DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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June 27, 2006

Richard Sheridan, J.D.
General Counsel
Scripps Health
4275 Campus Point Court
San Diego, CA 92121

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA)-1294 and Federalwide Assurance FWA- 7338

Research Project: A Multicenter, Randomized, Double-Blind Study of the Sirolimus Coated BX Velocity Balloon Expandable Stent in the Treatment of Patients with De Novo Coronary Artery Lesions SIRIUS Protocol: P00-6302
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L01-003

Research Project: Symbiot III: A Prospective Randomized Trial Evaluating the Symbiot III Covered Stent System in Saphenous Vein Grafts
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L02-008

Research Project: JOSTENT SVG Trial: Investigational Device Exemption Protocol for the Jomed JOSTENT Coronary Stent Graft System
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L01-025

Research Project: TAXUS IV-SR: Treatment of De Novo Coronary Disease Using a Single Paclitaxel-Eluting Stent
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L02-011

Research Project: A Multicenter, Non-Randomized Study of the 4.0 mm Sirolimus-Eluting BX Velocity Balloon-Expandable Stent in The Treatment of Patients with De Novo Native Coronary Artery Lesions SIRUS - 4.0
Principal Investigator: Dr. Maurice Buchbinder

Project Number: L03-020

Research Project: Carotid Revascularization with EV3 Arterial Technology Evolution CREATE Trial
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L04-007

Research Project: A Randomized Study Comparing the Edwards Self-Expanding LifeStent vs. Angioplasty Alone In Lesions Involving the SFA and Proximal Popliteal Artery RESILIENT Study
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L04-012

Research Project: D.E.S.cover Registry Protocol
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L04-016

Research Project: SVG Protection is a Distal Embolic Protection Randomized Trial – Spider
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L04-020

Research Project: Carotid Artery Stenting with Emboli Protection Surveillance Post Marketing Study - CASES study
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L04-024

Research Project: WATCHMAN Left Atrial Appendage System for Embolic PROTECTion in Patients with Atrial Fibrillation (PROTECT AF)
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L04-030

Research Project: Carotid RX ACCULINK/ACCUNET Post-Approval Trial to Uncover Unanticipated and Rare Events CAPTURE
Principal Investigator: Dr. Maurice Buchbinder
Project Number: L04-031

Research Project: The SLK-View Side-Access Coronary Stent Non-Randomized Pivotal Study
Principal Investigator: Dr. Maurice Buchbinder
Project Number: LM03-008

Dear Mr. Sheridan:

The Office for Human Research Protections (OHRP) has reviewed Scripps Health's (Scripps) August 10, 2005 and May 12, 2006 reports responding to determinations of noncompliance with

Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46).

Based upon its review, OHRP makes the following additional determination regarding human subjects protections at Scripps:

(1) OHRP finds that the Scripps institutional review boards (IRBs) do not have written institutional review board (IRB) procedures that adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(a) and 46.103(b)(4) and (5): The procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, any department or agency head, and OHRP of: (a) any unanticipated problems involving risks to subjects or others; (b) any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB; and (c) any suspension or termination of IRB approval.

OHRP notes that, while the Scripps written IRB procedures do include procedures for prompt reporting of adverse events to the IRB, not all unanticipated problems involving risks to subjects or others are adverse events. Additionally, the IRB procedures do not include procedures for reporting to institutional officials, any department or agency head, and OHRP. OHRP also acknowledges that while the Scripps written IRB procedures do include procedures for prompt reporting of suspension or termination of IRB approval to OHRP and sponsors, the procedures do not include procedures for reporting to institutional officials. In addition, the procedures for reporting of noncompliance only apply to noncompliance of investigators; OHRP notes that other individuals may be noncompliant with 45 CFR part 46, including IRB members, IRB staff, and institutional officials.

Required Action: Please provide OHRP with corrective actions to address the above finding no later than August 8, 2006.

OHRP has the following additional questions and concerns:

(2) [Redacted]

(3) [Redacted]

(4)[Redacted]

OHRP has the following additional guidance regarding the Scripps written IRB procedures:

(a) OHRP notes that the minutes of IRB meetings indicate that IRB members who do not vote on projects because they are absent from the room are listed as "abstained." Please note that members who are not present for the vote, especially if they are not present due to a conflict of interest, are not abstaining but are recused, and they cannot be counted toward the quorum.

(b) The Policy "Distinguishing between Research Protocols and Quality Assurance Projects" states that "Some data collection and analysis activities....are not intended to have any application beyond the specific organization in which they are conducted" and implies that such activities are not research. They also state: "when the purpose of an activity is to assess the success of an established program in achieving its objectives and the information gained from the evaluation will be used to provide feedback to improve that program, the activity is not human participants research." OHRP notes that such activities could be human subjects research. Regarding public health activities, the policy states: "surveillance...and program evaluations do not meet the DHHS definition of human subjects research and do not have to be reviewed by an IRB." OHRP notes that some such activities are human subjects research.

OHRP appreciates the continued commitment of your institution to the protection of human

research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Kristina C. Borror, Ph.D.
Director, Division of Compliance Oversight

cc: Ms. Barbara G. Bigby, Director, Scripps IRB Office
Dr. Robert L. Bjork, Jr., Chair, Scripps IRB #1
Dr. Joel I. Bernstein, Chair, Scripps IRB #3
Dr. Maurice Buchbinder, Scripps
Commissioner, FDA
Dr. David Lepay, FDA
Dr. Bernard Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael Carome, OHRP
Ms. Shirley Hicks, OHRP
Dr. Irene Stith-Coleman, OHRP
Mr. Patricia El-Hinnawy, OHRP
Ms. Janet Fant, OHRP