DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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October 24, 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 7, and September 28, 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).

In its June 27, 2006 letter OHRP made the following determination regarding human subjects protections at Scripps:

> (1) OHRP found that the Scripps institutional review boards (IRBs) do not have written 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. In its August 24, 2006 letter, OHRP found that the Scripps written IRB procedures still did not include the procedures by which unanticipated problems involving risks to subjects or others will be reported to appropriate institutional officials, any department or agency head, and OHRP. OHRP also found that the Scripps written IRB procedures still did not include the procedures for ensuring prompt reporting of suspension or termination of IRB approval to appropriate institutional officials.
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> **Corrective Action:** OHRP acknowledges that the Scripps written IRB procedures now include a description of the reporting of unanticipated problems involving risks to subjects or others to appropriate institutional officials, any department or agency head, and OHRP. In addition, the Scripps written IRB procedures now include the procedures for ensuring prompt reporting of suspension or termination of IRB approval to appropriate institutional officials.

In its August 24, 2006 letter, OHRP made the following additional determination, among others, regarding human subjects protections at Scripps:

> (2) OHRP found that Dr. Buchbinder enrolled a subject in protocol #L04-020 prior to obtaining legally effective informed consent from her, in violation of HHS regulations at 45 CFR 46.116.
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> **Corrective Action:** OHRP acknowledges that Scripps suspended Dr. Buchbinder's research privileges and required that he complete an IRB training module, which he did, and that he maintain 8 hours of continuing education in research ethics each year he continues to conduct research at Scripps. Scripps will periodically audit his clinical research documentation and monitor his consenting procedures, and he will be asked to attend IRB meetings to optimize his understanding of the review process. In addition, Scripps now has a requirement that investigators and non-investigators are to have initial and continuing education in research ethics, and each investigator must now submit a written affirmation of completion of research ethics training along with each research proposal.

OHRP finds that the above corrective actions are adequate and appropriate under Scripps's

FWA. As a result, there should be no need for further involvement of OHRP in this matter.

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 & #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. Carla Brown, OHRP