DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

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November 21, 2002

Donald C. Harrison, M.D.
Senior Vice President
University of Cincinnati
Room 250 Health Professions Building
Eden and Albert Sabin Way
Cincinnati, OH 45267-0663

**RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1138 and Federalwide Assurance (FWA) 00003152**

**Research Project A: Use of 5% Mafenide Acetate (Sulfamylon) Solution in Burn Wound Management**
**Principal Investigator: Dr. Glenn D. Warden**
**Project Number: 91-02-20-4**

**Research Project B: Autologous Cultured Skin Substitutes for Treatment of Full-Thickness Burns**
**Principal Investigator: Dr. Steven Boyce**
**Project Number: 90-5-7-1**

Dear Dr. Harrison:

The Office for Human Research Protections (OHRP) has reviewed the University of Cincinnati's (UC) September 27, 2000 report submitted in response to OHRP's August 7, 2000 letter regarding the above-referenced research. OHRP apologizes for the delay in its response.

Based on the review of your report, OHRP makes the following determinations regarding the above-referenced research:

(1) OHRP notes that (a) the Institutional Review Board (IRB)-approved protocols excluded pregnant women from participating in the above-referenced research; and (b) the subject in question was pregnant at the time of enrollment in Protocol # 90-5-7-1. Department of Health and Human Services (HHS) regulations at 45 CFR 46.103(b)(4) (iii) require that the IRB review and approve all proposed changes in a research activity, during the period for which IRB approval has already been given, prior to initiation of such changes, except when necessary to eliminate apparent immediate hazards to the subjects. OHRP finds no documentation that the investigator obtained UC IRB approval for inclusion of pregnant women for Protocol # 90-5-7-1.

OHRP notes that, although the subject did not receive grafting under this protocol, the subject did undergo collection of skin tissue for preparation of grafts as part of the research.

**Required Action**: By January 10, 2003, UC must submit to OHRP a satisfactory corrective action plan to address the above finding.

(2) In its August 7, 2000 letter, OHRP presented an allegation that the investigators failed to obtain the consent of the subject or the subject's legally authorized representative under circumstances that provided the parent with sufficient opportunity to consider whether or not to participate and that minimized the possibility of coercion or undue influence. OHRP notes that the letter from the complainant states, "**July 6th**, [subject's mother] was taken into a private room and presented with documents to sign. The Nurse said, 'The Doctors need these papers signed immediately. If she has any chance at all - this is the only chance she has.' No one at any time explained the documents to her and/or that they were consent for Experimental Programs." [Emphasis in original]

OHRP notes that your September 27, 2000 letter states:

> (a) "On Research Project A, the consent was obtained by Arline Miller, the research nurse, and co-signed by Dr. David Greenhalgh, a co-investigator. Both of these individuals explained the protocol in detail."
>
> (b) "The consent for Project B was obtained by Dr. Steven Boyce the day after admission to the hospital. As is the usual practice, Dr. Boyce explained the protocol in detail."

Based on the above statements, OHRP is unable to make a finding regarding this allegation.

(3) In its August 7, 2000 letter, OHRP presented an allegation that the investigators continued to conduct research on a subject after the subject's family withdrew permission for her participation in the research. Based on materials submitted with your September 27, 2000

report which indicated that the above-referenced protocols were discontinued upon request of the subject's family, OHRP finds that this allegation could not be substantiated.

At this time OHRP has the following additional guidance:

(4) OHRP notes the following regarding Protocol # 91-02-20-4:

(a) The IRB-approved protocol stated "The proposed research is aimed at demonstrating that a 5% Sulfamylon solution (Mafenide acetate) is a safe and effective alternative for antimicrobial therapy in the pediatric and adult burn population."

(b) The IRB-approved informed consent document stated "I understand that the following alternative procedures or courses of treatment are available that might be advantageous to me: Established treatment with other antibiotics in solution, **which may not control infection as well as the study drug**." [Emphasis added]

Since the stated purpose of the protocol was to evaluate the effectiveness of Sulfamylon solution, the above statement from the IRB-approved informed consent document may have inflated the potential benefits to the subjects.

Please forward your response to the above required action so that OHRP receives it no later than January 10, 2003.

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,

Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Ms. Mary Belkis, Director, Institutional Research and Compliance Services, UC
Dr. Peter Frame, Chair, IRB #1A, UC
Dr. James Mulchahey, Chair, #1B, UC
Dr. Margaret Miller, Chair, IRB #2, UC
Dr. Glenn Warden, Director of Research, Shriners Burn Institute

Dr. Steven Boyce, UC
Mr. Carlos Lott, Director, Cincinnati VA Medical Center
Dr. John Mather, Director, Office of Research Compliance and Assurance, Department of Veterans Affairs
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Dr. Greg Koski, OHRP
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