO) for research.

For Protocols A through D, we reviewed IRB and R&D Committee documents. We examined documents pertaining to radiation safety violations associated with Protocol C, reviewed radiation safety committee documents, waste disposal logs, and visited the location used by the facility to store its hazardous wastes. On site, we physically inventoried certain radioactive wastes described in documents associated with Protocol C. We examined scopes of practice for research coordinators and other personnel involved in Protocols A, B, and C. We also contacted another VA medical center (hereafter Facility 2) for additional information concerning the scope of practice of these personnel while previously employed by Facility 2. We reviewed documents related to

[9] *Review of Security and Inventory Controls Over Selected Biological, Chemical and Radioactive Agents Owned by or Controlled at Department of Veterans Affairs Facilities*, Report No. 02-00266-76, March 14, 2002.
[10] VHA Handbook 1200.17, *VA Research and Education Corporations Authorized by Title 38 United States Code (U.S.C.) Sections 7361 through 7368*, December 17, 2001.
[11] VHA Notice 2005-01 rescinded VHA Handbook 1200.13, *Financial Conflicts of Interest in Research*, on February 1, 2005.

the publication of unapproved research associated with Protocol D. We examined IRB documents pertaining to a fifth protocol (Protocol E) after identifying a deficiency in the data safety monitoring plan during the course of our inspection. Finally, we examined IRB and R&D committee documents pertaining to actions taken against a researcher involved in a sixth protocol (Protocol F).

The inspection was performed in accordance with the *Quality Standards for Inspections* published by the President's Council on Integrity and Efficiency.

Inspection Results

Issue 1: Safety and Human Subject Protection in Protocols A, B, and C

A. Performance of Health Care Activities by Unlicensed Personnel

We substantiated the allegation that one unlicensed physician (hereafter Researcher 1) with a scope of practice designated for a "research coordinator," performed at least two muscle biopsies in Protocol A at the facility. The PI, a licensed physician supervising Researcher 1, did not have privileges to perform muscle biopsies at the time these procedures occurred. The facility identified these issues prior to the date of our inspection and reported them to the Office of Research Oversight (ORO). However, Researcher 1 also performed numerous physical examinations and in several instances determined when it was appropriate to increase the dosage of a diabetes medication[12] in accordance with the protocol. These activities were not reported to ORO. The PI has since obtained privileges to perform muscle biopsies, and Researcher 1 is no longer involved with research at this facility.

During our inspection, we determined that Researcher 1 performed muscle biopsies at Facility 2 prior to working for the facility. We notified Facility 2, which reviewed medical records and verified that 11 muscle biopsies were performed by this individual. Facility 2 had no completed Scope of Practice for Researcher 1. The consent form designated his title as M.D., which was contrary to Facility 2 and IRB policy in that Facility 2 considers this to represent to the research subjects that the individual is a licensed physician. Facility 2 stated that non-licensed physicians could be considered as non-credentialed non-privileged trainees in terms of their scope of practice and could perform procedures with supervision. Documentation provided by Facility 2 acknowledges that there were at least five unlicensed individuals performing such procedures under the supervision of an attending physician as of December 8, 2006.

Whether or not Researcher 1 operated under the supervision of a licensed physician, he was not in a credentialed training program such as a university-affiliated program for the training of resident physicians and medical students. Researcher 1 could not practice

[12] The medication involved was pioglitazone, an oral medication for diabetes.

medicine, regardless of supervision. State law defines the practice of medicine for purposes of licensure. While the definition varies from state to state, statutes generally include the diagnosis and treatment of disorders or disease states in their definition of the practice of medicine. For example, Arizona State law defines the practice of medicine as follows:

> "Practice of medicine" means the diagnosis, the treatment or the correction of or the attempt or the holding of oneself out as being able to diagnose, treat or correct any and all human diseases, injuries, ailments, infirmities, deformities, physical or mental, real or imaginary, by any means, methods, devices or instrumentalities.…

Conducting a physical exam has no reasonable purpose other than to diagnose a disorder or to exclude its presence by negative findings. Performing a physical exam, particularly while wearing a name tag labeling the individual performing the exam as an M.D., could also constitute holding oneself out as being able to diagnose and treat medical conditions.

At the facility, a medical record review of the records of 55 patients (10 patients who consented for Protocol A, 9 patients who consented for Protocol B, and 36 patients who consented for Protocol C) revealed that at least 1 additional unlicensed physician (Researcher 2) performed physical examinations on patients and interpreted laboratory results to determine the presence or absence of disease states. The notes were received by the supervising physician after the date of the patient encounter. Researcher 2 performed these activities within the scope of practice granted by the facility on May 11, 2005. The facility defined Researcher 2's scope of practice to include performing physical examinations, muscle biopsies, and glucose clamp experiments under supervision. The scope of practice granted to a researcher, however, cannot supersede state or Federal laws or regulations prohibiting the practice of medicine without a license.

In addition, a Registered Nurse (Researcher 3) employed by the facility as a research coordinator completed notes documenting preparation for muscle biopsies, muscle biopsy procedures, glucose and insulin infusions, and a type of exercise testing that was performed with electrocardiogram (EKG) monitoring. Progress notes contained no evidence of supervision by a licensed independent health care provider at the time of our inspection. Researcher 3's scope of practice permitted her to administer intravenous solutions and medications, but did not indicate that she could perform muscle biopsies or exercise testing with EKG monitoring. We notified the facility of concerns that Researcher 3's activities did not fall within the scope of practice generally accepted for research coordinators, or within the facility's scope of practice for this individual. On December 19, 2006, and December 20, 2006, addenda were added to the progress notes reflecting that the muscle biopsies involved were performed by licensed physicians. These addenda do not, however, address whether licensed independent practitioners supervised the patients receiving exercise testing with EKG monitoring in Protocol B. In

some instances, the licensed physician writing the addenda was not listed on the consent forms as being the PI or a researcher involved in the protocol.

When the facility initially reported the two muscle biopsies performed by Researcher 1, the IRB instituted an action plan on September 21, 2005. The plan required that the IRB initial review form contain verification that any health care practitioner participating in the study holds a valid license and that, in the process of initial and continuing review of protocols, requests to perform procedures would precipitate a review of credentials, privileges, and scopes of practice. ORO closed the case on October 11, 2005, based upon the facility's reported action plan. Physical exams and exercise testing by unlicensed providers or those acting outside their scope of practice continued to occur without documentation of independent licensed health care provider involvement beyond the date of the action plan. These documentation issues persisted at the time of our inspection.

B. Radioactive Materials Management

We substantiated that the PI of Protocol C utilized radioactive materials in an unapproved area. Protocol C involved labeling glucose with a radioactive isotope, tritium,[13] and administering it along with insulin to patients for purposes of testing how insulin affects enzymes present in muscle tissue. A radioactive substance, tritium, has a half-life of 12.5 years.[14] It emits very small amounts of radiation, and is a hazard only if taken internally. Nevertheless, tritium is regulated by the NRC. The complainant alleged that there were numerous irregularities in Protocol C, including use of tritium in unapproved areas. The facility holds a Materials Permit authorizing the facility to possess tritium among other radioactive materials.

The facility has a history of violations in this area. In 1999, prior to VHA's National Health Physics Program (NHPP) assuming responsibility for materials management, the NRC inspected the facility, noting three violations, including failure to amend the permit prior to utilizing radioactive materials in certain areas. In 2000, NHPP identified four violations, again referencing failure to obtain an amendment to the permit authorizing use of radioactive materials in certain areas. On November 18, 2004, the facility obtained an external audit of the research radiation safety and quality assurance programs. The report concluded that "significant effort needs to be made to bring the paperwork for the in vitro[15] and in vivo[16] use of radioactive material into compliance with your license." It further stated that the VA had "no viable option" for the disposal of solid tritium contaminated wastes. On December 8, 2004, the minutes of the RSC state: "an audit of the research service was performed and there were significant problems with the paperwork for both the in vivo and in vitro research programs."

[13] Tritium (chemical symbol H^3) is a radioactive isotope of the element hydrogen, whose chemical symbol is H.
[14] Half-life is the time it takes half of the radioactive atoms to decay naturally.
[15] *In vitro* is a term used to indicate that the substance was used in laboratory experiments but not in the body.
[16] *In vivo* means that the substance was used within the body.

On December 13, 2004, 25 days after completion of the external audit, another inspection by NHPP disclosed continued use of radioactive materials in unapproved areas. The inspection also disclosed improper disposal of tritium contaminated laboratory supplies by soaking them in a commercial decontamination solution and then placing them in unregulated laboratory trash. Since the date of that inspection, and prior to our own, the facility amended the permit to include the room utilizing tritium in Protocol C. Minutes from the Subcommittee on Research Safety further disclose that, as of September 20, 2006, all in vivo work at the facility is now performed with non-radioactive substances.

Finally, the facility terminated the unapproved tritium disposal method following the inspection and accumulated tritium contaminated solid waste in a detached storage building. In a Memorandum to the Director of VHA's NHPP dated February 10, 2005, the facility Director indicated that these materials would be stored in the building "until a specifically licensed contractor can pick up, treat, and dispose of our dry waste composed of disposable laboratory glassware, tubing, pipette tips, and other supplies contaminated with long-lived radioactive materials." At the time of our onsite inspection, these wastes remained in the facility. However, the facility informed us on January 9, 2007, that a contractor had removed all tritium contaminated solid waste from the storage facility.

Additional procedures governing the inventory of radioactive wastes are contained within the facility's Radiation Safety Manual. The Manual requires radioactive wastes to be labeled with the name of the radioisotope, activity, date of disposal, and the radiation worker's full name and telephone number. The Manual also requires a radioactive waste disposal log, stating that "[All] of this information is necessary to correctly classify the waste for disposal."

During the course of our inspection, we obtained an inventory of tritium contaminated solid waste held in storage at the facility. The inventory indicated storage dates in the building beginning in May 2004 and continuing through June 2005. This was tracked by e-mail, in that the individual responsible for placing the materials in the storage building would e-mail the Research Safety Officer with the date, number of bags, and amount of radioactivity of each bag placed in the building. The Research Safety Officer then compiled this into a list of materials deposited in the building. Together with the AO for Research and the Research Safety Officer, we compared the inventory list against a direct physical inspection of the materials in the building. One bag of tritium contaminated solid waste listed on the inventory could not be located in the storage building at the time of our inspection, and five bags in the storage building did not appear on the inventory list. In addition, there were discrepancies between dates on the inventory list, the e-mails, and the bags located in the shed.

We requested that the facility reconcile the inventory list and e-mails pertaining to the storage of tritium with the physical inventory, report discrepancies to appropriate regulatory agencies, and follow up regarding a radioactive waste disposal plan. On December 13, 2006, the facility provided us with a certification and reconciliation of

waste inventory. The facility reported the missing bag of tritium contaminated solid waste as being present in the shed but mislabeled. The other five bags were placed in the building while the RSO was on extended leave. Multiple tag errors were noted concerning the correct amount of radioactivity. The facility stated that they reconciled all discrepancies and that the AO for Research contacted a manager at NHPP who said these were minor deficiencies that appeared to be addressed locally but suggested further review by the RSC. The facility also implemented an action plan which involved stoppage of the practice of holding a bag in the lab after it was sealed; improved documentation of waste bags including posting a waste log inventory sheet in the building to allow updates to be done when materials are placed in the building; and scheduling another independent audit of the Research Radiation Safety Program in the next fiscal quarter.

The RSO is the official in VHA policy responsible for a facility's radioactive waste management program. VHA Handbook 1105.1 outlines an extensive list of highly technical duties and responsibilities of the RSO as follows:

> The facility RSO is the functional and operational arm of the facility RSC for implementing policy, development of procedures, and ongoing oversight of local uses of radioactive materials as described in a permit. The RSO:
>
> (1) Is appointed in writing by the medical facility Director.
>
> (2) Investigates overexposures, accidents, spills, losses, thefts, and unauthorized receipt, use, transfer or disposal of radioactive materials, medical misadministrations…and other deviations from approved radiation safety practices and implements corrective actions as necessary.
>
> (3) Develops and recommends to the RSC local procedures in writing for acquisition, receipt, storage, inventory, safe use, emergency procedures, surveys, equipment performance checks, disposal, personnel training, and user and facility record keeping requirements.
>
> (4) Briefs medical center management at least once each year on the status of the facility radiation safety program.
>
> (5) Develops and recommends to the RSC investigational action levels for personnel exposures, contamination, and surveys.
>
> (6) Assists the RSC in the performance of its functions, including its annual evaluation of the facility radiation safety program.
>
> (7) Performs periodic onsite evaluations of all activities involving the use of radioactivity in the medical facility including, but not limited to, visits to

all areas of use, examination of required records, and evaluations of radiation safety procedures.

To perform these duties, the Handbook specifies the RSO must have "the education and professional experience needed for the position." A single RSO is listed on the Materials Permit for the facility.

The facility's Radiation Safety Manual dated June 30, 2005, however, indicates the RSO and the Research Safety Officer "manage the Radiation Safety program in a dual capacity." The Manual specifies that both individuals will manage daily operations and are responsible for compliance.[17] The RSO at the facility is a Board certified radiologist with training in nuclear medicine. The Research Safety Officer was hired as a research scientist. He indicated that he had received no formal training in radioactive waste management, had never been an RSO for the VA, and was appointed to the position about 2.5 years ago. Minutes from the Subcommittee on Research Safety identified that the "Radiation Safety Officer needs a backup who is at a senior level." When we interviewed the RSO, he believed that all radiation safety issues pertaining to research or occurring in research areas were the responsibility of the Research Safety Officer. This would mean that the Research Safety Officer would be required to perform all of the above technical duties in research areas, despite the absence of any training in these areas.

C. Publication of Research

We substantiated the allegation that a researcher at the facility (Researcher 4) presented the results of unapproved research in the form of a poster presentation at a professional society meeting. VHA Handbook 1200.5 defines research as "the testing of concepts by the scientific method of formulating a hypothesis or research question, systematically collecting and recording relevant data, and interpreting the results in terms of the hypothesis or question." The Common Rule (38 CFR 16) defines research as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalized knowledge."

Researcher 4 presented data on a case series of six patients with a relatively rare form of cancer. The data was obtained as part of routine medical care. No patients were harmed. The expressed intention of the poster presentation was to demonstrate the possibility of a higher incidence of this type of cancer in the VA population than previously reported. Researcher 4 reported the incident to the IRB on September 22, 2006. The IRB and R&D Committees determined that the case series did constitute research and requested that Researcher 4 submit a protocol so that the work could receive the appropriate approval. Neither committee otherwise sanctioned Researcher 4.

[17] The facility's previous *Radiation Safety Manual*, issued in 2002, also stated that the Research Safety Officer had the same duties as the RSO in research areas.

D. Additional Human Subject Protection Issues

Although not an allegation, during the course of our inspection, a PI disclosed that she had not accessed laboratory data pertaining to Protocol E since approximately February of 2006. This study involved laboratory data for 309 non-veteran patients. The facility's role was to analyze data in accordance with the terms of a Memorandum of Understanding (MOU) executed between the affiliated university and the facility. The laboratory data included serum concentrations of immunoglobulins.[18] Significant abnormalities of these values can be indicative of certain rare forms of cancer and immune deficiencies. VHA Handbook 1200.5 requires research proposals to "make adequate provisions for monitoring the data collected to ensure the safety of subjects (38 CFR 16.111(a)(6))." Policy Memorandum ERS/151-01[19] also states that "the research plan must make adequate provisions for monitoring the data collected to ensure the safety of subjects."

Protocol E did not have a Data Safety Monitoring Plan that addressed abnormal immunoglobulin levels despite being approved by the facility IRB. In addition, the MOU for Protocol E stated that the PI at the facility "will be responsible for, perform, or supervise all medical aspects of the collaborative research performed at the VAMC." The PI of the study at this facility was not a clinician. The PI stated in December 2006 that she had not accessed this laboratory data since approximately February of 2006 because of computer access issues. By not accessing the laboratory data, this created the possibility that abnormal laboratory results of clinical significance would not be detected and communicated to the patients' physicians in a timely manner, resulting in a failure to diagnose and treat those patients appropriately. In addition, because the PI was not a clinician, she would not necessarily have had the skills or experience to evaluate and recognize the clinical significance of these abnormalities even had she reviewed the laboratory results in a timely manner.

We notified the facility of this issue during our onsite inspection. The facility submitted a Corrective Action Plan stating that the normal lab notification process did not apply because the patients were not VA patients and the laboratory did not have identifying information for the patients. The facility reviewed the data from these patients and determined in a report dated January 11, 2007, there were nine patients with abnormalities of potential clinical significance. These results were reported to the regional IRB for purposes of attempting to identify the patients and subsequently inform their primary care providers. The facility IRB completed review of the Data Safety and Monitoring Plan for Protocol E by December 22, 2006. Testing of blood was halted until clinical oversight of laboratory results could be delineated.

[18] Immunoglobulins are proteins that play a key role in the body's immune response to foreign substances, including bacteria and viruses.
[19] Carl T. Hayden VA Medical Center Phoenix, AZ, Policy Memorandum No. ERS/151-01, *Research and Development Committee*, June 8, 2004.

Issue 2: Penalties for Human Subject Protection Violations

The complainant alleged that, while the IRB imposed no sanctions against the PIs involved in Protocols A through E, it barred Researcher 5 from participation in research activities for relatively minor non-compliance in Protocol F. In addition, the complainant further stated the delay and ultimate termination of Protocol F resulted in two patient deaths because they were unable to receive sleep studies and subsequent treatment for sleep apnea. We substantiated that Researcher 5 was barred from research activities at the facility, while the privileges of the PIs of Protocols A through D had not been curtailed or revoked for the infractions discussed in Issue 1. However, nothing in VHA or facility policy expressly limits the IRB and R&D Committee's discretion in the application of such penalties. Further, while we found that two patients did not receive sleep studies prior to their deaths, we did not substantiate that this resulted in these deaths or that it was related to IRB actions affecting Protocol F.

Researcher 5 submitted Protocol F, which was disapproved by the IRB on January 12, 2005. This was his first submission to the facility IRB. He then resubmitted the study, which was tabled by the IRB because of multiple irregularities in submission forms. Additionally, the IRB made recommendations for changes to the protocol and informed consent. Researcher 5 made additional changes and the project was approved by the IRB on May 11, 2005, subject to minor revisions to the informed consent. The R&D Committee approved the protocol on May 25, 2005, but requested the addition of a plan for statistical analysis of the data. Researcher 5 complied with the request.

During the course of audit activities conducted by the research compliance officer (RCO), the facility identified several issues with Researcher 5's protocol. These included no documentation of the consent process in the medical record, use of an unapproved consent form for five patients, discrepancies in handling research funds, and difficulty in locating source data. On July 6, 2006, the R&D Committee suspended Researcher 5 from research activities including membership in the R&D Committee until resolution of these issues.

The R&D Committee also formed an ad hoc committee to review these issues, which subsequently found four abstracts published by Researcher 5 without IRB approval. The subcommittee also found that research data was taken offsite and the PI could not provide adequate source documentation for the published abstracts. The ACOS/R&D reported that, while the subcommittee "determined there was evidence to suspect research misconduct," he did not find the evidence presented met the threshold of research misconduct. His findings were reported to ORO, which concluded that the ACOS/R&D's determination was "supported by a reasonable assessment of the evidence."

The facility's IRB and R&D Committee required that the PI find a replacement PI for his ongoing research study and present a safety plan providing for continuing care of patients

enrolled in the study. The IRB found the PI's response to be inadequate and closed the study on August 18, 2006. The facility notified ORO of the study closure. Finally, the IRB, R&D Committee, Research Integrity Officer, and Medical Center Director decided to bar Researcher 5 from "engaging in all future research activities at the Carl T. Hayden VA Medical Center."

The complainant maintained this punishment seemed inequitable, considering that neither the IRB nor the R&D Committee took action against the PIs in Protocols A, B, C, and D for the problems identified in Issue 1. While Researcher 5 provided explanations for many of the above discrepancies in documentation, we are unaware of VHA or facility policy limiting the severity of penalties that may be imposed by the IRB or R&D Committee for Researcher 5's infractions. Therefore, although we substantiated that the facility barred Researcher 5 from research activities, while the PIs of Protocols A through D had privileges to conduct research at the facility during the inspection, we note that this action does not appear to expressly violate VHA or facility policy.

Finally, the complainant alleged that the facility's action in failing to approve this protocol in a timely manner resulted in at least two patient deaths because of delays in receiving a diagnostic test known as polysomnography.[20] The purpose of this test is to diagnose sleep apnea, a disorder that results in low oxygen levels during sleep and which can contribute to the development of cardiac arrhythmias and a variety of chronic health problems. Patients enrolled in Protocol F would have received an in-home version of polysomnography in accordance with the protocol.

Researcher 5 evaluated the first patient clinically on October 25, 2005, and believed the patient had sleep apnea. The progress note of that date states that the patient would be evaluated again after polysomnography. The patient subsequently died in January 2006. A note entered on May 10, 2006, indicated that the patient did not undergo polysomnography prior to his death. Medical record documentation of the informed consent process occurred on May 10, 2006, after the date of the patient's death. Researcher 5 evaluated a second patient clinically on September 7, 2005, and stated that the plan was to schedule polysomnography. The patient subsequently expired in October 2006 without receiving this test. No documentation exists to explain why the polysomnography studies were not scheduled. We do not, however, substantiate that failure to schedule the polysomnography studies contributed or resulted in these patients' deaths. Both deaths occurred outside the hospital; the patients involved had multiple chronic health problems. Neither received an autopsy.

[20] Polysomnography, or a "sleep test," is a test in which the patient's oxygenation is monitored during sleep for purposes of diagnosing sleep apnea.

Issue 3: Alleged Conflict of Interest in the Operations of CTHMRF

The complainant alleged that a member of the Board of Directors of CTHNPC violated VA conflict of interest policies by voting on a grant for himself that was administered by the corporation. We can neither substantiate nor refute the allegation that the complainant voted on the grant due to the failure of the facility to maintain voting records.

Criminal and civil conflict of interest laws prohibit Government employees from participating, when the employee has a personal financial interest as defined in 18 United States Code, Section 208. We were not provided any evidence that the award of the grant benefited the researcher financially.

Notwithstanding the issue of whether the researcher benefited financially, we can neither substantiate nor refute the allegation that he voted on the award he received because the vote was conducted by e-mail and the facility did not maintain records of the Board's e-mail votes. Both current and draft versions of the nonprofit's by-laws permit the Board to vote "by unanimous written consent," which specifically includes e-mail. Because the vote had to be unanimous, even if the researcher recused himself from the process, the outcome would have been the same.

Issue 4: CTHMRF Meeting Minutes and IRB Correspondence

We substantiated that a research official in one case altered the minutes of the Board of Directors' meeting, but we found that this was to correct an error and did not violate VHA policy or procedure. We are unable to substantiate or refute allegations related to documentation irregularities in IRB correspondence. We further are unable to substantiate or refute whether the research official in question is solely responsible for the documentation irregularities.

The complainant alleged that a research official altered minutes of Board of Directors Meetings. An example included one set of minutes which described events at three separate Board meetings. The research official provided the Executive Director with a summary of what transpired at one of these meetings after the Executive Director was asked by the research official to leave the room. E-mails provided to us indicate that at least one other board member disagreed with the summary of events described in the minutes of that meeting. This Board member was able to comment on the summary because it was disseminated among Board members for their comments and approval. Disseminating the minutes for comment would not be consistent with a deliberate attempt to maintain inaccurate minutes.

However, during the course of our review of the Board of Directors Meeting minutes, we determined that the minutes did not consistently contain enough information to determine whether votes by Board members were in compliance with current by-laws (enacted in

1997) or by the draft by-laws, pending final approval by the Board at the time of our inspection. Both the 1997 version and the current draft of the by-laws state: "At each meeting, minutes shall be kept by the Secretary or someone appointed by the Chairman of the Board." We found at least one instance in which three meetings were consolidated into one set of minutes. In addition, the by-laws require a majority vote for approval of motions. The minutes do not contain sufficient voting information to confirm that a majority of the Board voted in favor of certain approved motions.

The complainant alleged that the same research official wrote a memorandum on behalf of the Chairman of the IRB and had another member of the R&D Committee sign it without approval of the IRB Chairman. We obtained e-mails demonstrating both that a draft memorandum did circulate between these individuals and that a researcher at the institution reported this situation to other research officials within the institution.

However, when we interviewed the Chair of the IRB, he denied that this incident occurred. We therefore can neither substantiate nor refute who actually wrote the memorandum in question or how it came to be attached to an e-mail originating with the research official who forwarded it to another member of the R&D Committee for signature.

Conclusion

While not substantiating allegations of violations of VHA policies concerning certain documentation issues and the inequitable application of IRB penalties, the problems identified in the areas of credentialing and privileging of research personnel, radioactive waste management, reporting of clinically relevant abnormal laboratory values, and conflict of interest in the setting of a VA-affiliated NPC suggest systemic issues in the management of research activities at this facility. Complicating our review was the absence of VHA policy in the areas of financial conflict of interest in terms applicable to research activities and in the credentialing and privileging of research personnel.

The facility has experienced significant changes in leadership recently, with both a new facility Director and a new Chief of Staff. We further note, the facility addressed several of the issues identified prior to the date of our inspection within the context of specific cases. However, the breadth of problems identified in the research arena at this facility warrant addressing deficiencies from a systems perspective. In addition, the finding that unlicensed research personnel performed minor procedures on patients at Facility 2 suggests at least the possibility that this particular condition could persist elsewhere. As a result, OHI will include in the Combined Assessment Program (CAP) an assessment of the scope of practice for unlicensed research personnel, as well as an assessment of the physical inventory of tritium at VHA facilities. We also make the following recommendations:

Recommendations

We recommend the VISN Director ensure that the Facility Director:

Recommendation 1. Prevents unlicensed physicians who work in VA research from engaging in activities which constitute the practice of medicine by ensuring (a) they have an appropriate scope of practice and (b) their research activities fall within that scope of practice.

Recommendation 2. Establishes procedures for ensuring that the storage, use, and disposal of radioactive wastes are managed in compliance with all applicable VHA and Federal regulations and policies.

Recommendation 3. Reviews the credentials of senior research managers and principal investigators to ensure that they have the requisite skills, training, and/or experience to perform their assigned or assumed administrative and research related duties.

Recommendation 4. Clearly delineates in policy the duty of the facility's laboratory to notify principal investigators or responsible clinicians of abnormal clinically significant laboratory data obtained for research purposes.

Recommendation 5. Reviews all conflict of interest policies pertaining to the facility or to CTHMRF for compliance with Federal ethics rules and regulations.

Comments

The VISN Director and facility Director concurred with the findings and recommendations of this inspection. In addition, the facility Director submitted a detailed corrective action plan regarding notification of PIs or responsible clinicians of abnormal clinically significant laboratory data obtained for research purposes (Recommendation 4) on December 7, 2006. On December 15, 2006, the facility Director also submitted a detailed plan to correct and prevent problems related to tritium-contaminated solid waste stored at the facility (Recommendation 2). Following the issuance of the draft report, the VISN Director and facility Director provided further comments and implementation plans. (See Appendix A, pages 18–24 for the complete text of their comments.)

We believe that the comments, along with the corrective action plans submitted in December, meet the intent of our recommendations. We will follow up on all planned actions until they are completed.

(original signed by:)
JOHN D. DAIGH, JR., M.D.
Assistant Inspector General for
Healthcare Inspections

Appendix A

VISN Director Comments

Department of Veterans Affairs **Memorandum**

Date: March 23, 2007

From: Network Director (10N17), VA Southwest Health Care Network, Mesa, AZ

Subject: Healthcare Inspections - Research Practices at Carl T. Hayden VA Medical Center, Phoenix, Arizona

To: Assistant Inspector General for Healthcare Inspections

THRU: Director, Management Review Service (10B5)

I concur with the facility response. See Medical Center Director's Comments for specific actions. Please contact Joan Funckes, Executive Assistant to the Network Director, VISN 18 at 602.222.2692, for any questions.

Patricia A. McKlem

PATRICIA A. MCKLEM

Network Director

VISN Director's Comments to Office of Inspector General's Report

The following VISN Director's comments are submitted in response to the recommendations in the Office of Inspector General's report:

OIG Recommendations

We recommend the VISN Director ensure the Facility Director:

Recommendation 1. Prevent unlicensed physicians who work in VA research from engaging in activities which constitute the practice of medicine by ensuring (a) they have an appropriate scope of practice and (b) their research activities fall within that scope of practice.

Concur **Target Completion Date:** Complete

See Medical Center Director's Comments for specific actions.

Recommendation 2. Establish procedures for ensuring that the storage, use, and disposal of radioactive wastes are managed in compliance with all applicable VHA and Federal regulations and policies.

Concur **Target Completion Date:** Complete

See Medical Center Director's Comments for specific actions.

Recommendation 3. Review the credentials of senior research managers and principal investigators and ensures they have the requisite skills, training, and/or experience to perform their assigned or assumed administrative and research related duties.

Concur **Target Completion Date:** Complete

See Medical Center Director's Comments for specific actions.

Recommendation 4. Clearly delineate in policy the duty of the facility's laboratory to notify principal investigators or responsible clinicians of abnormal clinically significant laboratory data obtained for research purposes.

Concur **Target Completion Date:** April 28, 2007

See Medical Center Director's Comments for specific actions.

Recommendation 5. Review all conflict of interest policies pertaining to the facility or to CTHMRF for compliance with Federal ethics rules and regulations.

Concur **Target Completion Date:** Complete

See Medical Center Director's Comments for specific actions.

Appendix B

Facility Director Comments

Department of Veterans Affairs **Memorandum**

Date: March 23, 2007

From: Medical Center Director (644/11Q), Carl T. Hayden VA Medical Center, Phoenix, AZ

Subject: Healthcare Inspections - Research Practices at Carl T. Hayden VA Medical Center, Phoenix, Arizona

To: Network Director, VA Southwest Health Care Network (10N18), Mesa, AZ

1. The draft report of the Healthcare Inspection – Research Practices was reviewed. The facility's comments and implementation plan are attached for the recommendations.

2. If you have any questions regarding this report, please contact Ms. Sally Compton, QM Program Manager, Quality Management Department at 602.277.5551, ext. 6777.

DONALD E. MOORE, R.Ph., M.B.A.

Facility Director's Comments to Office of Inspector General's Report

The following Facility Director's comments are submitted in response to the recommendations in the Office of Inspector General's report:

OIG Recommendations

We recommend the VISN Director ensure the Facility Director:

Recommendation 1. Prevent unlicensed physicians who work in VA research from engaging in activities which constitute the practice of medicine by ensuring (a) they have an appropriate scope of practice and (b) their research activities fall within that scope of practice.

Concur **Target Completion Date:** Complete

There have been no biopsies performed by an unlicensed physician since 2005. This incident was immediately reported to the Office of Research Oversight (ORO) and appropriate action was taken following ORO's guidance. There have been no occurrences since 2005.

The Research template review checklist has been changed to include instructions to specifically identify unlicensed physicians. Research scopes of practice for unlicensed physicians were reviewed and revised as needed. In order to improve the overall process, the following changes were made. Separate forms were designed for licensed and unlicensed personnel. This will assist the R&D Committee to identify unlicensed physicians and ensure that their scopes of practice are congruent with their research duties. The Chief of Staff and Director will approve every new or revised Research scope of practice.

Scopes of practice for unlicensed physicians will be attached to protocol materials which are reviewed by R&D and IRB committees. A statement has also been added to the Protocol Checklist that asks if duties assigned to an unlicensed physician fall within their scope of practice.

Recommendation 2. Establish procedures for ensuring that the storage, use, and disposal of radioactive wastes are managed in compliance with all applicable VHA and Federal regulations and policies.

Concur **Target Completion Date:** Complete

The Research Radiation Safety Manual has procedures for ensuring that the storage and disposal of radioactive wastes are managed in compliance with all applicable VHA and Federal regulations and policies and the facility's Radioactive Materials permit. The use of radioactive materials is protocol specific in experiments to be carried out by licensed users.

Stored long-lived radioactive waste is being picked up quarterly, as needed, by a licensed broker.

Recommendation 3. Review the credentials of senior research managers and principal investigators and ensures they have the requisite skills, training, and/or experience to perform their assigned or assumed administrative and research related duties.

Concur **Target Completion Date:** Complete

Credentials of senior research managers and principal investigators have been reviewed and they have the requisite skills, training, and/or experience to perform their assigned or assumed administrative and research-related duties.

The protocol review process includes a copy of the principal investigator's curriculum vitae for the R&D Committee's review in order to ensure that they have appropriate skills and research training to carry out the proposed project.

Recommendation 4. Clearly delineate in policy the duty of the facility's laboratory to notify principal investigators or responsible clinicians of abnormal clinically significant laboratory data obtained for research purposes.

Concur **Target Completion Date:** April 28, 2007

Facility Policy Memorandum No. CS/113-8, Procedure for Reporting Critical Laboratory Results, provides instructions on reporting critical laboratory results. A critical value denotes a test result that requires immediate attention by a responsible caregiver because the result has clinical significance to the patient. This policy is being amended to include telephonic notification to the responsible principal investigator if a research protocol is involved.

Facility Policy Memorandum No. CS/113-14, Procedure for Reporting Abnormal Laboratory Results, will be amended to report abnormal laboratory results for de-identified research subjects via e-mail message to the principal investigator or designee.

Recommendation 5. Review all conflict of interest policies pertaining to the facility or to CTHMRF for compliance with Federal ethics rules and regulations.

Concur **Target Completion Date:** Complete

The following directives and policies were reviewed to ensure that Research and the CTHMRF are compliant with Federal ethics rules and regulations: (1) VHA Directive 1200, VHA Research and Development, (2) VHA Handbook 1200.17, VA Research and Education Corporations Authorized by Title 38 USC Section 7361 Through 7368 Handbook, and (3) DVA Memorandum dated September 23, 2005 from Chief Research and Development Officer, Subj.: Financial Conflicts of Interest in Research. In addition, the CTHVAMC Standard Operating Procedures for R&D/IRB includes a section on financial disclosure and conflict of interest.

Appendix C

OIG Contact and Staff Acknowledgments

OIG Contact	Andrea Buck, M.D., J.D., Medical Consultant Washington, DC (202) 565-8496
Acknowledgments	Linda DeLong, Director Karen Moore, Associate Director Maureen Regan, J.D. Roxanna Osegueda

Appendix D

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