UCSB Audit and Advisory Services

Internal Audit Report

Human Subjects

April 26, 2017

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Report No. 08-17-0008

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April 26, 2017

To: Karen Hanson, Assistant Vice Chancellor for Research
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Office of Research

Distribution

Re: **Human Subjects**
Audit Report No. 08-17-0008

As part of the 2016-17 audit services plan, Audit and Advisory Services has completed an audit of human subjects protocol processes. Enclosed is the report detailing the results of our review.

The purpose of this audit was to determine whether the Research Integrity unit within the Office of Research has implemented appropriate processes to ensure compliance with federal and state requirements, and in accordance with University of California (UC) and University of California, Santa Barbara (UCSB) policies and procedures relating to the protection of human subjects in research. The scope of the audit covered general administration and current operating procedures of human subject protocols from July 2015 through January 2017, including Human Subjects Committee policies and procedures, training requirements, and protocol review process.

The audit found overall compliance with federal and state regulations in the areas included in the scope of our work. Although we found that there are adequate processes and internal controls in place, we did highlight opportunities for improvement in areas such as the approval process, post-approval reviews, communication by external IRBs, training for researchers, and documenting information security controls.

Detailed observations and management corrective actions are included in the following sections of the report. The management corrective actions provided indicate that each audit observation was given thoughtful consideration, and positive measures have been taken or planned in order to implement the management corrective actions.

We sincerely appreciate the cooperation and assistance provided by Research Integrity personnel during the review. If you have any questions, please contact me.

Respectfully submitted,

Jessie Masek

Jessie Masek
Acting Director
Audit and Advisory Services

Enclosure

Distribution:

Interim Vice Chancellor for Research Joe Incandela
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cc: Chancellor Henry Yang
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UCSB Audit Committee
Interim Senior Vice President and Chief Compliance and Audit Officer John Lohse

PURPOSE

The purpose of this audit was to determine whether the Research Integrity unit within Office of Research has implemented appropriate processes to ensure compliance with federal and state requirements, in accordance with University of California (UC) and University of California, Santa Barbara (UCSB) policies and procedures relating to the protection of human subjects in research. This audit is part of the fiscal year 2016-17 audit services plan of UCSB Audit and Advisory Services.

SCOPE, OBJECTIVES AND METHODOLOGY

The scope of the audit covered general administration and current operating procedures of human subject protocols from July 2015 through January 2017, including:

- Human Subjects Committee.
- Policies and procedures.
- Training requirements.
- Protocol review process.

The objectives of our review were to determine whether the Office of Research has adequate operating procedures and whether human subject protocols are managed in accordance with federal and state regulation and University policies.

To accomplish our objectives, we:

- Reviewed federal and state regulation, UC and UCSB policies and procedures concerning human subjects use in research. See Table 1 for relevant human subjects UC policies and regulation.

- Reviewed relevant UC and UCSB audit and advisory work, related to human subject research (see Table2).

- Conducted interviews with Research Integrity personnel to obtain a better understanding of the processes and internal controls in place and to identify areas of concern.

- Assessed risks in selected areas based on the results of interviews, governance body, regulation, University policies, training requirements, oversight of external institutional review boards (IRB), data privacy, and prior audits.

- Performed a review of Research Integrity operational procedures to determine whether University procedures comply with federal and state requirements.

- Reviewed research protocols managed by external IRBs to determine whether the University has implemented adequate oversight of UCSB protocols managed by external IRBs.

This audit was conducted in conformance with the *International Standards for the Professional Practice of Internal Auditing.*

Table 1 **Relevant Human Subjects UC Policies and Regulation**

Policy	Description
Code of Federal Regulation Title 45 Public Welfare Department of Health and Human Services Part 46 - *Protection of Human Subjects*	Applies to all human subjects research conducted, supported, or otherwise subject to regulation by any federal department or agency, which elects to make the policy applicable.
Code of Federal Regulation Title 32 National Defense Part 219 - *Protection of Human Subjects*	Regulations covering human subjects research when Department of Defense funding is involved.
Federal Register, Vol. 63, No. 216 – *Categories of Research That May Be Reviewed by the Institutional Review Board Through an Expedited Review Procedure*	Provides information on what research may qualify for an expedited review procedure. Expedited review may be done by the IRB chair or by one or more IRB members designated by the chair.
California Health and Safety Code Sections 24170-24179.5 *Protection of Human Subjects in Medical Experimentation Act*	Provides minimum statutory requirements regarding human experimentation and provides penalties for violations.
University of California Policy, *Protection of Human Subjects in Research*	Systemwide policy regarding the protection of human subjects involved in biomedical and behavioral research, regardless of the funding source.
University of California Policy, *HIPAA and Research*	Requires researchers wanting to use Protected Health Information (PHI) to conduct research to obtain authorization of the subject or satisfy an exception to the authorization requirement.
UC Contract and Grants Manual - Chapter 18 - *Protection of Research Subjects*	The Contract and Grants Manual provides guidance on systemwide policies as they relate to the requirements of major sponsors, the federal government, and the State of California.
UCSB Research Circular No. D.2 – *Policy on the Use of Human Subjects*	Currently undergoing revisions, this policy covers the ethical principles, responsibilities, and review process for the use of human subjects in research.
UCSB Human Subjects Committee *Member Binder*	Provided to each member of the Human Subjects Committee, this binder includes information on training, membership, ethical guidelines, policies, regulations, standard operation procedures, additional resources, and guidance for reviewing protocols submitted for review.

Source: Auditor analysis

BACKGROUND

University of California, Santa Barbara Office of Research[1]

The Office of Research helps the university community secure support for their research and creative activities. They work with all academic units to promote research throughout the

[1] Source: UCSB Office of Research webpage, http://www.research.ucsb.edu.

university, and have special responsibility for research done collaboratively across disciplines, departments, and schools. They ensure the integrity of UCSB research and provide assurance to governmental and private funding agencies and to the public that the research is conducted in accordance with the highest ethical standards.

UCSB Human Subjects Committee

The UCSB Human Subjects Committee (HSC) is an independent administrative committee mandated by the US Department of Health and Human Services and responsible to the Human Research Protections Program Office (HRPPO). At UCSB, HSC serves as the Institutional Review Board (IRB) for reviewing research applications involving human subjects. The primary mission of the HSC is to ensure the protection of the rights and welfare of human subjects who participate in research conducted by university faculty, staff, and students. The HSC is charged with ensuring compliance with federal regulations, state and local laws, and UC policies review and approval by the HSC is required before starting research involving human subjects.

The HSC review and approval process involves performing a risk assessment of the proposed research, which may include additional review by relevant departments on campus, as necessary. The research protocol application, IRB review, and approval process are documented in the Office of Research Application for the use of Human Subjects (ORahs) system.

Table 2 Relevant Previous Work by UC Audit and Advisory Services

Report Name	Year	Campus
Human Subjects Research - Policy Compliance	2003	UC Santa Barbara
Campus Monitoring of Human Subjects Research	1999	UC Santa Cruz
Participant Support and Payments to Human Subjects	2015	UC Berkeley
Internal Audit of Institutional Review Board (IRB) – Human Subjects	2005	UC Riverside
Clinical Research Compliance – IND Program and Protocol Registration System	2014	UC San Diego
Laboratory Compliance for Stem Cell Research	2010	UC San Diego
Phase II Trial of Levodopa for Angelman Syndrome - Regulatory Review Project	2013	UC San Diego
Office of Research Affairs Human Subjects	1999	UC San Francisco
Human Research Protection Program Post Approval Event Reporting	2014	UC San Francisco

Source: Auditor analysis

Research Integrity

The Research Integrity Department, a unit within the Office of Research, provides broad oversight, resources, and education for compliance issues relating to the conduct of research at UCSB.

The UCSB Human Subjects Office is a subunit within Research Integrity that provides administrative pre-reviews of proposed research activities and ensures researchers follow

federal, state, and university regulations when using human subjects as research participants. See Table 3 for main federal and state human subject requirements. The UCSB Human Subjects Office offers advice on and assistance with the development of human subjects protocol applications, and supports the HSC. The UCSB Human Subjects Office also provides education and outreach to the campus community and acts as a liaison between various campus departments, researchers, the HSC, and governmental agencies.

Table 3 Federal and State Human Subject Requirements

Category	Description
Approval for Protocol Submissions	IRBs must review and approve, require modification, or disapprove of all research activities related to human subjects.
Risks and Reasonableness of Risks	Risks to subjects are reasonable and are minimized by using procedures consistent with sound research design and using procedures already being performed, if appropriate.
Informed Consent or Waiver	IRBs must require informed consent and be documented, but may waive documentation in accordance with provisions in the federal regulations.
Written Notification to Approve Research	Investigators and institutions must provide written notification of the IRB's decision to approve or disapprove a proposed research activity. If disapproved, the written notification must include reasons for the decision and allow the investigator to respond.
Subject Privacy and Confidentiality of Data	When appropriate, IRBs must find that the protocol makes adequate provisions to protect subject privacy and maintain confidentiality of data.
Provisions for Monitoring Ongoing Research	When appropriate, IRBs must find that the protocol makes adequate provisions for monitoring the data collected and ensuring subject safety.
Expedited Review only for Minimal Risk	IRBs may use an expedited review procedure to review research involving minimal risk, or minor changes in previously approved research within one year (or less) of the original approval.

Source: Federal and state regulation.

ORahs 2.0

Office of Research Application for the use of Human Subjects (ORahs) is the system used for the submission of research protocols to HSC for review. Investigators submit a proposal through the application and receive system notifications (via email) regarding the progression of the protocol through the review process. Both UCSB Human Subjects Office and the HSC use the system for viewing and commenting on protocols prior to formal review. The UCSB Human Subjects Office may communicate with the investigator by requesting more information. After review, the system generates a letter notifying the investigator whether the protocol was approved or denied. The system is also used for any changes or updates to the protocol, if needed, while research is underway. Notifications are automatically generated to inform investigators of the need to renew a protocol and staff uses the system to monitor ongoing research.

ORahs access control is synchronized with the campus Identity Management system. There are three main roles: HS Coordinators, Researchers, and HS Committee members. Principal investigators (PIs) are granted access to their protocols. PIs must request access for any additional people on their research projects in ORahs. Usually when a protocol is submitted, the research group is already listed and given access, including PIs. The only time PIs would need to

add people is if they are not listed on the protocol. ORahs only includes the approval process for research protocols. ORahs does not handle sensitive data, which is limited to the protocol review and approval process.

SUMMARY OPINION

The audit found overall compliance with federal and state regulations in the areas included in the scope of our work. Although we found that there are adequate processes and internal controls in place, we did highlight opportunities for improvement in areas such as the approval process, post-approval reviews, communication by external IRBs, training for researchers, and documenting information security control.

Audit observations and management corrective actions are detailed in the remainder of the audit report.

DETAILED OBSERVATIONS AND MANAGEMENT CORRECTIVE ACTIONS

A. Procedures

We found that the Office of Research has formalized a set of procedures that help researchers to comply with federal and state regulation requirements related to human subject research. Table 4 outlines the procedures covering regulation requirements. Appendix A includes the complete list of the Human Subject Committee Standard Operating Procedures (HSC SOP).

Table 4 Federal and State Human Subject Requirements Covered by HSC SOP

Category	Rating	UCSB Procedure
Approval for Protocol Submissions	✓	HSC SOP-013 Submission Requirements.
Risks and Reasonableness of Risks	✓	HSC SOP-014 Initial Review Section 3: Policy and Procedure; Subsection 3.1: Minimum Criteria for Approval of Human Subjects Research
Informed Consent or Waiver	✓	
Subject Privacy and Confidentiality of Data	✓	
Written Decision to Approve Research	✓	HSC SOP-014 Initial Review Section 6.1.2
Provisions for Monitoring Ongoing Research	✓	HSC SOP-017 Continuing Review
	✓	HSC SOP-019 Monitoring of Ongoing Research
Expedite Reviews for Qualifying Protocols	✓	HSC SOP-015 Exemption Review
	✓	HSC SOP-016 Expedited Review

Source: Human Subject Committee Standard Operating Procedures

B. Compliance with Regulation and Best Practices

Our review of research protocols oversighted by external IRBs and by HSC highlighted that the Research Integrity unit within Office of Research has implemented appropriate processes to ensure compliance with federal and state requirements, in accordance with UC and UCSB policies and procedures relating to the protection of human subjects in research. However, we found opportunities for improvement, including pre-approvals of Department of Defense (DOD) protocols, post-approval monitoring reviews, incident reporting for external IRBs, training for researchers, and documenting information security controls. Table 5 summarized our findings:

- One protocol with DoD funding was approved by the HSC and a copy of the Human Research Protection Program Office (HRPPO) review was not submitted to the HSC.[2]

- Research Integrity does not perform post-approval monitoring of human subject research projects due to limited staff. For example, all applicable protocols in our sample included approved consent forms. However, there is no oversight to assure that researchers are providing and collecting consent forms.

[2] Research Integrity updated its procedures to include this requirement as part of current procedures.

- External IRBs do not usually provide formal progress reports or incident report regarding the UCSB research project that they manage.[3]

- Research Integrity suggested that there are opportunities to improve the content and frequency of human subject training for the UCSB research community. There is available a more robust training without extra cost. Additionally, researchers should take refresher trainings. Currently, researchers only have to take the training one time.

- As part of the protocol submission process, principal investigators provide a brief description of how identifiable research data is stored and protected.[4] However, there is no detailed information regarding:

  - Retention period of identifiable research data and location.
  - Information security practices and controls to comply with privacy requirements.

- There are no regular reviews of ORahs user accounts. Research Integrity relies on the campus identity management system to disable user accounts when researchers leave the University.

Table 5 Compliance with Regulation, University Policy, and Best Practices

Category	Rating	Comments
1. Appropriate Approvals	Partial	One protocol sponsored by the Department of Defenses (DoD) did not include HRPPO review.
2. Support documentation required for submission	✓	
3. Risk analysis and risk to subjects	✓	All applicable protocols included a risk and benefits analysis. There is a standard reporting document.
4. Consent forms and information sheets used	Partial	No post-evaluation review to validate whether researchers provided and collected consent forms.
5. Letter communicating approval or denial of submission	✓	
6. Data storage information	✓	There is no consistent information regarding retention period and research data location.
7. Confidentiality / Privacy requirements	✓	Protocols included a description of data privacy requirements. However, there is no details of how information is stored and protected.
8. Reporting[1]	Partial	Agreements with external IRBs do not include requirements to provide formal progress reports.

Source: Auditor analysis
✓: Full compliance.
Partial: Partial compliance.
1: Best practice not required by UC policy or federal or state regulation.

[3] In the case of Cottage Hospital, there are monthly meetings that discuss projects.
[4] ORahs only keeps information related to protocol submission and approval, but not research data.

We recommend Research Integrity to update or formalize new procedures to include the following enhancements:

- Request the Human Research Protection Program Office (HRPPO) review for all DoD protocols.
- Evaluate implementing a post approval monitoring process that includes the review of consent forms.
- Request researchers with projects managed by external IRB to report to HSC:
    - Any unanticipated problems or unexpected adverse events.
    - If the research has placed subjects at a greater risk of harm than was previously known or recognized.
    - Any significant changes or serious protocol non-compliance associated with their project.
- Evaluate replacing the current training for researchers for a more robust training and establish a minimal frequency for refresher training.
- Define minimal information security information to be presented with the protocol submission.

Management Corrective Actions

Research Integrity will update their procedures to include the following enhancements:

- Request the Human Research Protection Program Office (HRPPO) review for all DoD protocols.
- Evaluate implementing a post approval monitoring process that includes the review of consent forms.
- Request researchers with projects managed by external IRB to report to HSC:
    - Any unanticipated problems or unexpected adverse events.
    - If the research has placed subjects at a greater risk of harm than was previously known or recognized.
    - Any significant changes or serious protocol non-compliance associated with their project.
- Evaluate replacing the current training for researchers for a more robust training and establish a minimal frequency for refresher training.
- Define minimal information security information to be presented with the protocol submission.

Audit and Advisory Services will follow up on the status of these issues by July 31, 2017.

Appendix A	Human Subject Committee Standard Operating Procedures

Procedure	Description
HSC SOP No: 001.02 - Review and Approval Process	Establishes the process for creating and updating standard operating procedures and supporting documents.
HSC SOP No: 002.02 - Resource Development Distribution	Establishes the procedure for creating and updating committee resource documents.
HSC SOP No: 003.02 – Meeting Conduct	Establishes the procedure for the conduct of committee meetings.
HSC SOP No: 006.02 – Membership Managing Conflicting Interest	Establishes the procedure for the identification and management of conflicting interests of committee members.
HSC SOP No: 007.02 – Chair Discussion Leader Assignment	Establishes the procedure for the Chair or designee to assign committee members to serve as discussion leaders for protocols subject to full board review, or to conduct an expedited review of research that involves minimal risk.
HSC SOP No: 008.02 – Consultants	Establishes the procedure for the committee to obtain Consultants once the need for one is identified.
HSC SOP No: 009.02 – Membership Addition	Establishes the process for the addition of a new committee member.
HSC SOP No: 010.02 – Membership Removal	Establishes the process for the removal of a committee member.
HSC SOP No: 011.02 – Minutes	Establishes the process for recording committee meeting minutes.
HSC SOP No: 012.02 – Records	Establishes the procedure for maintaining Office of Research Human Subjects and the Human Subjects Committee records.
HSC SOP No: 013 – Submission Requirements	Requires investigators submit protocol applications for IRB review and outlines the submission requirements for protocols.
HSC SOP No.: 014 – Initial Review	Establishes the procedure for the IRB review process and sets forth the minimum criteria for the approval of human subject research.
HSC SOP No.: 015 – Exemption Determination	Establishes the procedure for the IRB to determine whether research activities fall under the categories of research that are exempt from federal regulations.
HSC SOP No.: 016 – Expedited Review	Establishes the procedure for an expedited review process for eligible research activities listed in the Federal Register Volume 63, No. 216.
HSC SOP-017 Continuing Review	Requires the IRB to conduct continuing review of research at intervals appropriate to the degree of risk, but no less than annually.
HSC SOP No.: 018 – Amendments	Requires all changes/modifications to approved research be submitted to the IRB for review and approval prior to implementation.
HSC SOP No: 019 – Monitoring of Ongoing Research	Establishes procedures for concurrent monitoring and periodic review of research activities in order to determine whether the research should be continued, modified, or terminated.
HSC SOP No: 020 – Data Collection without IRB Approval	Policy and procedure for IRB review when data is obtained from non-exempt research without prior IRB approval. Gives the circumstances when data is considered to have been collected without approval and the actions following data collected without approval.

Appendix A	Human Subject Committee Standard Operating Procedures

Procedure	Description
HSC SOP No: 021 – Protocol Deviations and Non-Compliance	Requires and outlines the procedure for IRB review and response to allegations of potential protocol deviations and/or non-compliance regarding approved research protocols.
HSC SOP No: 022 – Suspension or Termination	Grants the IRB the authority to and outlines the policy and procedure for the suspension or termination approved research, which is not conducted in accordance with IRB requirements or has been associated with unexpected serious harm to subjects.
HSC SOP No: 023 – Unanticipated Problems or Adverse Events	Fulfills federal requirements of having written procedures for the reporting of any unanticipated problems involving risks to subjects or others. This sets forth the institutional expectations and obligations of investigators.
HSC SOP No: 024 – International Research	Affirms that the IRB requires the same standards for all human subject research, no matter where the research is conducted. This policy also outlines the additional responsibilities assigned to Investigators conducting research at international locations.
HSC SOP No: 025 – Special Conditions: Pregnant Women, Fetuses, and Neonates	Federal regulations require additional protections when human subject research involves “vulnerable” populations. These policies address those requirements outlined in subparts B, C, and D of the Code of Federal Regulation Title 45 Public Welfare Department of Health and Human Services Part 46 - Protection of Human Subjects.
HSC SOP No: 026 – Special Considerations: Children	
HSC SOP No: 027 – Special Considerations: Prisoners	
HSC SOP No: 030 – Research Involving the Department of Defense	Outlines the additional responsibilities and requirements, which apply to all non-exempt human subject research involving the DoD. Also has guidance for identifying research that involves the DoD.

Source: Auditor analysis