Title: **UCLA Perinatal Biospecimen Repository**

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Signature Page

By signing and dating this clinical protocol, I provide the necessary assurance that this study will be conducted according to all stipulations of the clinical protocol, including all statements regarding confidentiality of information.

- I agree to protect the privacy, health, and welfare of the research participants and to ensure the integrity of the data collected.
- I agree to conduct the study in compliance with best practice guidelines, and applicable regulatory federal, state, and university requirements.
- I agree to conduct the study in accordance with the current clinical protocol and will not make changes to the research conducting without obtaining UCLA IRB approval, except, when necessary, to protect the safety, rights, or welfare of the research participants.

Sponsor-Investigator:

Signature: Date:

Name: Yalda Afshar, MD, PhD

UCLA, Division of Maternal Fetal Medicine, Department of Obstetrics and Gynecology, University of California, Los Angeles

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Legal notice

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ABBREVIATIONS

AE	Adverse Event
CFR	United States Code of Federal Regulations
CHD	Prenatal Vascular Phenotype in Congenital Heart Disease
Co-PIs	Co-Investigators
CRF	Case Report/Record Form (paper or electronic)
DMC	Data Monitoring Committee
DMP	Data Management Plan
DNA	Deoxyribonucleic Acid
DUA	Data Use Agreement
EC	Endothelial Cell
eCFR	electronic Case Report Form
EDC	Electronic Data Capture
FDA	Food and Drug Administration
FFPE	Formalin-fixed Paraffin Embedded
GCP	Good Clinical Practice
hESC	Human Embryonic Stem Cell
HIPAA	Health Insurance Portability and Accountability Act
HUVEC	Human Umbilical Vein Cell
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IP	Internet Protocol address numbers
IRB	Institutional Review Board
ISBER	International Society for Biological and Environmental Repositories
LEP	Limited English Proficiency
MTA	Material Transfer Agreement
NIH	National Institutes of Health
PAR	Post-Approval Reporting Requirements
PHI	Protected Health Information

PI	Principal Investigator
PII	Privately Identifiable Information
POC	Product of Conception
RHI	Research Health Information
RI	Restricted Information
RNA	Ribonucleic Acid
SAE	Serious Adverse Even
SAP	Statistical Analysis Plan
TORCH	Infections: toxoplasmosis, rubella virus, cytomegalovirus, and HIV
UCLA	University of California, Los Angeles
URL	Web Universal Resource Locator
WHO	World Health Organization

Abstract

The purpose of this investigator-initiated prospective observational cohort study is to establish the new UCLA Perinatal Biospecimen Repository (Perinatal Repository) for collection, storage, and distribution the human data and biospecimens of the participants with perinatal pathology. The secure and shared high-quality resource of clinical data and biological specimens (Repository Materials), across pregnancy pathology related to research protocols at the Afshar`s Lab will be created. Core variables of interest include clinical characteristics and relevant biological samples. Intention to collect perinatal data is aiding the efficiency and effectiveness of de-identified biorepository for pregnancy-at-risk outcome research.

The primary aims of the project are:

- To design the Case Report Forms (CRFs) for the clinical and biospecimen data.
- To create and update the project-specific policies, agreements, and Standard Operating Procedures (SOPs).
- To develop the data management system to assure personal health information de-identification, data integrity, participants welfare, and protocol compliance.
- To develop and implement a quality management system for the Repository.
- To collect and record in the Repository protocol-related clinical information.
- To organize consistent system to bank high-quality biospecimens while protecting participant-donor safety and privacy.
- To establish the policies and procedures for Repository Materials dissemination and research collaboration.
- To analyze the scientific results of the Repository creation.

The secondary aim of the study is to provide a mechanism to store and share for the research purposes the de-identified biospecimen and information about participants at risk for adverse pregnancy outcomes.

Inclusion criteria: 1. Pregnant and postpartum birthing persons aged 18 and over with perinatal pathology; 2. Pregnant and postpartum birthing persons; 3. Non-pregnant birthing persons (volunteers).

Exclusion criteria: Pregnant and postpartum birthing person unwilling to give written informed consent to participate in the study.

Duration of the project – 5 years. Approximate number of participants – 1000. The number of visits – from one to 6. Duration of the subject's participation in the study - from 1 day to 10 months. Follow-up period: from enrollment to postpartum visit. Core variables of interest comprise of the birthing person's/ fetus'/ neonate's clinical characteristics and relevant biological samples: maternal blood, cord blood, plasma, serum, urine, breastmilk, placenta, umbilical cord, amniotic fluid, product of conception (POC), and cell lines. Collection and retaining of the biospecimens will be performed by study team across perinatal pathology cases at the UCLA Health Medical Centers for up to 15 years. Study medical procedures (blood drawing, assessment, physical examinations, medical record, etc.) will be conducted by appropriately licensed/ credentialed personnel working within the scope of their licenses and credentials. Dataset entry and specimens processing will be performed by the Afshar's Lab personnel at the University of California, Los Angeles.

Key words: Biospecimen, Perinatal, Pregnancy, Repository, Obstetrics

1 BACKGROUND INFORMATION AND RATIONALE

1.1 Introduction

According to the US Centers for Disease Control and Prevention, complications of pregnancy involve the mother's health, the neonate's / fetus' health, or both. Some birthing persons can have perinatal disorders that arise during or after pregnancy. Other patients have health problems before they become pregnant that could lead to pregnancy complications. It is very important to know the risk factors of perinatal disorders to prevent non-favorable pregnancy outcomes. For pregnant and postpartum persons and also for their neonates/ fetuses implementation the results of scientific study into clinical care mean to decrease the risk of pregnancy complications.

At the present time, Dr. Afshar is conducting and oversighting the series of scientific projects in the field of perinatal pathology, including the following:

- PRIORITY (Pregnancy CoRonavIrus Outcomes RegIsTrY). It is the nationwide study of pregnant or recently pregnant persons who are either under investigation for Coronavirus infection (COVID-19) or have been confirmed to have COVID-19. This research is being performed to help patients and healthcare providers better understand how COVID-19 impacts pregnant persons and the newborns.
- Prenatal Vascular Phenotype in Congenital Heart Disease (CHD). This project targets the mechanisms underlying the single heart ventricle vascular phenotype by linking molecular data and environmental clues. Single ventricle accounts for 25% of infant CHD deaths; only 50-70% babies with this disease survive beyond 5 years. Research results may improve treatment that arises from loss of vascular integrity.
- Endothelial Cells: Conduits of Translational Medicine. Evaluation of the umbilical cord vessels provides data to identify the biomarkers responsible for the underlying etiologies of preeclampsia, growth restriction, and other pregnancy-related disorders.
- The Umbilical Cord as a Model System. The project identifies a patient population with an unmet clinical need because of an underlying chronic dysfunction of hemodynamics related to endothelial cell dysfunction. The study analyses downstream complications and interventions that can improve quality of life in these patients with lifelong sequel related to an abnormal endothelial cell and vascular phenotype. The project focuses on altered flow acting as a modifier in development and contributing to CHD. Flow is a well-defined mechanism and provides a platform to study physical forces that alter hemodynamics and of critical importance of gene expression in prenatally diagnosed CHD with postnatal sequel related to the vascular phenotype.

Creation and maintenance of Perinatal Repository provides the Afshar's Lab with the possibility to pool perinatal clinical data and biospecimens into a single database that could be accessed by clinical investigators inside and outside the UCLA research team.

The secure and shared research data storage and high-quality resource of clinical data and biological specimens (Repository Materials), across pregnancy pathology related to research protocols at the Dr. Afshar's Lab will be created. Core variables of interest include clinical characteristics and relevant biological samples. Collection and retaining of the

biospecimen will be performed by study team across perinatal pathology protocols at the Afshar's Lab.

The core data variables are selected to match those agreed upon by the Afshar's Lab team members. Intention to collect perinatal data is aiding the efficiency and effectiveness of de-identified biorepository for pregnancy at risk outcome research.

1.2 Compliance Statement

This study will be conducted in full accordance with Good Clinical Practice (GCP) and as required by the following regulations:

- University of California, Los Angeles (UCLA), Office of Research Administration Research Policies and Procedures;
- UCLA Human Research Protection Program;
- UCLA IRB Guidance and Procedures;
- United States Code of Federal Regulations (CFR): 21 CFR Parts 11 (Electronic Records and Electronic Signatures), 50 (Protection of Human Subjects), 54 (Financial Disclosure by Clinical Investigators), 56 (Institutional Review Boards), and 45 CFR Part 46 (Protection of Human Subjects);
- Health Insurance Portability and Accountability Act (HIPAA): Privacy Rule and Security Rule;
- U.S. Department of Health and Human Services, Food and Drug Administration (FDA) Guidance Documents, as applicable;
- International Conference on Harmonization (ICH) guidelines, but not limited to Good Clinical Practice (ICH E6), Clinical Trials in the Pediatric Population (ICH E11), and Genomic Sampling (ICH E18);
- the Belmont Report; the Declaration of Helsinki;
- National Institutes of Health (NIH) Office of Extramural Research, Research Involving Human Subjects, as applicable;
- International Society for Biological and Environmental Repositories (ISBER) best practices;
- Applicable Federal, State, Local Regulations and Guidance.

Non-compliance issue, if any episode arises, will be timely documented. The PI will conduct the study in in due course with this clinical protocol, will obtain consent and assent (unless a waiver is granted), and will report unexpected issues in conformity with the UCLA IRB policies and procedures and applicable federal, state, and local requirements. Obtaining, recording, reporting and transmission of research data will comply with the regulations mentioned above to protect the privacy, health, and welfare of the research participants during and after the study and to ensure the integrity of the data collected.

2 STUDY OBJECTIVES

The purpose of this investigator-initiated prospective observational cohort study is to establish the new UCLA Perinatal Biospecimen Repository for collection, storage and distribution the human data and biospecimens of the participants with perinatal pathology.

As a result of the clinical protocol implementation, the secure and shared research data storage and high-quality resource of clinical data and biological specimens, across perinatal pathology related to research protocols at the Afshar's Lab will be created.

2.1 Primary Aims

The primary aims of the project are:

1. To design the case report forms (CRFs) for the clinical and biospecimen data.
2. To create and update the project-specific policies, agreements, and Standard Operating Procedures (SOPs).
3. To develop the data management system to assure personal health information de-identification, data integrity, participants welfare, and protocol compliance.
4. To develop and implement a quality management system for the Perinatal Repository.
5. To collect and record in the Repository protocol-related clinical information.
6. To organize consistent system to bank high-quality biospecimens while protecting participant-donor safety and privacy.
7. To establish the policies and procedures for Repository Materials dissemination and research collaboration.
8. To analyze the scientific results of the Repository creation.

2.2 Secondary Aim

The secondary aim of the study is to provide a mechanism to store and share the de-identified biospecimen and information about participants at risk for adverse pregnancy outcomes for the research purposes.

2.3 Hypothesis

There is no hypothesis for this patient repository study.

3 INVESTIGATIONAL PLAN

3.1 Study Design

This is a Phase 0, investigator-initiated, prospective, observational study design: Patient Registry.

Observational Model: Cohort.

Time Perspective: Prospective.

Follow-Up Duration: From enrollment to postpartum visit.

The study is designed to create Repository of biospecimen and clinical data that may allow earlier evaluation of the patient's risk of developing adverse pregnancy outcomes. Further in this protocol, the term "Material/ Materials" is used to refer to human data and/ or biospecimens collected from the research participants. This study will be conducted in UCLA Health collecting data of the inpatients and outpatients with perinatal pathology and birthing persons (volunteers). All study participants will continue to be managed by their personal physicians / pediatrician. Participants will receive the treatment recommended by their doctors; the study will not alter the treatment pathway and pregnancy management of the patients. This study does not restrict or introduce any therapeutic or surgery interventions, including medications.

Along with biological specimens, this Register aims to collect and record the current treatment and outcomes during and after the pregnancy of participants diagnosed with perinatal pathology. Participants' information and biospecimen will be obtained as described below in Study Procedures. The Repository will contain the new research database of perinatal pathology.

3.1.1 Description of the Collecting Site

Location of the collecting site: Afshar's Lab, Dep.: Obstetrics & Gynecology, UCLA; 200 Medical Plaza Driveway, Suite 430, Los Angeles, CA 90095; phone: 310-794-7274; email: yafshar@mednet.ucla.edu. The study site belongs to the UCLA Health System sites.

Collecting activities will start after the UCLA IRB approval of the Protocol.

3.1.2 Institutional Review Board Information

Protocol of the study will be sent to the local UCLA IRB that is registered by the OHRP/ FDA [https://ohrp.cit.nih.gov/search/IrbDtl.aspx].

Parent Institution/Organization: IORG0000105 - University of California Los Angeles.

Located at: Los Angeles, California, US.

Expires: 12/10/2021.

IRB00000172 - University of California Los Angeles - MIRB1 General Biomedical IRB #1 - General Biomedical - MIRB1-Biomedical

3.1.3 Overview of the Data Collection

After enrollment of the participant in the study, PI/ designee study personnel (according to Study Delegation Log) will conduct chart review, i.e., manually review patient chart in CareConnect. To contribute to the Perinatal Registry database, clinical information of inpatient and outpatient population will be collected. Patient encounters are related to Ronald Reagan Hospital and Santa Monica Hospital.

Biospecimens will be collected prospectively to the Perinatal Repository. Clinical data will be linked to the biospecimens. Dataset entry and specimens processing will be performed at the Afshar's Lab.

3.2 Study Duration, Enrollment and Number of Sites

3.2.1 Duration of the Study

Duration of the project – 5 years.
Duration of participation in the study - from 1 day to 10 months.
Duration of follow-up period – from enrollment to postpartum visit.

3.2.2 Total Number of Study Sites/ Total Number of Participants Projected

Total number of study sites:
Approximate number of participants screened – 1050.
Approximate number of participants enrolled – 1000.

3.3 Study Population

Ages Eligible for Study: Child, Adult
Sexes Eligible for Study: All
Accepts Volunteers: Yes
Sampling Method: Non-Probability Sample
Study Population: Any UCLA Health patient that is at risk for perinatal pathology.
Estimated Enrollment: 1000 participants.

3.3.1 Inclusion criteria:

- Pregnant and postpartum birthing persons aged 18 and over with perinatal pathology;
- Pregnant and postpartum birthing persons;
- Non-pregnant birthing persons (volunteers).

The study has no inclusion criteria based on gender, race, ethnicity, and language spoken. The protocol contains inclusion criteria for enrollment in the study associated with term "pregnancy/childbearing potential".

The nature of and scientific rationale for the inclusions:

This observational study will establish the new UCLA Perinatal Biospecimen Repository, to collect, storage and distribute the clinical data and biospecimens of the participants with perinatal pathology. Therefore, pregnant and postpartum birthing persons are target population for this clinical protocol.

3.3.2 Exclusion criteria:

- Pregnant and postpartum birthing person unwilling to give written informed consent to participate in the study.

The study has no exclusion criteria based on gender, race, ethnicity, and language spoken. The protocol contains inclusion criteria for enrollment in the study associated with term "pregnancy/childbearing potential".

The nature of and scientific rationale for the exclusions:

According to the low, only a person who has given informed consent can be enrolled in the study. If the birthing person has not given written informed consent, this person cannot be the study participant.

4 STUDY PROCEDURES

4.1 Data Collection Procedures

4.1.1 Data Collection

The original Material collection date: The day after the approval of the Protocol by the UCLA IRB. Inclusion and exclusion criteria are listed above. Duration of the study: 5 years. Duration of maintenance and using of the Repository: 15 years.

Approximate number of data records to be collected in the Perinatal Repository: data of 1000-1050 participants.

After enrollment of the participant in the study, PI/ designee study personnel (according to Study Delegation Log) will conduct chart review, i.e., manually review patient chart in CareConnect. To contribute to the Perinatal Registry database, clinical information of inpatient and outpatient population will be collected. Patient encounters are related to Ronald Reagan Hospital and Santa Monica Hospital.

Biospecimens will be collected prospectively to the Perinatal Repository. Clinical data will be linked to the biospecimens.

4.1.2. Schedule of Events

Recruitment of pregnant birthing persons and volunteers will happen consecutively at the UCLA Health facilities. Table 1 outlines the events and biospecimen collection schedule for the study.

Table 1. Schedule of Events

Procedures/ Assessments	**Enrolment/ Baseline Visit**	**The Stages of Pregnancy**				**Postpartum Visit[d]**
		1st Trimester (from conception to 12 weeks)	**2nd Trimester (from week 13 to week 27)**	**3rd Trimester: (from week 28 until birth)**	**Delivery/ End of Pregnancy**	
Eligibility Criteria	X					
Informed	X[a]					

Consent						
Medical History [c]	X	X[b]	X[b]	X[b]	X[b]	X[b]
Pregnancy Status	X	X[b]	X[b]	X[b]	X[b]	X[b]
Pregnancy Outcomes					X[b]	X[b]
AE	X	X[b]	X[b]	X[b]	X[b]	X[b]
Neonatal/ Fetal Status	X	X[b]	X[b]	X[b]	X[b]	X[b]
Neonatal/ Fetal Outcomes					X[b]	X[b]
Biospecimens Banking [e]**:**						
Blood [f]	X	X[b]	X[b]	X[b]	X[b]	X[b]
UC Blood					X[b]	
Urine	X[b]	X[b]	X[b]	X	X[b]	X[b]
Tissue: Placenta					X[b]	
Tissue: UC					X[b]	
Other Tissue: POC [g]					X[b]	
Amniotic fluid					X[b]	
Breastmilk						X[b]

Footnotes for Schedule of Events:

X: Required activities.

[a] : Informed Consent process should take place prior to undergoing any Protocol-specific procedures.

[b] : Optional, based on the PI decision.

[c] : Medical History includes, but not limited to: demographics, physical examination, concomitant medications, ECG, laboratory assessment. Laboratory assessment includes, but is not limited to hematology, blood chemistry, coagulation, endocrine function, urinalysis, serum/ urine pregnancy test, TORCH infections: toxoplasmosis, rubella virus, cytomegalovirus, and HIV. Procedures and assessments will be performed according to the routine standard at the UCLA Health, and are documented as available (with the exception of Informed Consent).

[d] : Postpartum Visit should take place within 6 months of delivery/ end of pregnancy.

[e] : For biospecimens banking, trained research team personnel will collect the biospecimens per standard operating procedures.

[f]: The study protocol provides for the collection of blood samples as a procedure combined with routine blood sampling for clinical laboratory testing. For research purposes, it is intended to collect additional amount of the venous blood – up to 20 mL per procedure. The blood will not be drawn for research more often than twice in a single week. Blood drawing will be performed as follow: Red Top Tube (Serology tube) – 10 mL and Lavender Top Tube (EDTA tube) – 10 mL. Blood samples will be collected for whole blood, plasma, and serum banking.

[g] : Other tissue: In case of a miscarriage, abortion, or stillbirth, the participant will be asked to donate POC tissue for Repository collection.

Participation in the Repository Protocol can be offered by the PI/ designee for the outpatients and inpatients. Eligibility criteria will be checked during baseline visit. Informed consent form should be signed at enrolment, following which baseline medical history will be collected. Medical history includes, but not limited to demographics, physical examination, concomitant medications, ECG, laboratory assessment. Information about pregnancy and fetal status will be recorded. Laboratory assessment includes, but is not limited to hematology, blood chemistry, coagulation, endocrine function, urinalysis, serum/ urine pregnancy test, TORCH infections: toxoplasmosis, rubella virus, cytomegalovirus, and HIV. Procedures and assessments will be performed according to the routine standard at the UCLA Health, and are documented as available (with the exception of Informed Consent).

Enrolment/ Baseline Visit: After consenting, the birthing person will be asked to donate blood (maternal blood) or/ and urine specimen to the Repository. Trained research team personnel will collect the biospecimens per standard operating procedures. The study protocol provides for the collection of blood samples as a procedure combined with routine blood sampling for clinical laboratory testing.

For research purposes, it is intended to collect additional amount of the venous maternal blood – up to 20 mL per procedure. The blood will not be drawn for research more often than twice in a single week. Blood drawing will be performed as follow: Red Top Tube (Serology tube) – 10 mL and Lavender Top Tube (EDTA tube) – 10 mL. Blood samples will be collected for whole blood, plasma, and serum banking.

Collection of the cord blood after delivery will be performed once as the same order. The research Protocol does not involve collecting any specimens of the vital neonates, such as venous blood or urine.

All biological sampling for the Repository (blood, urine, breastmilk, placenta, umbilical cord, i.e.) will follow the Afshar's Lab standard operating procedures, UCLA, local and federal guidance documents on the proper handling and processing of potentially infectious biospecimens.

After participant enrollment, the PI will monitor and record, if any, the AEs, and informs the UCLA IRB according to the established policy and regulations.

Follow-up Visits: For pregnant birthing persons, biospecimens donation during follow-up visits is optional, based on the PI decision. Repository Material will be collected by research team during follow-up research visits (each once per pregnancy trimester):

- 1st Trimester Visit (from conception to 12 weeks): medical history, pregnancy and fetus status, AE, biobank specimens: blood and urine.
- 2nd Trimester Visit (from week 13 to week 27): medical history, pregnancy and fetus status, AE, biobank specimens: blood and urine.
- 3rd Trimester Visit: (from week 28 until birth): medical history, pregnancy and fetus status, biobank specimens: blood and urine.

***Delivery/ End of Pregnancy Visit*:** Medical history, pregnancy status, pregnancy outcome, neonatal/ fetus status, neonatal/ fetus outcome, AE, biobank specimens: maternal blood, cord blood (UC blood), maternal urine, placenta, umbilical cord, amniotic fluid.

Umbilical cord and placenta are temporary fetus organs. For the Repository collection, placenta, umbilical cord, and therefore, cord blood, will be obtained for the Repository purposes after childbirth.

In case of a miscarriage, abortion, or stillbirth, the participant will be asked to donate POC tissue to the Repository.

***Postpartum Visit*:** Medical history, pregnancy outcome, neonatal status, neonatal outcome, AE, biobank specimens: maternal blood, maternal urine, breastmilk.

All biological sampling for the Repository (blood, urine, breastmilk, placenta, umbilical cord, i.e.) will follow Afshar's Lab standard operating procedures, UCLA, local and federal guidance documents on the proper handling and processing of potentially infectious biospecimens.

For non-pregnant volunteers, participation in the project is limited to the one-time biospecimens donation and granting access to their medical records.

4.1.3 Data Elements

In the Perinatal Repository, the following clinical data from the UCLA Health records will be linked to the collected biospecimens:

- Patient Demographics.
- Patient Identifiers.
- Encounters (including hospitalizations, outpatient visits, and other encounter types).
- Provider.
- Hospital Unit Transfers.
- Diagnoses.

- Procedures completed.
- Problem List.
- Appointments.
- Vital Signs and Other Flow sheet Data.
- Laboratory Test Results.
- Medication Orders (Prescriptions) or Med Administration.
- Social History.
- Family History.
- Allergies.
- Provider Notes (Clinical Documents).
- Pathology and Cytology.
- Imaging Orders and Results.
- Cultures / Isolates (Microbiology).
- Cultures / Isolates Susceptibility and Sensitivity (Microbiology).

After collecting the necessary clinical information, all personal identifiable information of the participant will be encoded. The PI will retain access to the codes.

In case of an MTA arrangement and providing access to the Repository to the third party, only de-identified participants' information and de-identified biospecimens can be shared.

4.1.4 PHI Elements Collected

In the course of the study, the PI/ designee will approach and collect personally identifiable health information (PHI) of research participants in accordance with Table 2.

Table 2 – List of the PHI collected by the PI

N	PHI Elements	Intention to collect	
1	First Name, Last Name, Middle Name	Yes	
2	All geographical subdivisions smaller than a state, including street address, city, county, precinct, zip code	Yes	
3	All elements of dates for dates directly related to the participant, including birth date, admission date, discharge date, date of death (if applicable)	Yes	
4	Phone numbers	Yes	
5	Fax numbers		No
6	E-mail	Yes	
7	Social Security number		No

8	Medical record number	Yes	
9	Health plan beneficiary numbers		No
10	Account numbers		No
11	Certificate/license numbers		No
12	Vehicle identifiers and serial numbers, including license plate numbers		No
13	Device identifiers and serial numbers		No
14	Web Universal Resource Locators (URLs)		No
15	Internet Protocol (IP) address numbers		No
16	Biometric identifiers, including finger and voice prints		No
17	Full face photographic images and any comparable images		No
18	Other unique identifying numbers, characteristic, or code		No

The five PHI core elements listed in Table 1 are subject to HIPAA regulations:

- Name;
- Address;
- Dates directly related to the participant;
- Phone number;
- Medical record number.

This study will use PHI that enters the participants' medical records and / or is used for standard healthcare services. As known, HIPAA regulations grant the PI and authorized team members the right to approach and use PHI necessary to conduct clinical research.

It is necessary to be emphasize that during the conduct of the study PI endeavor to collect and record the minimum of PHI.

In the UCLA Health clinical departments, the medical personnel participating in the study will perform the sampling procedures. An example of these procedures is taking blood into a test tube, placing the umbilical cord or pieces of the placenta in containers with a solution. A label should be attached to each container or tube containing information about the patient's name, date of birth, age, date of sample collection, date of hospitalization (if applicable), name of the physician who organized the collection of the sample, and medical record number.

After the samples are transported to the Afshar's Lab, the registration and processing of the biospecimens is carried out. All labels are removed from the test tubes / containers and pasted onto a A4 paper sheet/sheets. Next to the label, the following information should be

recorded: the participant's ID in the Repository, the date of the sample processing, the initials of the personnel performing processing, the final number of the biospecimens collected and stored.

The paper sheet with these labels and notes is considered to be the primary source document containing PHI.

To preserve the confidentiality of the participants, the primary source documents are kept by the PI in the separate closed cabinet in the Afshar's Lab, to which only authorized UCLA personnel has access.

The PHI of the participants will be collected in the Repository according to Table 3.

Table 3 – List of the PHI collected in the Repository

N	**PHI Elements**	**Intention to collect**	
1	First Name, Last Name, Middle Name		No
2	All geographical subdivisions smaller than a state, including street address, city, county, precinct, zip code		No
3	Dates directly related to the participant: birth date, admission date, discharge date, date of death (if applicable)	Yes	
4	Phone numbers		No
5	Fax numbers		No
6	E-mail		No
7	Social Security number		No
8	Medical record number	Yes	
9	Health plan beneficiary numbers		No
10	Account numbers		No
11	Certificate/license numbers		No
12	Vehicle identifiers and serial numbers, including license plate numbers		No
13	Device identifiers and serial numbers		No
14	Web Universal Resource Locators (URLs)		No
15	Internet Protocol (IP) address numbers		No

16	Biometric identifiers, including finger and voice prints		No
17	Full face photographic images and any comparable images		No
18	Other unique identifying numbers, characteristic, or code	Yes	No

At the site, 3 PHI elements will be maintained by the collector by collecting data: dates, MRN, and other unique identifying numbers, characteristic, or code. In adult participants, instead of the first and last name, the initials will be entered in the Repository. Dates directly related to the participant: birth date, admission date, discharge date, date of death (if applicable).

The participant's ID (e.g., the unique code assigned by the PI/ designee to code the data) and biospecimen processing dates are examples of the Research Health Information (RHI). RHI is outside the HIPAA jurisdiction, but is subject to the UCLA IRB and Office of Research Administration regulations. In the event, that another research Institution will be granted access to the Repository, information about participant's MRNs should be eliminated or encoded.

After the study is completed, personal identifiers and/ or codes linking the data and/ or specimens to the personal identifiers will be maintained for future research. Only the PI will have access to these identifiers and/ or codes after study completion.

Specific measures to assure de-identification/ coding of Material for future research collaboration include:

- Confidentiality agreement with each investigator, granted this investigator access to the research Material.
- Use of firewalls.
- Utilization of honest broker model – coding identifiable Material by independent third-party entity/ vendor.

Therefore, the Repository creation will be accompanied by the collection of the minimum amount of the PHI, using study identifiers, that contribute to the maximum protection of the privacy and confidentiality of the study participants.

4.1.5 Screening

The UCLA IRB approved ICF for this study should be signed and dated by each participant before any protocol-related procedures are performed. For the potential participants of this study, the outpatients/ inpatients clinical routine procedures may be administered before signing the ICF.

A copy of the signed ICF should be handed to the participant by the person who provided the consent process.

The patient's attending physician makes an appropriate entry in the medical records confirming the implementation of the informed consent process. The name and surname of the person who carried out the consent process, position, date of signing the form is recorded in the medical records. In addition, the date of signing the form is entered directly into the study register.

PI / co-PIs must assess each participant for risk that affects the collection of biospecimens. Any AEs considered by the PI to be related to the biospecimens collection procedures, should be documented in the patient's medical record and administered according to the GCP and this protocol. Information about AE should also be captured in the study register.

Additional research data of the results from the genomic analysis will be documented and utilized in the register as part of this protocol.

4.1.6 Screen Failures

Participants who sign and dated the ICF will be considered screen failures for this study under the following conditions:

- Participant fails to undergo blood /or placenta/ or umbilical cord/ or breast milk collection procedure.
- Participant is otherwise found by PI / designee to be ineligible to the study engagement.

4.1.7 Study Termination and Participants Withdrawal

This clinical study can be terminated at any time for any reason by the PI. The PI will be responsible for informing the UCLA IRB and the participants (if applicable) of the termination of the study.

Participant may voluntarily withdraw from this clinical protocol. Any future planned biospecimens collection after consent withdrawal will be discontinued, as will clinical assessment of the participant. The participant is not obliged to provide an explanation of the reasons for termination of participation in a clinical study. However, the PI should make appropriate efforts to clarify the primary reason for the participant's withdrawal from the study.

The PI / designee can use phone calls, messages, e-mail, the Internet, and other communication channels to make contact to the participant. The results of this communication should be documented in the study register. If the participant withdraws from the study, the PI will still collect the output of the data collected from these studies up to moment of the participant's withdrawal.

For participants, whose status is undetermined because they fail the study visits without expressing an intention to discontinue or withdraw the study participation, the PI and study personnel must show "due diligence". Reasonable steps taken to contact the participant should be documented in the research records like dates of phone calls, messages, e-mails, etc. A participants cannot be considered as lost to follow-up until the time point of participants planned end of study visit has passed.

Participant may be dropped from participating in the Repository at the discretion of the PI at any time. The PI / designee will document the reason for the discontinuation in the research documents. Date and reason for discontinuation should also be recorded on the Repository. If the participant withdraws the ICF, the Dr. Afshar's Lab will continue to maintain and use all research data that have already been collected per protocol. All biospecimens not yet analyzed at the time of withdrawal may still be used for further testing/analysis in accordance with the terms of this clinical study. If the participant withdraws

from the study, the PI will still collect the output of the data collected from these studies up to moment of the participant's withdrawal.

4.2 Biospecimens

Repository biospecimens collection (blood drawing, fetus tissue obtaining, etc.) will be performed by appropriately licensed / credentialed study personnel working within the scope of their licenses and credentials.

4.2.1 Procedures

Repository biospecimens collection (blood drawing, fetus tissue obtaining, etc.) will be performed by appropriately licensed/ credentialed study personnel working within the scope of their licenses and credentials. Biological specimens may include, but are not limited to, human tissue (e.g., placenta, umbilical cord, POC), blood, urine, breast milk, and cell samples.

Donors of the Repository biospecimens are the birthing people with perinatal pathology, their fetuses, and adult volunteers. Adult persons will donate blood, urine, breast milk. After the pregnancy is over, the following fetal biospecimens will be collected and processed: cord blood, placenta, umbilical cord, POC.

The Repository personnel will obtain and store according to the SOPs the following specimens:

- Blood: whole blood, plasma, serum;
- Placenta samples: RNAlater, snap freeze, 70% Alcohol, FFPE;
- Umbilical cord: snap freeze, FFPE;
- POC: 70% Alcohol and FFPE;
- Cell Lines: HUVEC, trophoblastic, and other;
- Protein, RNA, DNA;
- Breastmilk;
- Urine;
- Other biospecimens.

In the dataset, the following clinical data will be linked to the biospecimens:

- Clinical data – human with PHI;
- Clinical data – human with Limited Data Set;
- Clinical data – human, de-identified.

5 BANK ADMINISTRATION

5.1 Study Organization

The Perinatal Repository will be created and maintained by investigator, initiated this project – Dr. Yalda Afshar, and designee - the Dr. Afshar's Lab. personnel. Dr. Yalda Afshar, PI, as a chief of the UCLA Perinatal Biospecimen Repository Advisory Committee is ultimately responsible for the Repository. According to the Committee Policy, the PI has right to delegate some of the PI's authority to manage and ensure the proper operation of the Repository to other Committee / Dr. Afshar's Lab members.

5.1.1 Request of the Repository Biospecimens and/ or Data by the Investigators or other Entities

Dr. Yalda Afshar is investigator, initiated this clinical research project.

The original task of the Perinatal Repository creation is to provide Afshar's Lab resources for ongoing and future clinical and non-clinical research.

Access to the Repository Material may be granted to:

- the PIs from the UCLA;

- the PIs from other universities;

- the institutions/ entities engaged in research in the field of the health science and biotechnology.

The PI, external to the Afshar's Lab, may contact chief of the Repository for preliminary information. If the Perinatal Repository stores samples and data necessary for the research, the PI fills out and sends a written request to the Afshar's Lab according to the attached Request Form for the UCLA Perinatal Biospecimen Repository Advisory Committee.

The adequacy of requests to obtain data and/or biospecimens is reviewed by the Committee on the terms and conditions established by the UCLA Perinatal Biospecimen Repository Advisory Committee Policy.

In case of a positive decision of the Committee, the applicant-investigator receives a written response from the Afshar's Lab explaining the next steps. Research projects planning to use the Repository Material must be approved by the UCLA IRB.

Then the applicant-PI fills out and submit Request for the Receipt of Materials for Research Purposes. Negotiation and arrangement of the Material Transfer Agreement (MTA) or Data Use Agreement (DUA) is carried out by Dr. Afshar / designee and by direct support of the UCLA Technology Development group.

After signing and registering the MTA/ DUA, the PI is granted access to the particular biospecimens and / or biospecimens and data in accordance with the agreed provisions.

5.1.2 Distribution Rules

Distribution rules and criteria used to determine the adequacy of investigators' requests to acquire the Material from the Repository are set forth in the "UCLA Perinatal Biospecimen Repository Advisory Committee" Policy and "Request Form for the UCLA Perinatal Biospecimen Repository Advisory Committee".

5.1.3 The Structure of the Repository

Figure 1 represents the structure of the Perinatal Repository.

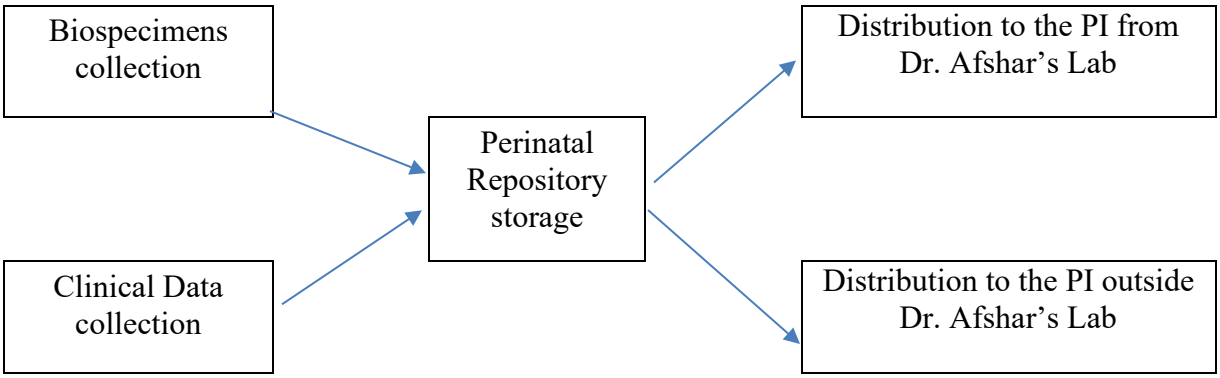

Figure 1. The Structure of the Perinatal Repository

5.1.4 The Person Responsible for Maintaining the Repository

Perinatal Repository will be created and maintained by investigator, initiated this clinical project – Dr. Yalda Afshar, and designee - the Afshar's Lab. personnel. Dr. Yalda Afshar, PI, as a chief of the UCLA Perinatal Biospecimen Repository Advisory Committee, is ultimately responsible for the Repository. According to the Committee Policy, the PI has right to delegate maintaining the Repository, stripping identifiers, coding and distribution biospecimens and dataset to the Repository Director and other Afshar's Lab personnel. The specific tasks of each project member will be indicated in writing in the Study Delegation Log. The PI considers the qualification, training, experience and licensing/ credentials of each individual team member when determining personnel eligibility to carry out the assigned task within the framework of this project.

5.1.5 Long-Term Storage of Biospecimens for Future Research

Collected biospecimens may be kept and used by the PI for up to 15 years after the study is completed. See also Study Termination and Participants Withdrawal section, for sample handling if a participant withdraws consent.

5.2 Data Collection and Management

To ensure human subject protection and reliability of the study results, the PI and the research team establish their approach to computer system validation on a risk assessment. The intended use of the research software and potential for the future use of the Repository Material are taken into consideration.

The Repository data collection and management will be conducted using Box (Box, Inc.), the cloud-based content management platform at UCLA. The Box platform and associated products are compliant with HIPAA, HITECH, and the final HIPAA Omnibus rule since November 2012. All PHI collected and stored in Box is secured in accordance with HIPAA, and Box signs Business Associate Agreements with all clients who plan to store PHI in the cloud. Box is a secure, metadata-driven electronic data processing system. This web-based research validated tool designed for data collection, scientific collaboration, and data analysis. Investigational team can develop new databases to collect clinical and biospecimen data. Box allows to audit data records and trace the users' activity. Created raw data and syntax files may be exported to common statistical packages: R-system, SPSS, Stata R, SAS.

5.2.1 Computer System

The Perinatal Repository based on Box platform conforms to the UCLA IRB's established requirements for computer data system validation: completeness, accuracy, reliability, and stable intended performance. The UCLA IRB and other regulatory authority may inspect computer software during a research site inspection.

The project-related Data Management System will be created and maintained for using Box application. Creation of the DMS is one of the primaries aims of the study.

5.2.2 Participants' Privacy

The PI will maintain participants' privacy providing all protocol-related activities and procedures in strong adherence to the requirements of the UCLA OHRPP Quick Guide "Protecting Privacy and Maintaining Confidentiality". The Afshar's Lab researchers, assigned by the protocol implementation, have / will have completed the CITI Program and UCLA IRB HIPAA trainings on the participants privacy topic.

To protect the Repository participant's privacy, the protocol plans to use the Acceptable Recruitment Methods. The potential study participants will be identified and contacted using:

- Dissemination of appropriate information about the study through advertisement, flyers, notices, Internet, and media.
- Disclosing the certain privacy protection provisions in the Informed Consent Form.
- Sending introduction letters to the PI's colleagues to notify the physicians and eligible patients interested in research participation.
- Contacting those patients that qualify to determine interest by primary care staff.
- Providing necessary information about the project to patients under direct medical care of the PI and co-investigators who are licensed clinical specialists, qualified by education, training and experience.

Participant's privacy is also protected by Appropriate Method of Material collection:

- Respecting sensitivity of the information being gathered.
- Interviewing each participant individually, in a room or area where conversations cannot be overheard by others in the research setting.
- Conducting study procedures in the manner, that give the participants possibility to feel comfortable.

5.2.3 Participants' Confidentiality

The PI will maintain data confidentiality conducting all study-related activities and procedures in strictly adherence to the requirements of the UCLA OHRPP Quick Guide "Protecting Privacy and Maintaining Confidentiality".

The Afshar's Lab personnel have / will have completed the CITI Program and UCLA IRB HIPAA trainings on the data confidentiality topic.

To protect the data confidentiality, the protocol contains special provisions, including, but not limited to:

- Maintaining of identifiable research Material.
- Addressing an extension of participants privacy issues.
- Statement of the PI agreement about confidentiality maintenance.
- Accessibility of the participants identifiable information by the study team.

Conducting the study per this protocol, the PI protects the participants' confidentiality from inappropriate disclosure of PHI.

With reference to the HIPAA the following measures will be implemented:

- Study design: Clinical Protocol is designed according to "minimum necessary" standard of the participants PHI.
- Collecting and maintaining of the identifiable Material: Clinical Protocol safeguards PHI and data security regarding the risk from disclosure.
- Provisions to maintain confidentiality of the Material: in Clinical Protocol and ICF, confidentiality of the PHI is offered; study will be performed in strict adherence to the applicable international, federal (including the HIPAA), state, and UCLA requirements; the risk of unauthorized disclosure of the PHI during the study is minimized.
- Limit access to the Repository: Repository Materials provided to authorized, non-UCLA institutions will not contain identifiable information about the research participants.
- ICF indicates study personnel who has access to the participants' personal health information and biospecimens.

In the Repository records, the research participants data will be coded.

Participants' privacy data and records generated during the study will be kept confidential in accordance with applicable federal, state and local low, the UCLA Office of Research Administration Research Policies and Procedures, the UCLA Human Research Protection Program, and the UCLA IRB Guidance and Procedures. The PI and study team will use the Protected Health Information, the Privately Identifiable Information, and the Research Health Information solely for the purpose of conducting approved clinical research. The use of participants' privacy data for purposes other than those listed above is prohibited.

To limit access to the identifiable Material, the study personnel are granted different level of data access. All team members have received CITI Program and UCLA IRB HIPAA training and certification. Only PI and designee (in writing, according to the Study Delegation Log) will have access to the participants identifiable information.

5.3 Material Collection and Management

Repository biospecimens collection (blood drawing, placenta obtaining, etc.) will be performed by appropriately licensed / credentialed study personnel working within the scope of their licenses and credentials.

Biological specimens may include, but are not limited to, human tissue (e.g., placenta, umbilical cord, POC), blood, urine, breast milk, and cell samples.

Donors of the Repository biospecimens are the birthing people with perinatal pathology, their fetuses, and adult volunteers.

Adult persons will donate blood, urine, breast milk.

After the pregnancy is over, the following fetal biospecimens will be collected and processed: cord blood, placenta, umbilical cord, amniotic fluid, and/ or POC.

The Repository personnel will obtain and store according to the SOPs the following specimens:

- Blood: whole blood, plasma, serum;
- Placenta samples: RNAlater, snap freeze, 70% Alcohol, FFPE;
- Umbilical cord: snap freeze, FFPE;
- POC: 70% Alcohol and FFPE;
- Cell Lines: HUVEC, trophoblastic, and other;
- Protein, RNA, DNA;
- Breastmilk;
- Urine;
- Other biospecimens.

In the dataset, the following clinical data will be linked to the biospecimens:

- Clinical data – human with PHI;

Clinical data – human with Limited Data Set;

Clinical data – human, de-identified.

5.3.1 Research Data Ownership and Transfer

The UCLA Health holds in demesne the primary research results generated from all research, development, and related activities conducted under this protocol. The UCLA Health owns clinical data recorded in both paper and electronic medical records.

Consistent with the academic tradition and its Intellectual Property regulations, the UCLA Health does not claim ownership of the Afshar's Lab copyrightable research works that will appear due to this clinical protocol implementation.

In the event the PI leaves the UCLA and wishes to take Repository to her/ his new institution, ownership of the Repository Research Data may be transferred to the new institution with the documented approval of the UCLA IRB and the UCLA Office of Research Administration and, if applicable, with the permission of the study sponsor. Like this would happen, the UCLA will execute a written MTA with the new PI's institution. The situation wherein the Repository data will eventually be used by both institutions.

According to the MTA, the new PI's institution should admit all legal and financial obligations for the Repository maintenance. The MTA should ensure the UCLA's access to the original Repository data if that should become essential. If the conclusion and observance of the MTA will be impossible due to any circumstances, the PI may take with her/ him a copy of the primary source documents, assuming no third-party limitations.

If co-investigator, another then the PI, leaves the UCLA, hi/ she may apply to the PI regarding primary source documents transcribing. If the PI considers it reasonable to give written permission to duplicate data, the co-investigator may to copy the primary Research Data obtained due to his/ her immediate professional actions in the Afshar's Lab within the framework of this protocol.

5.3.2 Missing Variables and Outliers

The study team will make all attempts to collect the necessary data per protocol. As missing information is expected to be minimal, no imputation will be performed for missing variables.

Any qualitative and quantitative values that appear to be erroneous or inexplicit based on the PI clinical judgment will be investigated as the potential outliers.

If variable is identified as outlier, statistic sensitivity analyses will be undertaken to examine the impact of including or excluding this data point to the data set. Any significant differences found from the sensitivity analyses will be reported in the final study report and publications.

5.3.3 Statistical Analysis Plan

Developing this research project, we have followed the UCLA OHRPP recommendations for research involving use and storage of data and/ or human biological specimens, and data and specimen repositories [https://ohrpp.research.ucla.edu/policies-and-guidance/].

UCLA OHRP Guidance "Data and Specimen Repositories (April 13, 2009)" does not provide instruction about developing the Statistical Analysis Plan (SAP) for repositories. There is also no statistics section in the template repository protocol (IMAGING / DATA BANK TEMPLATE) recommended by OHRPP.

Taking into account all aspects of the clinical protocol design and reporting specific for non-interventional methods of Material collection, we do not create the SAP for this study.

5.3.4 Providing Results to Participants

Research (non-validated) test results that are of uncertain clinical significance will not be reported back to the participants and their families. The PI also does not intend to routinely share the results of the research tests with the participant's primary care physician / pediatrician unless the latter is a delegated study team member.

If there is written consent / statement from the particular participant, the results of research tests may be included in the medical records if the PI deems it appropriate and reasonable to do so.

5.4 Regulatory and Ethical Considerations

5.4.1 Risks and Benefits

5.4.1.1 Potential Benefits of Participation

Potential direct benefits (physical, psychological, social, or other) to study participants:

There are no direct benefits to the study participants. But the person's decision to donate biospecimens to Repository will significantly contribute to solving problem of perinatal disorders. Also, the study participant can help another patient with pregnancy complications. The study results will benefit other birthing persons and their babies/ fetuses in the future by providing important information about the risk factors of perinatal disorders. Implementation the results of research study into clinical care may decrease the risk of pregnancy complications and therefore prevent non-favorable pregnancy outcomes.

Some study participants receive the indirect psychological and social benefits from being involved in research as documented in the literature.

Potential benefits to society:

Community gets new generalizable knowledge about regarding social significant diseases as perinatal pathology. The research society, the Dr. Afshar's Lab and collaborators, get access to the high quality biospecimens and reliable clinical data to facilitate clinical research in the field of the maternal and child health.

5.4.1.2 Potential Risks

Risk for birthing person:

There is minimal risk study for both pregnant and postpartum birthing person with perinatal pathology, and for health birthing person. Sociological, economic, and legal risk for participation in the Registry is no higher, than in general population.

There is minimal physical and psychological risk associated with venous blood drawing. Blood sampling by performing standard medical procedures may cause fainting or lightheadedness or some discomfort. Other risks include bleeding or bruising where the needle enters the body. A small blood clot may form where the needle enters the body or swelling of the surrounding skin may occur. There is also a small risk of a minor infection at the blood draw site. During pregnancy, the birthing person will be asked to donate blood samples from one to 4 times. After labor, it is planned to collect the specimens one or two times.

Birthing persons may be asked also to donate urine samples and, after labor, small amount (2-3 teaspoons) of breastmilk. Physical and psychological risk associated with these procedures is no higher, than in general population.

Risks associated with loss of privacy and confidentiality:

Participation in the study may involve a loss of privacy and confidentiality for the birthing person and the neonate/ fetus.

Risks Associated with Loss of Privacy in Genomic Research:

- Since some genetic variations can help to predict the future health problems of your child, this information might be of interest to health providers, life insurance companies, and others. Patterns of genetic variation also can be used by law enforcement agencies to identify a person or his/ her blood relatives. Therefore, your fetus/newborns genetic information could potentially be used in ways that could cause you or your family distress. There also may be other privacy risks that we have not foreseen.
- Genetic information that results from this study does not have medical or treatment importance at this time. However, there is a risk that information about taking part

in a genetic study may influence insurance companies and/ or employers regarding health-related decisions. To further safeguard participant's privacy, genetic information obtained in the research will not be placed in the participant's medical record.

- In the event of an unexpected breach of confidentiality, a federal law called the Genetic Information Non-Discrimination Act (GINA) will help protect the participant from health insurance or employment discrimination based on genetic information obtained about neonate/ fetus. In general, this law makes it illegal for health insurance companies, group health plans, and most employers to discriminate against the person based on the child's genetic information. However, it does not protect the neonate against discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

Therefore, special precocious designed to respect and protect participants' privacy and data confidentiality.

Risk for neonates/ fetus:

There is minimal physical and psychological risk associated with cord blood drawing. Blood sampling is often performed after birth as the standard medical procedure for fetal blood gas, pH, and hematocrit evaluation. Percutaneous fetal blood sampling is not planned in this study and will not be performed for the project purposes. The collection of a small amount of cord blood after birth poses no real risk to the neonate participating in the study. Cord blood collection from the clamped umbilical cord is safe for the infant and its mother, with no complications reported in the research publications.

The collection of fetus tissue (e.g., placenta, umbilical cord) poses after birth no risk to the neonate.

The potential risk of privacy and confidentiality breaches due to the inclusion of the neonates/fetuses in the study is outlined above.

Therefore, the Perinatal Repository represents the minimal risk study for neonates/ fetuses. Physical, psychological, sociological, economic, and legal risk for participation in the Registry is no higher, than in general population.

5.4.1.3 Risk/ Benefit Analysis

Study medical procedures (blood drawing, assessment, physical examinations, medical record, etc.) will be performed by appropriately licensed / credentialed study site personnel working within the scope of their licenses and credentials.

To alleviate the participant's physical and psychological discomfort, the study protocol provides for the collection of blood samples as a procedure combined with routine blood sampling for clinical laboratory testing. For research purposes, it is intended to collect additional amount of the venous blood – up to 20 mL per procedure.

If qualified study staff will have difficulty in obtaining the blood sample, the staff will attempt the blood draw no more than two times per one day, with the consent and approval of the patient.

Special precocious will be taken by the study personnel to prevent breach of the participants' privacy and confidentiality.

There is minimal risk study for the birthing persons and their neonates/ fetuses. Possible risks, associated with the study participation, are no higher, than in general

population. The risks to the participants are reasonable in relation to the importance of the knowledge that may be expected upon the study completion.

5.4.2 Standard of Care

Screening and enrollment of study participants will be organized on the labor and delivery units at both Ronald Reagan Medical Center and Santa Monica Hospital. High-professional physicians, nurses, midwives, and staff of the Department of Obstetrics and Gynecology represent the nationally and internationally recognized leaders in the delivery of women's medical care. The provision of patient care is carried out in accordance with the strict standards of medical care implementation at the David Geffen School of Medicine at UCLA.

Whatever the birthing person does consent / or does not consent the participation in the study, it will not change the person's labor management.

5.5 Recruitment Strategy

Recruitment will be maintained according to the UCLA policies, state's and Federal regulations. Participants' rights participate/ do not participate/ withdraw at any time will be explained by the PI or designee (physician) during informed consent process.

Participants' privacy will be maintained according to the UCLA policies, state's and Federal regulations. PI or designee (physician) will contact potential study participants during visits.

5.6 Informed Consent

Informed consent process should be performed by the PI/ designee in accordance with the UCLA OHRP Guidance "Obtaining and Documenting Informed Consent (March 2, 2021)". Consenting will be arranged in the private room in non-emergency or emergency setting of the UCLA Health. Signed and dated ICF will be obtained from the research participant. Prospective study participants will be provided with sufficient opportunity to consider whether or not to participate in the study:

- The PI/ designee meets the prospective participants/ families to review the ICF and provide an oral explanation of the study. Individuals will be given a chance to ask questions before making a considered decision about taking a part in the study.
- Prospective study participants/ families will have the opportunity to take the ICF home and discuss the documents with others prior to making decision.
- The persons will be given unlimited time until childbirth to decide whether they wish to participate in the study.

Investigator or study team member will evaluate person's comprehension of the information conveyed during the consent process. The PI/ designee provides initial assessment of patient's capacity to consent trough routine interactions with the potential study participant.

The PI should ensure that the patient understands the following information:

- Writing the ICF means enrollment the persons as the research participant to the study "The UCLA Perinatal Biospecimen Repository".
- Participation in research is completely voluntarily. The birthing person may agree to participate in the study or disagree to participate without any negative consequences. The research participant has the right at any time to refuse to participate in the project without explanation and withdraw the consent.

- Participation in the Protocol means donation of patient's biospecimens and clinical data to the study team.
- Protocol-specific procedures will take place according to the Schedule of events.

The Perinatal Repository in non-interventional minimal risk study without direct benefits to the birthing persons and their neonates/ fetuses.

- Research participants receive copy of the signed ICF with contacts of the Afshar's Lab and UCLA OHRP. If the participants have questions about the study or experiences problems or changes their opinion regarding participation, they can reach out to the investigator or UCLA Research Administration using that information.

By signing and dating the ICF, the PI/ designee confirms that the birthing person has the decision-making capacity and expresses the choice to participate in this study.

In case of doubts about the correctness of the information received by the individual about participation in the project, the use of the Decision-Making Capacity Assessment Tool (UCLA OHRP Form: Decision-Making Capacity Assessment Tool (August 22, 2012)) is provided. Signed and dated permission, as part of the ICF, will be obtained from the birthing person to enroll the neonate/ fetus in the study under the informed consent procedure.

5.6.1 Vulnerable Population

The study will include vulnerable populations as research participants. Adult research participants (birthing persons) may be the persons with Limited English Proficiency (LEP), illiterate persons, unable to read and write, or visually impaired, or deaf persons.

Enrollment of the research participants will be provided at the Los Angeles County Area - one of the most culturally and ethnically diverse cities in the US. The likelihood of encountering eligible participants with limited English proficiency is high. With respect to the cultural and ethnic diversity of Los Angeles population, recruitment of the LEP and / or illiterate birthing persons will be arranged according to the UCLA OHRP Guidance "Research Involving Non-English Speaking Research Participants (May 9, 2019)".

In case of LEP, the informed consent process will be conducted using the services of the qualified interpreters using one of the two available consent methods: Preferred Method or Short-Form Method.

For Spanish research subjects, the ***Preferred Method*** of enrollment of the non-English speaking research participants will be used. After IRB approval of the ICF English version, this form will be translated by qualified translator into the Spanish language, send to the IRB as an amendment for reviewing and subsequent approval. The IRB approval of the Spanish ICF version should be obtained by the research team before enrollment of the Spanish birthing persons with LEP. Potential study participants will be given the opportunity to review the ICFs in Spanish. Additionally, the PI, or the member of the research team, or qualified interpreter, who speaks Spanish and English, will be available during the study to answer questions and conduct the project. If Spanish speaking patient decides to participate in the research, the patient prints, signs, and dates the ICF. Then person conducting consent process, also prints, signs, dates ICF, and provides the copy of the ICF to the birthing person.

For the occasional and unexpected enrollment of the ***non-Spanish research subjects*** with LEP, the ***Short Form Method*** may be implemented during enrollment. The UCLA

OHRP documents: "Checklist for Using the "Short Form" Method of Consent for Non-English Speaking Research Participants (February 20, 2020)" and "Research Participant Bill of Rights/ Experimental Subjects Bill of Rights (July 12, 2021)" (Bill of Rights) will be used to assure all UCLA IRB requirements are met.

The Short Form Method is appropriate for enrollment the participants under certain circumstances:

- The patient wants to be study participant and is otherwise eligible, but did not speak English or Spanish;
- the PI has not sufficient time to translate the ICF and obtain the IRB approval before planned date of the participant's enrollment;
- the research project is the minimal risk study;
- the study has a short window to enroll the birthing person.

The Short Form informed consent procedure will be as follows:

- The study personnel upload from the UCLA OHRP website the Bill of Rights on the birthing person's native language, or language, that the patient is fluent in.
- If the UCLA OHRP website does not contain the Bill of Rights on the necessary language, and the PI would like to enroll the patient, the study personnel arrange the professional/ certified translation of the Bill of Rights into the patient's language.
- The statement "The elements of consent from the consent form were presented orally" is added to the translated Bill of Rights.
- Lines for the participant's printed first and last names, signature, and date are added to the Bill of Rights.
- Lines for the PI/ designee's printed first and last names, title, signature, and date are added to the Bill of Rights.
- Lines for the Interpreter/ Witness's printed first, and last names, signature, and date are added to the Bill of Rights.
- The PI secures the qualified interpreter who speaks both English and the birthing's person language to obtain, document and sign the consent documents.
- The PI/ designee explains the research to the birthing person, using Patient-Centered approach, answers questions, and assess participant's comprehension of the study.
- Study participant prints first name and last name on the translated Bill of Rights, signs, and dates the document.
- Study participant prints first name and last name on the English version of the ICF, signs, and dates the document.
- After consenting, the PI gives the copy of the signed Bill of Rights and English version of the ICF to the birthing person.
- The researcher documents all details of the informed consent process in the research document.
- Within 30 days after consenting, the study personnel arrange translation of the ICF from the English to the participants own language, that is the language used during Short Form Method.
- The PI/ designee submits the Post Approval Incident Report to the UCLA IRB, notifying them of about implementation of the Short Form Method for enrollment the birthing person into the Perinatal Repository Protocol. The amendment should be submitted to the IRB

along with the translated ICF and copy of the Bill of Rights. The PI provides the IRB with the description of the plan, including timing, to provide the full translated ICF to the study participant.

- After obtaining the IRB approval of the translated ICF, the PI provide the birthing person with the translated ICF in person during visit or by mail/ email. All details are recorded by study personnel in the research records.
- At the time of the Continuing Review, the PI summarizes any and all uses of the Short Form Method.
- During the participant's visits, the PI, or the member of the research team, or qualified interpreter, who speaks the target subject population will be available to answer questions and conduct the project.

A special approach will also be applied to ***visually impaired persons*** and ***illiterate*** persons who understand English. The ICF will be read aloud, explained, and checked by the PI / designee for comprehension.

For consenting ***deaf participant***, the PI will use deaf service available through the UCLA Health System Interpreter/ Translation and Deaf Services program.

By answering and asking questions, the PI/ designee determines whether the potential participant comprehends the consent information to ensure the informed consent is valid. An impartial third-party witness will confirm the informed consent process has taken place. Both the PI and the witness will sign and date the ICF. The copy of the ICF will be provided to the research participant.

5.6.2 Additional Protection for Pregnant Birthing Person and Neonate/ Fetus

According to 45 CFR 46: Protection of Human Subjects under United States Law (1974), the additional protections for pregnant birthing persons, neonates, and fetuses are provided in the Protocol. Additional protection of Repository participants will be arranged according to the UCLA OHRP Guidance: "Special Populations – Pregnant Women, Fetuses, Neonates or In Vitro Fertilization" and "Chart for Regulatory Requirements for Pregnant Women, Fetuses and Neonates".

The Repository does not imply direct benefits to the birthing person, both the birthing person and the fetus/ neonate. Risk for the study participant is minimal.

The research participants will be recruited during perinatal visits. The birthing persons may also be recruited and consented while they are in early labor (infrequent contractions (less than 3 per minute) and cervix < 4 cm.

The study will not recruit and seek to consent research participant under the following conditions:

- birthing person is in active labor: contractions every 3-4 minutes, cervix > 4 cm;
- birthing person is distracted, exhausted, and in a degree of pain or discomfort that could preclude valid consent;
- patient is sedated.

Results of the Protocol implementation make the substantial scientific contribution to the prevention of the non-favorable clinical outcome for high-risk pregnancy. Creation of the Perinatal Repository address an important clinical issue. It is necessary postulate that the

birthing person will not be provided inducements like money to terminate the pregnancy. The PI and co-PIs do not have part in determining the viability of the fetus. Postpartum, no research tests of infants for research purposes will be performed. Repository Material records clinical data on the newborns condition. The research will not terminate the functioning of the heart and respiration of the nonviable neonate. After delivery, the viable neonates ate protected by the protections allotted to normal study participants and the additional protections of children.

Therefore, there is no added risk to the fetus/ neonate and the birthing person. . Intention to collect perinatal data is aiding the efficiency and effectiveness of de-identified biorepository for pregnancy at risk outcome research. The results of the study are important and cannot be obtained through other means.

5.7 Payment to Participant/ Families

There is no financial incentive foreseen in this study. No payment will be provided to the participants/ families.

5.8 Confidentiality

All study Materials, data and records generated per this protocol will be kept confidential in accordance with UCLA Health policies and guidance. Special HIPAA compliance activities for this study are outlined above. The PI and the study personnel will not use biospecimens and linked clinical data for any purpose other than conducting the study per protocol.

The safeguards to maintain participant's privacy and confidentiality are described above. To ensure compliance with the HIPAA requirements, separate measures have been developed in case the PI moves to another university, as well as in case of the future dissemination of the scientific institutions and organizations. The additional safeguard measures are set forth under Data Collection and Management section.

5.9 Ethical Considerations

Under implementation of this Protocol, the researchers plan to conduct study specifically involving following populations/ specimens:

1. Pregnant birthing persons/ fetuses.
2. Adults who are competent to give written informed consent.
3. Participants unable to read, speak, and/ or understand English.
4. Fetal tissue.
5. Neonates (clinical data only).

Inclusion of the vulnerable patient populations is necessary to achieve the purpose the study and implement the objectives of the research project. Additional safeguards are developed to protect this population from coercion, undue influence, and exploitation. The PI/ designee will provide assessment of capacity to consent for the birthing person as the primary additional safeguard measure. If upon assessment the potential participant will be found as person unable to give informed consent, or person with diminished capacity to consent, the PI/ designee will not seek surrogate consent for their participation in the Perinatal Repository Protocol.

6 SAFETY MANAGEMENT

The Perinatal Repository is a minimal risk study.

6.1 Clinical Adverse Events

Unanticipated problems involving risks to subjects and others will be monitored throughout the study according to the UCLA OHRP Guidance "Decision Tree: Adverse Events (February 20, 2021)".

6.2 Adverse Event Reporting

Since the study procedures are not greater than minimal risk, SAEs are not expected. If any unanticipated problems related to the research involving risks to subjects or others happen during the course of this study these will be reported to the IRB in accordance with UCLA IRB Guidance and Procedure: Post-Approval Reporting Requirements (PAR) for Investigators: Reporting of Unanticipated Problems, Including Adverse Events as well as Protocol Violations, Deviations and Incidents and the Reporting of Updated Study Safety Information.

7 PUBLICATION POLICY

The PI reserves the right to make public presentation of the scientific data in any way related to this clinical study. Study participants' identifiers will not be used in public presentation.

Acquaintance of the scientific community with research data can be carried out in the form of research publications, articles, reviews, abstracts at research congresses, oral / video presentations, reports, press releases, publication of information about the research on the Internet and in other ways, opted by a discrete PI decision.

Public presentation of the research material may be implemented during the preparation of this clinical study, throughout the conducting of the study, and upon completion of the study for an unlimited period of time.

The PI should assure that the actual information relating to the study will be publicly available on the Internet at the website www.clinicaltrials.gov.

The inclusion of illustrative cases in the presentation of study is not intended. If, in the future, during the implementation of the research project, special circumstances arise that may result in disclosure of identifiable information, or may create opportunities for such disclosure, the PI will promptly notify the IRB in writing. Study presentation approval should not be withheld unreasonably.

In case of a difference of opinion regarding the data reported and publication, the PI will contact the UCLA Office of Research Administration for a prompt review and a decision that satisfies all concerned parties.

Any scientific work designed and generated in connection with this protocol will be the intellectual property of the PI / Afshar's Lab as author and owner of copyright for such document.

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