THE UNIVERSITY OF IOWA

Human Subjects Office/
Institutional Review Board (IRB)
105 Hardin Library for the Health Sciences
600 Newton Road
Iowa City, Iowa 52242-1098
319-335-6564 *Fax* 319-335-7310
irb@uiowa.edu
http://research.uiowa.edu/hso

IRB ID #: 201010715

To: Jeffrey Murray

From: IRB-01 Univ of Iowa, DHHS Registration # IRB00000099, DHHS Federalwide Assurance # FWA00003007

Re: National Children's Study Formative Research Project: Placental Study

Protocol Number:
Protocol Version:
Protocol Date:
Amendment Number/Date(s):

Approval Date: 10/12/10

Next IRB Approval Due Before: 10/12/11

Type of Application:	**Type of Application Review:**	**Approved for Populations:**
☒ New Project	☐ Full Board:	☐ Children
☐ Continuing Review	Meeting Date:	☐ Prisoners
☐ Modification	☒ Expedited	☐ Pregnant Women, Fetuses, Neonates
	☐ Exempt	

Source of Support: US Department of Health & Human Services, National Institutes of Health

Investigational New Drug/Biologic Name:
Investigational New Drug/Biologic Number:
Name of Sponsor who holds IND:

Investigational Device Name:
Investigational Device Number:
Sponsor who holds IDE:

This approval has been electronically signed by IRB Chair:
Catherine Woodman, MD
10/12/10 1443

IRB Approval: IRB approval indicates that this project meets the regulatory requirements for the protection of human subjects. IRB approval does not absolve the principal investigator from complying with other institutional, collegiate, or departmental policies or procedures.

Agency Notification: If this is a New Project or Continuing Review application and the project is funded by an external government or non-profit agency, the original HHS 310 form, "Protection of Human Subjects Assurance Identification/IRB Certification/Declaration of Exemption," has been forwarded to the UI Division of Sponsored Programs, 100 Gilmore Hall, for appropriate action. You will receive a signed copy from Sponsored Programs.

Recruitment/Consent: Your IRB application has been approved for recruitment of subjects not to exceed the number indicated on your application form. If you are using written informed consent, the IRB-approved and stamped Informed Consent Document(s) are attached. Please make copies from the attached "masters" for subjects to sign when agreeing to participate. The original signed Informed Consent Document should be placed in your research files. A copy of the Informed Consent Document should be given to the subject. (A copy of the *signed* Informed Consent Document should be given to the subject if your Consent contains a HIPAA authorization section.) If hospital/clinic patients are being enrolled, a copy of the signed Informed Consent Document should be placed in the subject's chart, unless a Record of Consent form was approved by the IRB.

Continuing Review: Federal regulations require that the IRB re-approve research projects at intervals appropriate to the degree of risk, but no less than once per year. This process is called "continuing review." Continuing review for non-exempt research is required to occur as long as the research remains active for long-term follow-up of research subjects, even when the research is permanently closed to enrollment of new subjects and all subjects have completed all research-related interventions and to occur when the remaining research activities are limited to collection of private identifiable information. Your project "expires" at 12:01 AM on the date indicated on the preceding page ("Next IRB Approval Due on or Before"). You must obtain your next IRB approval of this project on or before that expiration date. You are responsible for submitting a Continuing Review application in sufficient time for approval before the expiration date, however the HSO will send a reminder notice approximately 60 and 30 days prior to the expiration date.

Modifications: Any change in this research project or materials must be submitted on a Modification application to the IRB for prior review and approval, except when a change is necessary to eliminate apparent immediate hazards to subjects. The investigator is required to promptly notify the IRB of any changes made without IRB approval to eliminate apparent immediate hazards to subjects using the Modification/Update Form. Modifications requiring the prior review and approval of the IRB include but are not limited to: changing the protocol or study procedures, changing investigators or funding sources, changing the Informed Consent Document, increasing the anticipated total number of subjects from what was originally approved, or adding any new materials (e.g., letters to subjects, ads, questionnaires).

Unanticipated Problems Involving Risks: You must promptly report to the IRB any serious and/or unexpected adverse experience, as defined in the UI Investigator's Guide, and any other unanticipated problems involving risks to subjects or others. The Reportable Events Form (REF) should be used for reporting to the IRB.

Audits/Record-Keeping: Your research records may be audited at any time during or after the implementation of your project. Federal and University policies require that all research records be maintained for a period of three (3) years following the close of the research project. For research that involves drugs or devices seeking FDA approval, the research records must be kept for a period of three years after the FDA has taken final action on the marketing application.

Additional Information: Complete information regarding research involving human subjects at The University of Iowa is available in the "Investigator's Guide to Human Subjects Research." Research investigators are expected to comply with these policies and procedures, and to be familiar with the University's Federalwide Assurance, the Belmont Report, 45CFR46, and other applicable regulations prior to

conducting the research. These documents and IRB application and related forms are available on the Human Subjects Office website or are available by calling 335-6564.

Mount Sinai

Program for the Protection of Human Subjects

Mount Sinai School of Medicine and Mount Sinai Hospital
One Gustave L. Levy Place, Box 1075
3 East 101st Street, First Floor
New York, NY 10029-6530
Phone: (212) 824-8200
Fax: (212) 876-6789

APPROVAL OF RESEARCH

Date: February 1, 2011

To: **Philip Landrigan, M.D. (philip.landrigan@mssm.edu)**

On **1/27/2011**, an Institutional Review Board of the Mount Sinai School of Medicine, in accordance with Mount Sinai's Federal Wide Assurances (FWA#00005656, FWA#00005651) to the Department of Health and Human Services approved the following human subject research from **1/27/2011** until **11/10/2011** inclusive.

Type of Review:	**Modification**
Project Title:	**FORMATIVE RESEARCH PROPOSAL PROJECT 18- PLACENTAL STUDIES 18.2 AND 18.4**
Investigator:	**Philip Landrigan, M.D.**
MSSM Project #:	**GCO#: 05-0269(0002)(01) CM**
Funding Agency:	**NIH NICHD**
IND or IDE (if any):	**No INDs; No IDEs**
Submission Details (if any):	modification: 18.2 and 18.4 are now being added as a part of the larger protocol that was submitted with 05-0269(2) and are now being started at MSSM; submitting an updated abstraction form; removing Elena Rahona as a coordinator; submitting a revised Visit Information Sheet.

Before **10/12/2011** or within 30 days of study close, whichever is earlier, you are to submit a completed FORM HRP-212: Continuing/Final Review Progress Report and required attachments, in order to request continuing IRB approval or study closure. If IRB continuing review approval is not granted before the expiration date of 11/10/2011, IRB approval of this research expires on that date.

The IRB has determined that this research involves no greater than MINIMAL RISK. Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. (45CFR.46.102; 21CFR50.3).

In conducting this research you are required to follow the requirements listed in the *Investigator Manual*. If stamped approved consent forms are attached, use copies of these forms to document consent. IRB approval does not constitute or imply institutional support for the conduct of this research.

Sincerely yours,

Jeffrey H. Silverstein, MD

Jeffrey H. Silverstein, M.D.
Chair, Institutional Review Board
Program Director, Program for the Protection of Human Subjects
Associate Dean, Research

cc: Study Contact: Anne Golden anne.golden@mssm.edu

South Dakota State University

Office of Research/Human Subjects Committee
SAD Room 124
Box 2201 SDSU
Brookings, SD 57007

To: Natalie Thiex and Bonny Specker, National Children's Study/E.A. Martin Program

Date: November 9, 2010

Project Title: NCS Placental Studies

Approval #: IRB-1011007-EXP

The committee approved the above referenced activity using expedited procedures as described in 45 CFR 46.110. The activity was deemed to be no greater than minimal risk, and the following expedited category from 63 FR 60364-60367 was found to be applicable to your activity:

(3) Prospective collection of biological specimens for research purposes by noninvasive means.

One-year approval of your project will be dated starting 11/9/10. If you require additional time to complete your project, please submit a request for extension before 11/8/11. Protocol changes must be approved by the Committee prior to implementation. Forms may be found on the Human Subjects web page. If there are any unanticipated problems involving risks to subjects or others, please contact the SDSU Research Compliance Coordinator. At the end of the project please inform the committee that your project is complete.

If I can be of further assistance, don't hesitate to let me know.

Sincerely,

Norm

Norman O. Braaten
SDSU Research Compliance Coordinator

INSTITUTIONAL REVIEW BOARD
University of California, Davis

PROTECTION OF HUMAN SUBJECTS – DECLARATION / ASSURANCE OF IRB APPROVAL

Principal Investigator	Protocol No.	Approval Date	Expiration Date	Risk Level
Cheryl Walker MD	201018244-1	10/18/10	10/17/11	Minimal Risk
PI Department	**Sponsor Name**	**Level of Review**	**Expedited Category**	**Status**
MED: OBSTETRICS & GYNECOLOGY	NIH	Expedited	2b ,3	New

The following research study has been reviewed by the IRB in accordance with the Common Rule and any other governing regulations:
The Effects of Time, Temperature and Storage on Neonatal Hematopoietic and Mesenchymal Stem Cell Populations

The above referenced activity has been determined to meet the definition of human subjects research as defined by Federal Regulations and UC Davis IRB Policy. As principal investigator for a study involving human subjects, you assume certain responsibilities, specifically:

1. You will conduct the study according to the protocol approved by the IRB. As the PI you will be accountable for your own research and the protection of human subjects. You will ensure, at all times, that you have the appropriate resources and facilities to conduct this study. You will ensure that all research personnel involved in the conduct of the study have been appropriately trained on the protection of human subjects, in addition to the study procedures.
2. Any unanticipated problems involving risks to participants or others will be reported to the IRB in accordance with IRB policy. Changes in approved research initiated without IRB approval to eliminate apparent immediate hazards to the participant, are to be reported to the IRB in accordance with the policy "Reporting of Unanticipated Problems Involving Risks to Participants or Others."
3. Any changes in your research plan must be submitted to the IRB for review and approval prior to implementation of the change. Proposed changes in approved research cannot be initiated without IRB approval, except when necessary to eliminate apparent immediate hazards to participants.
4. Your protocol must be renewed prior to expiration of the study. Although a courtesy renewal notice will be issued to you three months prior to expiration, should you fail to receive this notice it is your responsibility to contact the IRB Administration for a duplicate copy. Failure to submit renewal documents to the IRB Administration by the Administrative Due Date may result in termination of the study by the IRB.
5. Advertisements for the recruitment of subjects must be approved by the IRB prior to implementation.
6. If you plan to collect protected health information, you are required to comply with HIPAA requirements.
7. Studies conducted at the CCRC must be reviewed and approved by the VA Research & Development Committee prior to initiation of the study. Contact the VA R&D Committee for submission requirements.
8. Should your study involve the use of investigational drugs, you are required to provide a complete copy of the approved protocol to the Investigational Drug Service Pharmacy.

If this is a Clinical Study, the Hospital Health System requires that:

- A complete copy of the IRB approved Description of Study and signed Consent Form be placed in the patient's medical record. Ensure that you have swiped the patient's name plate card or printed the patient's name at the top of page 1 of the consent document. Medical procedures should be documented in the patient's medical record.
- All investigational drugs be distributed through the UCDMC Pharmacy. A copy of the signed consent form must be submitted to the Pharmacy if investigational drugs are dispensed through the Outpatient Pharmacy.
- If the study involves radiation use, a copy of the IRB approved consent form be sent to: RUC, Health Physics, 2500 FSSB.

Name and Address of Institution: University of California, Davis IRB Administration 2921 Stockton Blvd., Suite 1400, Rm. 1429 Sacramento, CA 95817	**Signature : The IRB Chair/Designee signing below certifies that the information provided above is correct and that, as required, future reviews will be performed until study closure and certification will be provided.**
Institutional Administrator: Eric C. Mah, MHS Director, Institutional Review Board Administration ecmah@ucdavis.edu	**Name:** John Anderson MD
Phone No.(916) 703-9151	**Title:** Chair
Fax No. (916) 703-9160	**Date:** 10/18/2010

This Assurance, on file with the Department of Health and Human Services, covers this activity:

FWA No: 00004557 Expiration Date: August 17, 2013 IORG: 0000251

Informed Consent

If your study includes the use of a consent form(s), your study will require the use of the HIPAA *Research Authorization Form.* Please see the website address below for the form, instructions and requirements. Note: the IRB does not require submission of the *Research Authorization Form* with your IRB protocol application form.

- **http://compliance.ucdmc.ucdavis.edu/guidance/privacy/resauth.html**

DESCRIPTION OF STUDY

Principal Investigator: Cheryl Walker, MD

Title of the Study: The Effects of Time, Temperature and Storage on Neonatal Hematopoietic and Mesenchymal Stem Cell Populations

PURPOSE AND PROCEDURES:

1. Describe the study format and whether it is single or multi-center; industry-sponsored or investigator initiated; and the funding source.

   This is an investigator-initiated multi-center formative research study funded by the NICHD as part of the National Children's Study (NCS). It is designed to generate operational data to determine the appropriate and efficient conditions for collection, transport, storage and processing of cord blood and placental tissues, the results of which will advise scientists overseeing the National Children's Study. Here at UCD, we plan to study the influence of shipping conditions, including storage temperature and duration of time between birth and specimen processing on the numbers and functional characteristics of hematopoietic and mesenchymal stem cells (HSC and MSC, respectively) derived from human cord blood, umbilical cord matrix and placental tissues. Ultimately, we want to explore how these parameters relate to the development of both hematopoietic and immune systems and serve as potential mechanisms underlying differences in these cell populations that could be related to the etiology of and potential preventive strategies for preterm birth and diseases in childhood and throughout life.

   Sites for the Pilot Study to which tissue obtained from subjects at UC Davis will be sent and/or analyzed of from which tissue will be obtained include: UC Davis, University of Rochester, University of Wisconsin, Mount Sinai, University of Iowa, Brown University, University of Illinois, and University of Massachusetts.

   Sites for the Main Study from which tissues will be obtained include the following NCS Sites:

   University of California, Irvine
   South Dakota State University
   Mount Sinai University
   University of North Carolina at Chapel Hill
   Children's Hospital of Pennsylvania
   University of Utah
   University of Wisconsin, Madison
   Orange County Vanguard Center
   BYPL Vanguard Center
   Queens Vanguard Center
   North Carolina Vanguard Center
   Montgomery County Vanguard Center
   Salt Lake County Vanguard Center
   Wakesha County Vanguard Center

2. Briefly describe the specific aims of the study, research methods and procedures.

   A. Aims:

   The explosion of research into the therapeutic potential of neonatal stem cells has largely overlooked the reality that these stem cells are also a rich source of information about the neonates from which they derive and their prior fetal environment. Their numbers, distribution and functional capabilities provide a window into the health and resilience of the child at birth and suggestions as to the type and magnitude of antenatal insults. Further, they present a magnificent opportunity to study health and disease, both in general and in the individuals from whom they originate. In the future, neonatal stem cells stored at birth may provide the basis for personalized medicine, using neonatal cells to make patient-specific induced pluripotent stem cells (iPSC) with the ability to generate any tissue type and the promise of many avenues for the study of disease processes. In our study, we

Medical College of Wisconsin /
Froedtert Hospital
Institutional Review Board

To: Randall Kuhlmann
Sara Szabo, MD PhD
Andrew Webb
Steven Leuthner

Date: **October 6, 2010**

Re: **Study Full Title**: NCS Project 18, Placental Studies, Pilot Study: Pilot study for evaluation of feasibility of placental tissue collection for RNA isolation.

Study # & Link: PRO00013497

IRB Approval Date: 10/6/2010

IRB Expiration Date : 10/5/2011

The MCW/FH Institutional Review Board #5 has granted approval for the above-referenced submission in accordance with 45 CFR 46.111 by expedited review, Category #2b & #5. This letter also includes approval in accordance with 45 CFR 46 Subpart B (pregnant women, fetuses, and neonates).

The consent form and related HIPAA authorization are effective as of 10/6/2010. Signed consent forms for each subject must be kept on file as part of the project records.

The items listed below were submitted and reviewed when the IRB approved this submission. Research must be conducted according to the IRB approved protocol listed below:

Consent Ver. 2

Wisconsin IRB Consortium Project Description and Review Request Form

Protocol dated 7/26/10

The IRB also granted approval of a waiver of HIPAA authorization requirements at 45 CFR 164 and a waiver of informed consent requirements at 45 CFR 46.116 for the purpose of Records Review for Potential Subjects.

Any and all proposed changes to this submission must be reviewed and approved by the IRB prior to implementation. When it is necessary to eliminate hazards to subjects, changes may be made first. this should be followed promptly by a protocol deviation and amendment.

In accordance with federal regulations, continuing approval for this submission is required prior to 10/5/2011. The Continuing Progress Report (CPR) must be received by the IRB with enough time to allow for review and approval prior to the expiration date. Failure to submit the CPR in a timely manner may result in the expiration of IRB approval.

A Final CPR must be submitted to the IRB within 30 days of when all project activities and data analysis have been completed.

All Unanticipated Problems Involving Increased Risk of harm to Subjects or Others (UPIRSOs) must be reported promptly to the MCW/FH IRB according to the IRB Standard Operating Procedures.

If you have any questions, please contact the IRB Coordinator II for this IRB Committee, Dee Burns, at 414-456-8464 or dburns@mcw.edu.

Sincerely,

Patricia Witt, PhD
IRB Chair
MCW/FH Institutional Review Board #5