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GENE HASEGAWA
Chief Operating Officer
Vice Chancellor Health Sciences
0602

JENNIFER BRASWELL
Executive Director
Sanford Center
0695

**Subject: *Stem Cell Clinical Trial Accounting Review
Report 2016-23***

The final report for *Stem Cell Clinical Trial Accounting*, Report 2016-23, is attached. We would like to thank all members of the department for their cooperation and assistance during the review.

Because we were able to reach agreement regarding management action plans in response to the audit recommendations, a formal response to the report is not requested. The findings included in this report will be added to our follow-up system. We will contact you at the appropriate time to evaluate the status of the management action plans.

UC wide policy requires that all draft reports be destroyed after the final report is issued. We also request that draft reports not be photocopied or otherwise redistributed.

David Meier
Director
Audit & Management Advisory Services

Attachment

cc: David Brenner
 Judy Bruner
 Joseph Ciacci
 Bryan Clary
 Wolfgang Dillmann
 Bill Gentz
 Larry Goldstein
 Robert Henry
 Greg Kharabadze

David Kimber
John Lohse
Pierre Ouillet
Cheryl Ross
Amir Schangali
Marlene Shaver
Andy Walton
Dan Weissburg
Erika Wilson

UC San Diego

AUDIT & MANAGEMENT ADVISORY SERVICES

Stem Cell Clinical Trial Accounting Review
Report No. 2016-23
August 2017

FINAL REPORT

Performed By:

Aparna Handa, Auditor
Christa Perkins, Associate Director

Approved By:

David Meier, Director

TABLE OF CONTENTS

I. EXECUTIVE SUMMARY 2

II. BACKGROUND..... 3

III. AUDIT OBJECTIVE, SCOPE, AND PROCEDURES 5

IV. CONCLUSION..... 6

V. OBSERVATIONS REQUIRING MANAGEMENT ACTION 7

 A. Study Cost Transfers 7

I. EXECUTIVE SUMMARY

Audit & Management Advisory Services (AMAS) completed a review of Stem Cell Clinical Trial Accounting as requested by management. The objective of our review was to determine whether processes to allocate or transfer charges to donor gift funds, for the two designated clinical trials were effective, adequately supported, and compliant with donor commitments, sponsor agreements, and applicable clinical research billing policies.

We concluded that a process had been established to allocate and transfer charges to donor gift funds that was generally compliant with the donor commitment, sponsor agreements and clinical research billing policies. As of April 2017, a total of \$205,866 (#140248) and \$297,863 (#140261) had been provided by the Sanford Center as part of its financial commitment to support the clinical trials. We noted that the Sanford Center had developed documentation for study #140261 to track the total subject-related costs which had been funded through gift funds. A similar cost per subject analysis was pending for the other study (#140248), but had not yet been completed.

Our analysis of total subject specific costs charged to study indexes in comparison to total cost transfers indicated the need for additional transfers to be processed for both studies to fund subject charges to date. There may also be a need to reconfirm the financial commitment from Sanford for these studies. Management action plans to address this finding are summarized briefly below:

A. Study Cost Transfers

1. Sanford Center, the study team and appropriate study fund management personnel will coordinate to reconfirm Sanford Center's financial obligations to the department for both studies.
2. The Sanford Center or Alpha Clinic will prepare and present an analysis of cost per subject for study #140248.
3. Sanford Center will process cost transfers to meet their financial obligations as confirmed with the department (per A.1) as appropriate.

Observations and related management action plans are described in greater detail in section V. of this report

II. BACKGROUND

Audit & Management Advisory Services (AMAS) has completed a review of Stem Cell Clinical Trial Accounting as requested by management. This report summarizes the results of our review.

In October 2013, philanthropist T. Denny Sanford committed a \$100M donation to support UC San Diego's efforts to accelerate the development of drugs and therapies by harnessing discoveries derived from human stem cells and translating them to the clinic as rapidly as possible. This gift established the Sanford Stem Cell Clinical Center (Sanford Center), dedicated to establishing, promoting, and disseminating clinical programs for stem cell clinical trials and therapies.

The goal of the Sanford Center is to provide administrative and other relevant support to help with the execution and creative development of clinical trials of novel stem cell related therapies for a range of human disorders. The Sanford Center also is home to the UC San Diego Alpha Stem Cell Clinic (Alpha Clinic), funded through an award from the California Institute for Regenerative Medicine (CIRM). The clinic is one of three "alpha clinics" in a Network designated by CIRM, the state's stem cell agency. The Alpha Stem Cell Clinic is the cell therapy arm of Sanford Center and is intended to create the long-term, networked infrastructure needed to launch and conduct numerous, extensive clinical trials of stem cell-based drugs and therapies in humans, including those developed by independent California-based investigators and companies.

The Sanford Center offers funding from donor funds for direct costs specifically related to stem cell research, upon application by a Principal Investigator (PI) and approval by the Sanford Center Executive Steering Committee. In January 2014, the Executive Steering Committee approved Sanford Center support from donor gift funds for two Phase I stem cell studies which are co-funded by industry sponsors: IRB #140248 (Sponsor: NeuralStem; award fund managed by the Health Sciences Research Service Core on behalf of the Department of Surgery) and IRB #140261 (Sponsor: Viacyte; award fund managed by the Department of Medicine).

The Clinical Trial Agreement (CTA) with the sponsors for these studies specifies that Sanford Center is responsible for:

- For study #140248, the first \$150,000 of subject-specific charges per study subject, for up to eight subjects
- For study #140261, the first \$40,000 of subject-specific charges per study subject, for up to 15 subjects.

The CTAs further specify that the institution shall account for all subject-related charges during the course of each subject's enrollment and participation in the study according to the Final Budget in the CTA. For each agreement, the sponsor pays for subject-specific costs in excess of Sanford Center support, as well as other costs associated with conducting the clinical trial.

Within the UC San Diego accounting system, funds from the donor gift account cannot be transferred to the study clinical trial account due to fund source restrictions. Therefore, the process for funding the Sanford Center support to each study is through transfers of expenditures from the clinical trial account to the gift fund. Each study has a clinical trial index, and subject-specific charges must be

transferred to the donor gift index through cost transfers up to the committed threshold for each subject.

The process for charging clinical research costs which occur in UC San Diego Health (UCSDH) clinical space is managed by a complex process interfacing subject visit information in the Velos Clinical Trial Management System and charge information in the Epic Enterprise system. These hospital and professional (physician) charges accumulate in a Bulk Account, and each month this balance is transferred to a study index. Other hospital charges may be transferred via journal voucher from the hospital account to the study index.

Subject-specific charges related to the studies can include recharges from Clinical and Translational Research Institute (CTRI) for use of clinic facility, Study Coordinator (SC) time and pharmacy costs. In addition, hospital and professional charges for study procedures, including surgeries, clinic visits, laboratory tests and radiology procedures, either post directly to the study indexes or pass through the study Bulk Account. Other study charges could include scrip distribution to subjects, subject rehabilitation recharges and, external pharmacy study medication costs.

Interim Feedback

After beginning our review, we noted that cost transfers had not been initiated due to clinical research billing process issues that prevented the majority of subject-specific charges up to that point from posting correctly to the study indexes. We communicated to management various items that needed resolution to assure subject charges were flowing to the study indexes, before cost transfers could be initiated and audit work completed. These areas included:

- Clinical Research Charges – Subject specific charges were not posted to the study indexes or at correct rates due to a variety of factors relating to broader clinical research billing process issues, including
 - Associated hospital charges were on a bill hold status and not flowing to the study account,
 - Charges were erroneously billed to external parties rather than to the study or were written off,
 - Professional billing charges were not posted to the study index or captured at correct rates,
 - Unscheduled procedures were not consistently captured in Velos to interface with associated clinical charges in Epic, or
 - Study Coverage Analyses (CAs) did not capture all study related procedure codes required as part of the Epic-Velos interface for charges to flow correctly.
- Roles & Responsibilities – Administrative roles and responsibilities, in particular related to the unique funding arrangement for the two studies, were not defined at the initiation of the studies. We noted that the successful identification and transfer of costs to the donor fund required close coordination and exchange of information between study team members (including Principal Investigator (PI), SC, and fund managers) and Sanford Center staff which was not formally articulated.

Since communication of these issues, the Alpha Stem Cell Clinic has coordinated with the CRB office and SC to clear bill holds and correct research billing errors to allow study charges to post to the study indexes. This is planned to be an ongoing process with the Alpha Clinic monitoring study charges and associated statements, and assisting with reconciliation to study indexes.

In the future, for projects involving co-funding with an external sponsor, the Sanford Center will consider using commitment letters that include language for need of effective coordination with the study team to allow Sanford Center to meet their obligations under the agreement and ensure that roles and responsibilities of all parties are clear.

III. AUDIT OBJECTIVE, SCOPE, AND PROCEDURES

The objective of our review was to determine whether processes to allocate or transfer charges to donor gift funds for the two designated clinical trials were effective, adequately supported, and compliant with donor commitments, sponsor agreements, and applicable clinical research billing policies. We performed the following procedures:

- Reviewed applicable clinical research billing policies and Velos Guidelines;
- Reviewed the Donor Gift Agreement and sponsor CTAs for terms of Sanford Center funding;
- Reviewed a sample of commitment letters for Sanford Center projects;
- Analyzed Financial Link operating ledgers for both study indexes for subject-specific charges;
- Reviewed the study coverage analysis (CA)¹ for both studies;
- Discussed hospital case rate development and use of professional fee research rates for study procedures with the:
 - Director, Budget and Financial Forecasting, UC San Diego Health System (UCSDHS),
 - Senior Administrative Analyst, Budget and Financial Forecasting, UCSDHS,
 - Senior Administrative Analyst, Anesthesiology,
 - Operations Manager, Billing and Collections Management, Medical Group and,
 - Bulk/Research Billing Specialist, Billing and Collections Management, Medical Group;
- Discussed study procedure hospital billing process with the Clinical Research Billing (CRB) Manager, UCSDH Revenue Cycle;
- Met with the CTRI SC for both studies and conducted site visits to review study records for a sample of five study subjects for each study;
- Discussed cost transfer status and process with the:
 - Clinical Study Coordinator (CSC), Alpha Stem Cell Clinic,
 - Fund Managers for both studies;
 - Financial Analyst for #140261 study;
- Discussed study subject charges with the:
 - CTRI Business Office Analyst,
 - CTRI Administration Nurse Supervisor,

¹ A Coverage Analysis is a schedule of clinical research study events that provides a description of the protocol / clinical services and identifies whether the services are billable to insurance, the study sponsor and/or to the subject or guarantor. A coverage analysis links the description of services to a procedure (CPT/HCPCS) code or charge description master (CDM) code and a study event schedule. A billing modifier indicates the charge routing mechanism for the service: XS (for charges to be billed to study) and Q1 (for charges to be billed to subject/payor).

- Pharmacist, Medical Center Pharmacy,
 - Administrative Analyst Supervisor, Occupational Therapy;
- Reviewed Velos entries for study visits for a sample of five subjects for each study and evaluated study charges (hospital and professional fees) to determine how they were billed and/or posted to the study;
- Reviewed a sample of scrip issuance to sampled subjects for compliance with the payment schedule in the study Informed Consent Form (ICF) for the #140261 study;
- Analyzed study billing tracking sheets, cost transfer summaries, sponsor invoicing and other documentation provided for the #140261 study; and
- Summarized total patient costs charged to study indexes and compared to costs transferred to the Sanford gift fund account for both studies as of April 2017.

IV. CONCLUSION

Based on our review, we concluded that a process had been established to allocate and transfer charges to donor gift funds that was generally compliant with the donor commitment, sponsor agreements and clinical research billing policies.

As of April 2017, a total of \$205,866 (#140248) and \$297,863 (#140261) had been provided by the Sanford Center as part of its financial commitment to support the clinical trials. Of this total, \$183,629 (#140248) and \$284,794 (#140261) represented costs that had been transferred from the study indexes to the Sanford Foundation index and the remainder was direct support received from Sanford Center gift fund.

We noted that the Sanford Center had developed documentation for study #140261 to track the total subject-related costs which had been funded through gift funds. In some cases, the charges were subject-related but could not be attributed to specific individual subjects due to the nature of the charges and/or how they are recorded in the University financial system. In other cases, Sanford provided financial support for expenditures that were not directly subject-related but were incurred for providing study-related care to the study subjects (such as a percentage of payroll for study team members) based on discussion with the department. Sanford developed an approximate cost per subject for study #140261 based on the aggregate costs transferred divided by the number of subjects randomized to the study. Costs were averaged by randomized subjects since identifying and attributing costs by individual patient was a burdensome process and in some instances, not feasible considering how costs were presented. This method, although not strictly consistent with the requirement in the CTA to “account for all subject-related charges during the course of each study subject’s enrollment and participation” met the spirit of the CTA and the financial commitment by Sanford. We noted that a similar cost per subject analysis was pending for the other study (#140248), but had not yet been completed.

We also confirmed that, for study activity to date, the Alpha Clinic did not invoice the sponsor for study #140261 for the first \$40,000 of subject-specific charges for each subject (as related to the Final Budget, study visits 1-9). We noted that this was consistent with the sponsor agreement terms for the Sanford Center to finance the first \$40,000 in subject-specific costs. For study #140248, we confirmed that the sponsor had not been invoiced for any subject-specific costs as of May 2017.

Our analysis of total subject specific costs charged to study indexes in comparison to total cost transfers indicated the need for additional transfers to be processed for both studies to fund subject charges to date. There may also be a need to reconfirm the financial commitment from Sanford for these studies. These issues are further discussed in the remainder of the report.

V. OBSERVATIONS REQUIRING MANAGEMENT ACTION

A.	Study Cost Transfers
Overall cost transfers for study charges to date do not fully satisfy Sanford Center’s institutional commitment to the department as specified in the sponsor contract. Documentation of the cost transfers to subject for study #140248 had not been created.	
Risk Statement/Effect	
Lack of timely cost transfers, and associated documentation, can result in unfulfilled financial obligations, and non-compliance with the terms of the agreements.	
Management Action Plans	
A.1	Sanford Center, the study team and appropriate study fund management personnel will coordinate to reconfirm Sanford Center’s financial obligations to the department for both studies.
A.2	The Sanford Center or Alpha Clinic will prepare and present an analysis of cost per subject for study #140248.
A.3	Sanford Center will process cost transfers to meet their financial obligations as confirmed with the department (per A.1) as appropriate.

A. Study Cost Transfers – Detailed Discussion

The sponsor contracts state that the “Sanford Stem Cell Clinical Center at Institution is responsible for” the first \$150,000 (or \$40,000) of the Subject-specific charges per Study subject for eight (or 15) as applicable for each of those eight (or 15) Study subject’s participation in the study.

Based on Velos data, study #140248 enrolled a total of 10 subjects, with six screen failures and four subjects that underwent study surgeries. Based on the sponsor agreement this would equate to Sanford Center support of up to \$600K in subject-specific costs the for four randomized subjects. Similarly, for study #140261, 13 subjects were enrolled, with eight active, four that completed the study and one screen failure. Based on the sponsor agreement, this would equate to up to \$480K in support for the 12 randomized subjects.

As of April 2017, the Sanford Center has provided a total of \$205,866 (#140248) and \$297,863 (#140261) in financial support for the studies. This included charges that supported the trial but were

not necessarily subject-specific related. We did an analysis of the total charges posted to study indexes for #140248 (SURCI01) and #140261 (MEDHB03) which identified a total of \$244,946 (#140248) and \$472,828 (#140261) in subject-specific charges.

For both studies, the total cost transfers were lower than total subject specific costs incurred, and below the total Sanford Center financial commitment. This information is summarized in the table below:

Data as of April 2017	Study #140248	Study #140261
Number of Subject Randomized	4	12
Sanford Per-Subject Commitment	\$150,000	\$40,000
Total Sanford Commitment (to date, based on enrollment)	\$600,000	\$480,000
Subject Costs To Date	\$244,946	\$472,828
Cost Transfers for Subject Costs	\$183,629	\$218,661
Additional Sanford Support (not subject-specific)	\$22,237	\$79,202
Total Sanford Support	\$205,866	\$297,863
Remaining Costs	\$39,080	\$174,965

Sanford Center created and maintained documentation of the subject costs for study #140261 to comply with the terms of the CTA which require accounting of subject-related charges. A cost per patient was calculated based on the aggregate costs divided by the number of subjects enrolled in the study. As of March 2017, the Alpha Clinic cost transfer summary report identified that approximately \$24,822 of the \$40,000 per patient commitment had been transferred. A similar analysis has not been completed for the #140248 study to determine total cost transfers to be processed and document the accounting of subject-related charges to support cost transfers previously completed, or still needed.

The Executive Director for the Sanford Center has indicated that they do not anticipate processing any future cost transfers for the #140261 study since the study is now in receipt of sponsor payments and has a surplus balance in the study index. However, when the study was initiated the understanding was that funding support would come from the Sanford Center as documented in the CTA, and it was under this premise and terms that the clinical trial agreement was executed by the University. Current index balances for an in-progress study are unreliable indicators of financial needs over the duration of the study, and should not be used as a basis to discontinue committed financial support. The departments have an expectation that the Sanford Center will fulfill its financial obligations as stipulated in the contract.

Although the sponsor contract specifies Sanford center support for the study, there is currently no written agreement between the department and Sanford Center on how Sanford will meet its institutional commitment. A mutual agreement needs to be reached between the Sanford Center, the study PI and department to ensure that both parties expectations and commitments are clearly defined.