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May 26, 2009

Mark A. Slater, PhD  
Vice President, Research  
Scottsdale Healthcare  
10510 N. 92nd Street, Ste. 300  
Scottsdale, AZ 85258

**RE: Human Subject Protections Under Federalwide Assurance FWA-1751**

**Research Project: Molecular and Genomic Rationale for Adjunctive Hyperbaric Oxygen Therapy of Selected Crush Injuries Using DNA Microarray Analysis (CRUSH Study)**

**Principal Investigator: Dr. Dennis Weiland**

**Research Project: HOLLT study**

**Principal Investigator: Dr. Dennis Weiland**

Dear Dr. Slater:

Thank you for your May 5, 2009 report in response to our March 30, 2009 letter regarding determinations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR part 46) at Scottsdale Healthcare (SH). While the above-referenced research projects are not conducted or supported by HHS, we note that SH has voluntarily extended its Federalwide Assurance (FWA) to cover all human subjects research at SH, regardless of the source of support for the particular research activity. Based on review of your response, we make the following additional determinations regarding the above-referenced research:

A. Determinations Regarding the Above-Referenced Research

- (1) We determine that the protocol approved by the SH institutional review board (IRB) for the CRUSH study included little or no information about where the tissue would be biopsied from, the risks of the research, or how informed consent will be obtained, in contravention of the regulatory requirements at 45 CFR 46.111(a)(1),

(2), and (4) which require that in order to approve research, the IRB shall determine that risks to subjects are minimized; risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result; and informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116. In addition, the protocol stated that the biopsies would be of skin, but the informed consent documents referenced "damaged skin and tissue under the skin" and minutes of the May 23, 2007 IRB meeting stated "skin biopsies will be taken adjacent to the wound." Also, the IRB had insufficient information about previous studies of hyperbaric oxygen therapy, such as the Australian pilot study.

**Corrective Action:** We acknowledge your statement that the CRUSH study was closed April 22, 2009, and that SH has implemented a new policy, Research IRB Initial Review Policy, to improve processes and demonstrate compliance with HHS regulations at 45 CFR 46.111(a)(1), (2), and (4).

- (2) We determine that the IRB-approved informed consent document for the CRUSH study described DNA microarray analysis as "studying the pieces of DNA or genes on a glass or plastic slide" and does not appear to describe what will happen to subjects randomized to the control group, in contravention of the regulatory provision at 45 CFR 46.116(a)(1) which requires, among other things, that subjects be provided with the purposes of the research and an adequate description of the procedures to be followed.
- (3) We determine that the IRB-approved informed consent document for the CRUSH study did not adequately describe the amount of time the serious side effects may be experienced, the risks of not receiving hyperbaric oxygen therapy, the risks of pulmonary barotrauma, the risk of oxygen toxicity, the risks of anxiety and claustrophobia, and the risk of delay of healing time for injury, in contravention of the regulatory provision at 45 CFR 46.116(a)(2) which requires that subjects be provided with a description of any reasonably foreseeable risks or discomforts to the subject.
- (4) We determine that the IRB-approved informed consent document for the CRUSH study did not describe that hyperbaric oxygen therapy may be obtained outside of the research, in contravention of the regulatory provision at 45 CFR 46.116(a)(4) which requires that subjects be provided with a disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.

**Corrective Action:** We acknowledge your statement that SH has implemented a new policy, Research IRB Informed Consent Policy, to improve processes and demonstrate compliance with HHS regulations at 45 CFR 46.116.

We acknowledge your statement that the HOLLT study, about which we made determinations in our March 30, 2009 letter, was also closed April 22, 2009.

B. Recommendations

We recommend that SH ensure that investigators, IRB staff and IRB members receive training about the requirements of SH's Research IRB Initial Review Policy and the Research IRB Informed Consent Policy.

We determine that the above corrective actions adequately address the above determinations. At this time, there should be no need for further involvement by our office in this matter. Please notify us if you identify new information which might alter this determination.

We appreciate 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. Borrer, Ph.D.  
Director  
Division of Compliance Oversight

cc: Ms. Liz Brouchoud, IRB Coordinator, Scottsdale Healthcare  
Dr. Robert A. Marlow, IRB Chair, Scottsdale Healthcare  
Dr. Dennis Weiland, Scottsdale Healthcare  
Dr. Margaret Hamburg, Commissioner, Food and Drug Administration  
Dr. Joanne Less, Food and Drug Administration