Complete Final Version of the Cover Letter From the PI

(02-0898)

Dr. Kimberly Spence

Title: Precursor Preference in Surfactant Synthesis of Newborns

January 28, 2005

Office of OHRP

Dear Committee:

The human study protocol entitled "Precursor preference in surfactant synthesis of human preterm infants" is currently under review by the OHRP because of the recent change in human study criteria for studies performed in children who are considered "normals" if the risk is classified as"greater than minimal risk." For our particular study, the details are summarized in my protocol attached as well as in my F32 entitled, "Precursor preference in Surfactant Synthesis of Newborns." The most recent findings from our research indicate the kinetic parameters and substrate utilization of surfactant turnover change with age, specifically the turnover rate nearly doubles (manuscript attached). In order to provide context to our current data, we need to know if kinetic parameters we measured are different from those kinetics of infants born at term without lung disease. At this point it is not known if the patients have disrupted metabolism at birth or develop disrupted surfactant metabolism with chronic ventilation, or if the metabolism is the same pattern seen in term infants without lung disease. We are seeking to recruit 10 more *term infants less than 1 month of age* who are ventilated but do not have lung disease. These are infants who have normal respiratory function, but who are critically ill with extra-pulmonary disease and require mechanical ventilation. The information derived from these infants will not only provide the context for interpretation of studies in infants with lung disease, but it will also provide important information about normal surfactant metabolism in humans that cannot be approached in any other fashion.

Please find the following enclosed documents pertaining to the protocol submitted to you for your review: 1) Consent form for preterm infants with lung disease, 2) consent form for intubated term infants without lung disease, 3) 2004 updated protocol for the study, "Precursor preference in surfactant synthesis of human preterm infants," 4) Data safety and monitoring plan for this project including data reviewed from the project start until October 2004, 5) preparation protocol for the study's stable isotope infusions, 6) examples of certificates of analysis from the manufacturer of the stable isotopes, Isotec, Inc and Cambridge Isotope Laboratories, Inc., 7) examples of a certificates of presence of sterility from St. Louis Children's Hospital Microbiology Laboratory, and 8) certificates of the absence of pyrogenicity and particulate matter from the independent chemical assay company, Bio-Science Research Institute, Inc. These certificates are obtained on each new batch of isotope received. These methods have permitted us to successfully perform over 100 studies without incident.

My grant program administrator is: Sandra Hatch, M.D.
Medical Officer
Lung Biology and Disease Program
Division of Lung Diseases, NHLBI, NIH

6701 Rockledge Dr., MSC 7952
Bethesda, MD 20892-7953
(301)435-0222
e-mail: hatchs@nhlbi.nih.gov

Please feel free to contact me if I can provide additional information.

Sincerely,

Kimberly L. Spence, MD
Instructor of Pediatrics

Aaron Hamvas, MD
Professor of Pediatrics

Division of Newborn Medicine
Washington University / St. Louis Children's Hospital
1 Children's Place
St. Louis, MO 63110