



DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 240-453-8120
FAX: 240-453-6909
E-mail: Lisa.Rooney@hhs.gov

November 9, 2009

Arnold W. Strauss, M.D.
Chief Medical Officer
Cincinnati Children's Hospital Medical Center
3333 Burnet Avenue
Cincinnati, OH 45229

RE: Human Research Protections Under Federalwide Assurance FWA-2988

Research Project: A Prospective Randomized Multicenter Trial of
Amnioreduction vs. Selective Fetoscopic Laser for the
Treatment of Severe Twin-Twin Transfusion Syndrome
Principal Investigator: Timothy M. Crombleholme, M.D.
HHS Protocol Number: R01HD41149

Dear Dr. Strauss:

Thank you for your April 10, 2009 letter in response to our March 17, 2009 letter that included determinations, questions, and concerns. Based on the information submitted, we make the following determinations:

Determinations Regarding the Above-Referenced Research:

We determine that the Cincinnati Children's Hospital Medical Center (CCHMC) institutional review board (IRB)-approved informed consent documents for the treatment arm of the above-referenced study failed to: (i) explain that the echocardiograms and neuroradiologic evaluations conducted after one and four weeks of life to check for the subsequent development of brain abnormalities and the progression or regression of abnormal cardiac function were experimental, as required by Department of Health and Human Services (HHS) regulations at 45 CFR 46.116(a)(1); and (ii) describe the reasonably foreseeable risks or discomforts associated with these echocardiograms and neuroradiologic evaluations, as required by HHS regulations at 45 CFR 46.116(a)(2).

Corrective Actions: We note that CCHMC has instituted the following changes related to the preparation and review of informed consent documents:

- CCHMC investigators are provided with a template for preparing consent documents which includes specific instruction regarding the test/procedures as well as the reasonably foreseeable risks/discomforts that should be included in the consent form;
- CCHMC investigators are provided with an instructional document entitled “Guidance: Informed Consent: Process, Elements, Documentation and Waivers” which provides general guidance on preparing consent forms, including a description of the required elements of informed consent; and
- CCHMC IRB staff use a “Consent Pre-Review Form” which is completed during the pre-review process and included with the documentation that is provided to the IRB for use during the review process.

We determine that these corrective actions adequately address our determination and are appropriate under the CCHMC FWA.

We acknowledge CCHMC’s additional responses to the other questions and concerns noted in our March 17, 2009 letter. Moreover, we acknowledge the areas of concern that CCMHC uncovered while conducting its investigation. The additional corrective actions outlined in the April 10, 2009 CCHMC letter satisfactorily address these areas of concern and are appropriate under the terms of the CCHMC FWA.

We note that our March 17, 2009 letter failed to address one of the concerns noted in our December 21, 2007 inquiry letter; i.e., that the IRBs that reviewed and approved the above-referenced study may not have had sufficient expertise to review this complex research. We reviewed the February 6, 2008 CCHMC response to this concern and determine that the CCHMC IRB had sufficient expertise to review this research, namely that the CCHMC IRB utilized an external expert consultant when reviewing and approving this research.

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.

Sincerely,

Lisa A. Rooney, J.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Dr. Jennifer Ruocco, Director, Office of Research Compliance and Regulatory Affairs,
Cincinnati Children's Hospital Medical Center
Dr. Robert Frenck, Chair, Cincinnati Children's Hospital Medical Center IRB#1 and #2
Ms. Deborah Barnard, Director of Research Compliance and Regulatory Affairs, Children's
Hospital of Philadelphia
Dr. Mark Schreiner, Chair, Children's Hospital of Philadelphia IRB #1 and #2
Ms. Sharon K. Friend, Director, Human Research Protection Program, University of
California, San Francisco
Dr. Victor I. Reus, Chair, Parnus IRB #1, University of California, San Francisco
Dr. Susan H. Sniderman, Chair, San Francisco General Hospital, IRB #2
Dr. Alan P. Venook, University of California San Francisco, IRB #4
Dr. Timothy M. Crombleholme, Cincinnati Children's Hospital Medical Center
Dr. Joe Ellis, Office of Extramural Research, National Institutes of Health (NIH)
Dr. Sherry Mills, Office of Extramural Research, NIH
Dr. Duane Alexander, Director, National Institute of Child Health and Human Development,
NIH