UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
AUDIT AND ADVISORY SERVICES

HRPP Review – Follow-Up
Project #17-045

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University of California
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UCSF

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SUBJECT: Human Research Protection Program (HRPP) Follow-up Review #17-045

As a planned internal audit for Fiscal Year 2017, Audit and Advisory Services ("A&AS") conducted a follow-up on the HRPP review completed in 2014 to validate that corrective actions implemented have addressed the issues identified.

Our services were performed in accordance with the applicable International Standards for the Professional Practice of Internal Auditing as prescribed by the Institute of Internal Auditors (the "IIA Standards").

The preliminary draft report was provided to department management in February 2017. Management provided us with their final comments and responses to our observations in March 2017. The observations and corrective actions have been discussed and agreed upon with department management and it is management's responsibility to implement the corrective actions stated in the report. In accordance with the University of California audit policy, A&AS will periodically follow up to confirm that the agreed upon management corrective actions are completed within the dates specified in the final report.

This report is intended solely for the information and internal use of UCSF management and the Ethics, Compliance and Audit Board, and is not intended to be and should not be used by any other person or entity.

Sincerely,

Irene McGlynn
Director
UCSF Audit and Advisory Services

EXECUTIVE SUMMARY

I. BACKGROUND

The Human Research Protection Program (HRPP) reviews and monitors research involving human subjects at UCSF and several affiliate institutions to ensure the ethical and equitable treatment of the research subjects. The HRPP is comprised of these groups:

- The Institutional Review Board (IRB), which reviews human subject research studies;
- The Quality Improvement Unit (QIU), which conducts monitoring, education, and other QI activities; and
- The Human Gamete, Embryo, and Stem Cell Research (GESCR) Committee.

Audit and Advisory Services performed an HRPP audit in 2014; however, subsequent to the 2014 audit, HRPP has undergone organizational changes with turnover of key executives and staff members. As part of the re-organization, two positions, the QIU Coordinator and the Training Coordinator, were reallocated to IRB activities, resulting in routine site visits (RSV) activities being currently suspended and training courses reduced.

The Integrated Research Information System (iRIS) is used for online submission, tracking, and monitoring of Post Approval Event Reporting (PAER) compliance activities managed by QIU, including using the Adverse Event (AE) and Protocol Violation (PV) reporting forms. The number of AEs and PVs reported during calendar year 2016 and their dispositions were as follows:

Incident Reporting	AE Forms	PV Forms
Total Submitted	268	260
Noncompliance [1]	0	73
Reportable Events	25	12

The Common Rule 45 CFR 46 Subpart A and 21 CFR §56 requires prompt notification of reportable events, which include unanticipated problems (UP), serious or continuing non-compliance (S/CNC), suspension, and terminations, to ensure that timely actions are taken to protect human subjects from avoidable harm in clinical research.

[1] Noncompliance is defined as "failure to follow state federal regulation, or the University policies, or the requirements of the Veterans Health Administration Handbook 1200.5, or determinations of the IRB for the protections of the rights and welfare of study participants." While non-compliance is acknowledged, these events do not rise to the level of reportable events.

II. AUDIT PURPOSE AND SCOPE

The purpose of this review was to follow-up on the HRPP review completed in 2014 (report dated March 2014) and to validate that corrective actions implemented have addressed the issues identified.

The scope of the review included analyses of reportable events from August 2014 to September 2016.

Procedures performed as part of the review included interviews with QIU department personnel to understand the status of corrective actions implemented and examination of reportable events to determine compliance rate with internal policies and procedures as well as adherence to outside regulatory reporting guidelines.

Work performed was limited to the specific activities and procedures described above. As such, this report is not intended to, nor can it be relied upon to provide an assessment of compliance beyond those areas specifically reviewed. Fieldwork was completed in January 2016.

III. SUMMARY

Based on our review, QIU management has implemented actions that addressed the risks identified in the prior audit. These actions included the adoption of the 30-day target for reporting to outside agencies on reportable events and reducing the submission time period for the Principal Investigators (PI) to report to QIU on serious and unexpected adverse events and major protocol violations/incidents from 10 to 5 days from date of awareness. Additionally, an Agency Tracking report was developed to monitor timeliness with key hand-off points including PI submission date and notification dates to Institutional Officer and agencies.[2] The compliance rate for meeting the 30-day target for reporting to outside agencies increased from 62% in 2015 to 85% in 2016.

Other steps that QIU has taken to reduce notification delays to outside agencies include delegating the review of the notification letters previously conducted by the Associate Vice Chancellor of Ethics & Compliance to the Director; and concurrent notifications to the Institutional Official and the applicable federal agencies once a determination has been made. The determination of "noncompliance" outcome is now undertaken by the QIU coordinator and the Chair of the IRB Committee as opposed to solely reserving this for the IRB Committee.

While many of the action plans have been implemented, opportunities for improvement exist in the areas of capturing and reporting Veteran Affairs' (VA) reportable events, monitoring of compliance through RSV, implementing iRIS system enhancements to create efficiencies for compliance and monitoring reporting, and reducing excessive submissions of AE and PV reporting forms.

Further detail on the specific observations can be found in the next section on Observations and Management Corrective Action Plans.

[2] Agencies include Office of Human Research Protections (OHRP), Food and Drug Administration (FDA), and Department of Veterans Affairs Office of Research Oversight depending on studies' reporting requirements.

IV. OBSERVATIONS & MANAGEMENT CORRECTIVE ACTIONS

No.	Observation	Risk/Effect	Recommendation	Management Corrective Actions
1	**OHRP/FDA and the Institutional Official were not always notified of VA reportable events.** VA reportable events are tracked independently by VA HRPP staff and reported directly to the Federal Office of Research Oversight (ORO), which oversees all VA research. Four VA reportable events during our period of review were not reported to OHRP, FDA, or the UCSF Institutional Officer. It was noted that there may not be established procedures between UCSF and VA on VA reportable events. Upon clarification of reportable event processes between UCSF and VA, QIU discovered that VA reportable events should also be reported to the OHRP or FDA in addition to ORO.	Delayed reporting of reportable events results in non-compliance with federal regulations and may impact patient safety and increase liability for the University.	QIU management should develop procedures between UCSF and VA on VA reportable events to allow proper notifications to relevant agencies and parties. Additionally, awareness of this reporting requirement should be shared with other UC campuses that have VA research activities.	a) QIU has reviewed the current reporting procedures with the VA HRPP staff and provided training. A new SOP will be created specifically for VA reporting procedures. QIU will monitor VA reporting to all federal organizations. The new SOP will be completed by September 15, 2017. b) To correct the deficiency in not reporting to other federal agencies, all previous reports of SCNC or UPs will be sent to OHRP and/or FDA, as applicable. This will be completed by June 30, 2017.

No.	Observation	Risk/Effect	Recommendation	Management Corrective Actions
2	**Routine site visits for monitoring compliance are not being conducted.** QIU has suspended its RSV since April 2014 due to the department reorganization. The RSVs are an important oversight control activity for performing protocol compliance assessments to identify risks and non-compliance. They also provide opportunities for on the spot education and consultations and build relationships with the research community.	Risks and non-compliance may not be identified and adequately addressed.	QIU management should continue to consider reinstating the RSV program on a risk-based basis to align with its objective in enhancing compliance activities to ensure patient safety.	QIU management is working with the Associate Vice Chancellor's office to determine the feasibility of re-instating the Routine Site Visit Program. This is a resource issue and we are looking at how best to obtain additional resources. The assessment will be completed by September 15, 2017.

IMPROVEMENT OPPORTUNITIES

No.	Observation	Risk/Effect	Recommendation
1	**The iRIS application has additional functionality that could be leveraged to reduce manual efforts.** While the iRIS application has the potential ability to track reportable events and non-compliance outcomes, enhancements have not been made to allow this feature to be available. As a result, QIU continues to manually enter data from iRIS into a spreadsheet (Agency Tracking spreadsheet). This manual process is labor intensive and contributed to discrepancies on the spreadsheet. iRIS enhancements for compliance monitoring and reporting were recommended to Management in the 2014 audit review.	Manual tracking of reportable events is an inefficient use of limited resources and may result in errors impacting the accuracy of the metrics on reportable events.	QIU management should evaluate how the iRIS application could be effectively utilized to create efficiencies in reporting and compliance monitoring. Management should consider reaching out to other iRIS users within other academic research institutions to leverage how they have utilized system functionalities for improving reporting and monitoring.
2	**Additional training on criteria for AE and PV submissions could allow for more effective use of resources.** In 2016, about 20% of AE and PV submissions met the definitions of UP or S/CNC and were submitted for IRB review. Each submission requires time of the PI or research staff to enter detailed data and of the QIU coordinator for review and determination on whether it meets the criteria for IRB review. The processing of the excessive submissions may reduce resource availability for operations.	Limited resources within the research departments and QIU are being expended for submissions and subsequent review that could be utilized elsewhere.	QIU management should look into causes of excessive submissions and develop applicable solutions to reduce the number of submissions, including continuing to educate the PIs and their research staff on the type of incidents that warrant reporting and provide job aids where applicable.