

## BASIC STUDY INFORMATION

### 1.1 Indicate the appropriate IRB. NOTE:

- If you are unsure which IRB to select, please refer to the guidance or contact an IRB office for assistance.
- For studies that may qualify for review by the commercial (e.g., Western) IRB or NCI Central IRB, select the Health Sciences IRB below.

\*

Education and Social/Behavioral Science IRB

**Health Sciences IRB**

Minimal Risk IRB (Health Sciences)

### 1.2 Provide a short, lay-terms study title.

\* Metabolic Gene Profile on Aneuploidy Relevant to Fetal Growth Abnormalities

### 1.3 Provide the full, formal study title. NOTE: This is the title that will appear in correspondence.

\* Metabolic Gene Profile on Aneuploidy Relevant to Fetal Growth Abnormalities

### 1.4 Is this study being transferred from another institution?

\*  Yes  No

### 1.5 Identify the Principal Investigator.

\* JESUS IRURETAGOYENA

### 1.6 Identify the points of contact for this study (limit of four).

#### NOTE:

- Points of contact can edit the application and will receive email notifications about this submission. For the HS and MR IRBs only, points of contact can also submit materials on behalf of the PI.
- If the PI is serving as a study point of contact, indicate that here.

\*

[Redacted]

## PI STATUS

Principal Investigator: JESUS IRURETAGOYENA

### 2.1 Select which of the following criteria describe(s) how the person identified as the PI meets UW-Madison requirements to serve as PI:

\*

PI has a UW-Madison CHS appointment

2.1.1 If the PI does not meet any of the above criteria and an exception to allow the individual to serve as PI is being requested, indicate below why an exception is being sought and the person's qualifications to serve as PI. NOTE: Campus policy does not allow student researchers to serve as PI.

2.1.2 If required, upload "Request for Approval to Serve as Principal Investigator on a Human Subjects Protocol."

File

There are no items to display

### STUDY TEAM

NOTE: All members of the study team (key personnel) must be listed on this page. Study team members can be listed as having either edit/email access or read-only access, but all study team members (apart from the PI and POC) must be listed in one category or the other.

If the study team includes anyone (including students) who is not affiliated with (e.g., employed by, holds an appointment at) the UW-Madison, UWHC, or Madison VA (Wm S. Middleton VA Hospital) AND for whom you are requesting that UW-Madison serve as IRB of record, these individuals must be listed in either 3.1 or 3.2. If the study team includes anyone who is not affiliated with the UW-Madison, UWHC, or Madison VA (Wm. S. Middleton VA Hospital) for whom you are NOT requesting that UW-Madison serve as IRB of record, DO NOT list these individuals in either 3.1 or 3.2. The study protocol must include all external collaborators and their roles in this study.

**3.1 Identify study team members with edit/email access.** NOTE: Study team members listed here will be able to edit the application and receive email notifications regarding this study. Only the PI and Point of Contact can formally submit materials to the IRB.

JESUS IRURETAGOYENA

[REDACTED]

**3.2 Identify study team members with read-only access.** NOTE: Study team members listed here will be able to read the application but will not be able to edit the application or receive email notifications.

[REDACTED]

CYNTHIA BIRD

THADDEUS GOLOS

### STUDY TEAM: ROLES

NOTE: Depending on the nature of the study or project, it is possible that some or all study team members will not fit into the categories below. If this is the case, select Not Applicable.

**4.1 Identify the study team members who will be involved in identification and recruitment of subjects for this study, if applicable.**

Person

JESUS IRURETAGOYENA

[REDACTED]

Not applicable

**4.2 Identify the study team members who will be responsible for obtaining informed consent, if applicable.**

Person

JESUS IRURETAGOYENA

Not applicable

**4.3 Identify the study team members who will be intervening or interacting with subjects (e.g., administering surveys, conducting physical interventions), if applicable.**

Person

There are no items to display

Not applicable

**4.4 Identify the primary point of contact for this study. NOTE: If the PI is serving as the primary point of contact, indicate that here.**

\* [REDACTED]

**LEGACY DATA ANALYSIS**

**1.1 Is this study open ONLY for data analysis and NO changes of protocol other than those to key personnel or funding sources are likely to be submitted to the IRB in future?**

**IMPORTANT NOTES**

- Data analysis means that ALL study activities are complete for this study except for the analysis of data collected for the study.
- Answer yes to this question ONLY if the study is PERMANENTLY in data analysis.
- If you answer yes to this question, the ONLY changes of protocol that will be allowed will be to key personnel and funding sources. Should any other changes need to be made, the study team will need to submit a new application.
- Do NOT answer yes to this question if you think it is possible that a change of protocol will be submitted in future (e.g., to collect additional data, recontact study subjects).
- If this does NOT apply to this study (e.g., if this is an umbrella protocol), select no.

\*  Yes  No

**PROJECT SPONSORSHIP AND BILLING INFORMATION**

**6.1 Does this submission primarily represent a trainee project?**

\*  Yes  No

**6.1.1 If yes, identify the student(s)/trainee(s).**

Student/Trainee	Category	Course
JESUS	Fellow	Endocrinology Reproductive Physiology Program
<a href="#">View</a> IRURETAGOYENA		

**6.2 Is this an investigator-initiated project?**

NOTE: The UW-Madison Health Sciences IRBs define investigator-initiated research as research that is originated and designed by individuals, independently of any sponsor or funding agency. Such research is not conducted under the auspices of a formal sponsor, such as a pharmaceutical company, and the protocol is not developed or generated by a funding agency (e.g., National Cancer Institute, Cystic Fibrosis Foundation).

To be considered investigator-initiated research, the following must apply:

- The project receives no or very limited industry funding or support (e.g., support is limited to the provision of the drug or device)
- If an IND or IDE exists, it is held by an individual investigator and not a study sponsor

\*  Yes  No

**FUNDING: GENERAL**

**7.1 Identify the organization through which the PI will conduct the study.** NOTE: If you are requesting the UW-Madison defer to another IRB, select the organization with which the PI is affiliated.

\*

- 
- Madison VA (Wm. S. Middleton VA Hospital)
- 
- University of Wisconsin Hospital and Clinics (UWHC)
- 
- University of Wisconsin-Madison**

**7.1.1 If the University of Wisconsin-Madison, identify the specific department or organization unit under which the research study will be conducted:**

OBSTETRICS & GYNECOLOGY-GEN (A532800)

**7.2 Are you or do you plan on receiving funding to support this project (includes internal UW-Madison/UWHC/UWMF funds)?**

\*  Yes  No

**7.2.1 If the answer to 7.2 is Yes, will any of the funding be administered by the University of Wisconsin-Madison AND be at least one of the following types of accounts: 133 (not federally sponsored), 144 (federally sponsored), 233 (gift account), or 135 (WARF gift account).** NOTE: For a 136 revenue account, please answer No to this question.

Yes  No

**7.2.2 If the answer to 7.2 is Yes, will any of the funding be administered by the Madison VA (Wm. S. Middleton VA Hospital) or the UWHC?**

Yes  No

**FUNDED STUDIES**

**8.1 Identify all sources of funding for this study or project:**

\*

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Other

**8.1.1 If other, specify.**

Department of Ob/Gyn R&D funding

**8.1.2 If 8.1 is fee-for-service, provide information about the funding sources.**

Sponsor    UDDS    UW fund/account number    Accounting Point of Contact  
There are no items to display

**FUNDING INFORMATION FOR STUDY CONDUCTED UNDER UW-MADISON**

**10.1 Provide information about each funding source administered by the UW-Madison that will support the activities of the study.**

\*

Funding Source Information

Funding Source Type	Lite Project
Fund	233
MSN Number	No Value Entered
Project ID	233JX90
PI Name	Director,
Start Date	Mon Jan 1 00:00:00 CST 2007
End Date	Fri Dec 31 00:00:00 CST 9999
Sponsor	UWF - SMPH RESEARCH AND DEVELOPMENT
View Primary Sponsor	No Value Entered
Title	R & D PROGRAM SUPPORT FOR FELLOWSHIP
Status	Active
Federal	No
Pending	No
FA Rate	No Value Entered
Department ID	532860
Agency Reference Number	5/3/11
Budget	15000
Grant Application	

**10.2 Provide a back up account/project number (e.g., departmental funds, multidonor account, start up funds). NOTE: Check Not Applicable if you are not conducting this research under a School of Medicine and Public Health (SMPH) appointment.**

233-JX90

Not Applicable

**10.3 Identify the accounting point of contact for this submission.** NOTE: The accounting point of contact is the person who can be contacted for questions about accounting information related to this submission.

\* [REDACTED]

**CONFLICT OF INTEREST (COI)**

**13.1 Do ANY of the study team involved in the design or conduct of the research study, or their immediate family (spouse or dependent children), have a financial interest in an entity that (a) sponsors the study or (b) owns or licenses technology tested or evaluated in the study (including any agent, device, or software) that meets or exceeds one of the thresholds below:**

**(a) Compensation of \$20,000 or more in a calendar year from a publicly traded or**

**privately held business entity;**

**(b) An ownership interest in a publicly traded business entity valued at \$20,000 or more or a 5% or greater equity interest;**

**(c) Any ownership interest in a privately held business entity whatever the value;**

**(d) A combination of compensation and ownership interest in a publicly traded business entity valued at \$20,000 or more;**

**(e) A leadership position in a business entity (Leadership positions are positions with fiduciary responsibility, including senior managers (e.g., presidents, vice presidents, etc.) and members of boards of directors). Scientific advisory board membership is not a leadership position.**

\*  Yes  No

**13.1.1 If yes, identify the personnel who have this interest.**

Person

There are no items to display

**13.1.2 Upload the COI management plan(s).**

File

There are no items to display

**13.2 Do ANY of the study team involved in the design or conduct of the research study, or their immediate family (spouse or dependent children), have a proprietary interest in the research, such as royalties, patents, trademarks, copyright, or licensing agreement, that is relevant to this research study (including any agent, device, or software being evaluated as part of the research study)? NOTE: If this proprietary interest is managed through WARF, select Not Applicable.**

Yes  No

Not Applicable

**13.2.1 If yes, identify the personnel who have this interest.**

Person

There are no items to display

**13.2.2 Upload the COI management plan(s).**

File

There are no items to display

**13.3 Do ANY of the study team involved in the design or conduct of the research study have a financial interest that requires disclosure to the sponsor or funding source?**

\*  Yes  No

**13.3.1 If yes, identify the personnel who have this interest.**

Person

There are no items to display

**CONFLICT OF INTEREST (COI): CONTINUED**

**14.1 In addition to the sponsor(s) of this study or project, are other companies or business entities involved or potentially affected in a significant way by this study or project?**

\*  Yes  No

**14.1.1 If yes, list those companies/business entities.**

**14.1.2 If yes, describe the nature of each company/business entity's involvement.**

**14.2 Do ANY of the study team involved in the design or conduct of the study or project have any other financial interest that the investigator believes may interfere with his or her ability to protect subjects?**

\*  Yes  No

**14.2.1 If yes, identify the personnel who have this interest.**

Person

There are no items to display

**14.3 Do any of the study team receive any incentives for recruiting human subjects or any other purpose directly related to the study or project?**

\*  Yes  No

**14.3.1 If yes, describe the nature of the incentive.**

## **DETERMINATION OF VA STATUS**

**15.1 Indicate if any of the following apply to this study or project:**

\*

None of the above

## **SCIENTIFIC REVIEW: UW CARBONE CANCER CENTER (UWCCC) PROTOCOL REVIEW MONITORING COMMITTEE (PRMC) AND CLINICAL AND TRANSLATIONAL RESEARCH CORE (CTRC)**

**17.1 Is the scientific question of the protocol cancer related?**

\*  Yes  No

**17.2 Are you specifically targeting cancer patients for enrollment in this study?**

\*  Yes  No

**17.3 Does this study involve the review and/or use of biological specimens/data /images/records from cancer patients?**

\*  Yes  No

**17.4 Will this study use the Clinical and Translational Research Core (CTRC)?**

NOTE: If the answer to this question is Yes, you must upload a copy of the CTRC application to the Submit activity form. You will see the Submit activity form when you click on the Submit link to submit the completed IRB application.

\*  Yes  No

## SCIENTIFIC REVIEW: OTHER

### 18.1 Does this study require scientific review by ICTR Scientific Review Committees?

NOTE: If none of the options in 18.1.1 apply, scientific review is required.

\*  Yes  No

#### 18.1.1 If no, select why scientific review is not required.

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Not applicable, as this is a legacy application

## ICTR SUPPORT SERVICES

### 19.1 Select all of the research support services available through the Institute for Clinical and Translational Research (ICTR) that you consulted while preparing this study or project for submission. If none of these services were used, select Not Applicable.

\*

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Not Applicable

#### 19.1.1 If other, specify.

### 19.2 Is this study coordinated by the Office of Clinical Trials?

\*  Yes  No

## CLINICALTRIALS.GOV REGISTRATION

NOTE: Registration at Clinicaltrials.gov may be required in the following situations:

- Per FDA regulations, most studies involving the testing of a drug, biologic, or device must be registered.
- If publications resulting from this study will be published in a member journal of the International Committee of Medical Journal Editors (ICMJE) or in a publication that adheres to the standards of the ICMJE, the study must be registered.

Click on the help link above for additional information on these requirements.

### 20.1 Does this study need to be registered at Clinicaltrials.gov?

\*  Yes  No

#### 20.1.1 If yes, who has or will register the study prior to the enrollment of the first subject?

##### 20.1.1.1 If other, specify.

## TYPE OF APPLICATION

### 1.1 Indicate the type of application:

\* Initial review application: Full review



**STUDY LOCATION: GENERAL**

**1.1 Is this a multi-site study?** NOTE: A multi-site study involves at least one site or individual NOT affiliated with the UW-Madison/UW Health/Madison VA (Wm. S. Middleton VA Hospital). Select Yes if this study:

- Will be conducted at sites outside the UW
- Includes study team members NOT affiliated with the UW
- Involves sending or receiving samples/data/images to/from collaborators outside the UW

\*  Yes  No

**1.1.1 If yes, does the study have a coordinating center?** NOTE: A lead site or coordinating center is typically responsible for coordinating activities at all other sites, receiving and analyzing data, and developing and updating the study protocol as needed.

Yes  No

**1.1.1.1 If yes to question 1.1.1, is the UW-Madison/Madison VA (Wm. S. Middleton VA Hospital) serving as the coordinating center?**

Yes  No

**1.1.1.2 If no to question 1.1.1, how is it being ensured that all sites have IRB approval prior to initiating study activities?**

**1.2 Will UW-Madison, Madison VA (Wm. S. Middleton VA Hospital), or UWHC personnel or personnel under UW-Madison IRB purview conduct research activities at sites outside of the US?**

\*  Yes  No

**1.2.1 If yes, specify.**

There are no items to display

**STUDY LOCATION(S): UW-MADISON SITES**

**3.1 Select the UW-Madison/UW Health/Madison VA (Wm. S. Middleton VA Hospital) location(s) at which this study will occur. Check all that apply:**

Other UW-Madison/UW Health location (s) \_\_\_\_\_

**3.1.1 If other, specify.**

Planned Parenthood

**STUDY SUMMARY**

**1.1 Upload the stand-alone scientific protocol associated with this application.**

NOTE: A protocol is required for the types of studies listed below. This list is NOT exhaustive and the IRB may request a protocol in other cases as appropriate.

- All multi-site studies (regardless of risk level)
- All studies requiring scientific review
- All studies involving drugs or devices
- All studies posing more than minimal risk to subjects

File

There are no items to display

**1.1.1 If no protocol was uploaded, select the reason(s) below.**

Other

**1.1.1.1 If other, provide a justification.**

this study involves use of tissue originally obtained for non-research purposes.

**1.2 Will study activities involve interaction and/or communication with human subjects, even if only to obtain informed consent?**

\*  Yes  No

**1.3 Provide the expected duration of the study (i.e., the time from IRB approval to completion of all study activities).**

\* 1 - 3 years

**SPECIAL CONSIDERATIONS AND PROCEDURES****2.1 If your study involves any of the following special procedures or considerations, additional information may be needed. Select all that apply. If none apply, check Not Applicable.**

\*

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Collection and/or use of biological specimens for research purposes, which includes, but is not limited to, HIV or other infectious disease testing/illegal drug use. It does NOT include routine safety labs

**RESEARCH DESIGN AND PROCEDURES****1.1 What is the overall purpose of this project or study?**

\* Fetuses with abnormal number of chromosomes (aneuploidy) have abnormal growth; specifically they experience fetal growth restriction. Somatic growth is the final product of fetal metabolism. If the genes coding for the processing of nutrients like glucose, and fatty acid are abnormal then this could explain the growth abnormally. Many investigators have attempted to discover the gene profiling of aneuploidy fetuses. One example study is Chug et al., who analyzed different gene expressions in amniotic fluid cells of fetuses with Down syndrome using DNA microarray (1) for 102 genes involving brain function, muscle, apoptosis and housekeeping. They found 2 genes that were down regulated in Down syndrome fetuses compared to normal fetuses. This was one of the research efforts to try to develop the gene profile of Down syndrome. Many other investigations have pursued this type of work (2, 3,4, and 5) with the sole purpose of establishing the gene profile of trisomy 21, which then could explain the phenotype, i.e. findings associated with this condition. Presently there is no literature on gene profiling for metabolic pathways in aneuploidy fetuses.

**1.2 What are the specific aims of this project or study?**

\* Expression of the genes in fetuses with normal chromosomes will be compared to gene expression in fetuses terminated for known abnormal chromosomes obtained from amniocentesis or chorionic villus sampling. The study group with the abnormal chromosomes is previously identified since that will be the reason for termination. In these cases, the patient's primary care physician has referred the patient to Planned Parenthood for termination due to the abnormality. The PCP would typically call Planned Parenthood to discuss this information with Planned Parenthood Physicians prior to the patient coming in for an appointment. The reason for termination is then recorded in the Planned Parenthood record.

These two groups can be compared an specific genes can be identified as playing a role on the

causation of the growth restriction. This will allow further characterization of these genes with a better knowledge of how abnormal number of chromosomes (aneuploidy) is associated with growth restriction. The only information recorded will be gestational age, but there will be two groups, the control and the study one. The separate them, the study group(termination due to chromosomal abnormality) will still have a random identification number on the sample collection tube exactly as the control one, but the data sheet will include the chromosomal abnormality diagnosed by previous prenatal testing. The study nurse will know if a participant is part of the study group and she will record that in the confidential data sheet.

### 1.3 Background: What prior information or knowledge exists to support the conduct of this project or study?

\* There is limited information available on the underlying pathophysiology of growth restriction in fetus affected by aneuploidy (abnormal number of chromosomes). Many of these fetuses survive but continue to suffer morbidities from growth restriction. No therapeutic intervention exists at present to improve the fetal development in these cases. There is a potential for intervention to improve growth if we develop a better understanding of underlying mechanism. Many investigators have attempted to discover the gene profiling on aneuploidy fetuses. One example study is Chung et al., who analyzed different gene expressions in amniotic fluid cells of Down syndrome using DNA microarray (1) for 102 genes involving brain function, muscle, apoptosis and housekeeping. They found 2 genes that were down regulated in Down syndrome fetuses compared to normal fetuses. This was one of the first researches to try to develop the gene profile of Down syndrome. Many other investigations have pursued this type of work (2, 3, 4, and 5) with the sole purpose of establishing the gene profile of trisomy 21, which then could explain the phenotype, i.e. findings associated with this condition. Presently there is no literature on gene profile for metabolic pathways in aneuploidy fetuses.

### 1.4 Briefly describe the procedures and interventions that will be performed for this project or study and all study arms involved.

\* No procedures will be done for the purpose of this study. The tissue collected on the termination of pregnancy would otherwise be discarded. The order of events would be: 1. Patient presents to Planned Parenthood for termination of pregnancy. 2. Planned Parenthood nurse interviews the patient and consents her for the termination of pregnancy in 24 hours. 3. The day of the procedure, study nurse consents the patient for utilization of the fetal tissue and placental tissue obtained. This is set up in this way so that the study does not interfere at all with the standard process. The patient will be reassured that no changes will occur in the regular termination procedure regardless of her decision. 4. If the patient agrees to it, the fetal and placental tissue is collected through suction and deposited in a glass jar connected to the suction device,, as per Planned Parenthood protocol by [REDACTED] (physician performing the procedure). The only information that will be collected is the gestational age. 5. The tissue then is brought to [REDACTED] where RNA is extracted and microarray chips are arranged. 6. A computer program will analyze the intensity of the signal from the microarray and would allow for determination of which genes are upregulated or downregulated in each sample. 7. Statistical analysis will be preformed to find significant differences.

### 1.5 Will subjects be randomized?

\*  Yes  No

## RESEARCH DESIGN AND PROCEDURES: CONTINUED

NOTE: Depending on the nature of your study or project, these questions may not apply. If this is the case, select Not Applicable.

### 2.1 Describe the current alternatives to participation in this research study, including treatments subjects could undergo outside of the research study. If there is no

**accepted treatment or no effective treatment, state this.**

Not Applicable

**2.2 Describe how this patient population is treated clinically.**

pregnant women between 10 - 19 weeks of gestational age seeking termination of pregnancy (control), and pregnant women carrying a fetus affected by aneuploidy (study group) at similar gestational ages.

Not Applicable

**2.3 List the procedures that will be performed solely for research purposes (i.e., those that are not performed as part of standard of care).**

No procedures will be done for the purpose of this study. The tissue collected on the termination of pregnancy would be otherwise discarded. The order of events would be:

1. Patient presents to Planned Parenthood for termination of pregnancy.
2. Planned Parenthood nurse interviews the patient and consents her for the termination of pregnancy in 24 hours.
3. On the day of the procedure; Planned Parenthood nurse consents the patient for utilization of the placenta and fetal tissue obtained and otherwise discarded. This is set up in this way so that the study does not interfere at all with the standard process. The patient will be reassured that no changes will occur in the regular termination procedure regardless of her decision.
4. If the patient agrees to it; through suction and depositing into a glass jar connected to the suction device (as per Planned Parenthood protocol) a sample would be obtained from the placenta and fetal tissue. This procedure will be done by either [REDACTED] or [REDACTED], (physicians performing the procedure). The only information that will be collected is the gestational age.
5. The tissue is then brought to [REDACTED] and will be stored in freezers in [REDACTED]. The PI, Co-investigator, research coordinator, and research scientists will be responsible for the handling of the tissues. This location is a LOCKED facility and only these persons will have access to it.
6. Total RNA will be extracted with RNA STAT-60 following the manufacturer's directions (Tel-Test Inc., Friendswood, TX), and mRNA will be isolated and purified using the Micro-FastTrack 2.0 kit (Invitrogen, Carlsbad, CA). RNA integrity will be tested at the [REDACTED].
7. A computer program will analyze the intensity of the signal from the microarray and would allow for determination of which genes are upregulated or downregulated in each sample.
8. Statistical analysis will be performed to find significant differences.

Not Applicable

## **RISKS AND BENEFITS: GENERAL**

**1.1 Describe any potential direct benefits to subjects. If there are no direct benefits, state this.**

- \* no direct benefits or risks.

## 1.2 Describe the potential benefits of this research to society.

- \* The secondary aim of this study if we could identify a critical gene that could be mapped, is to tailor specific pharmacological therapies that may aid in the correction of the defective metabolic pathway.

The major implication of this study will be to understand the details in the metabolic pathways involved in the growth restriction. To determine which pathway and how is affected to produced the abnormal growth. This may correlate with specific gene products that may be amenable to be manipulated through pharmacologic therapies. In conclusion, it will allow a better understanding for future research and possibly a better outcome for fetuses with aneuploidy.

## 1.3 Does this study involve direct physical intervention with subjects? NOTE: A physical intervention refers to study procedures that may pose a risk (however minimal) to a subject's body (e.g., blood draws, MRI scans, drug or device trials, exercise, dietary restrictions/supplements). Examples of activities that are NOT physical intervention include obtaining informed consent and administering surveys.

- \*  Yes  No

## 1.4 Will subjects incur any costs as a result of study participation (e.g., pharmacy preparation fees, payment for a device, billing of study procedures to subject's insurance)?

- \*  Yes  No

1.4.1 If yes, describe any costs. NOTE: Costs to subjects must be included in the consent form.

## RISK/BENEFIT ANALYSIS

### 4.1 Describe any potential psychosocial risks to subjects, such as psychological stress or confidentiality risks (including risk to reputation, economic risks, and legal risks).

- \* Inadvertent breach of confidentiality and distress during the consent process.

### 4.2 Describe how ALL the risks of the study will be minimized.

\* All data is stored in a password secured computer. The label on the sample would not allow for identification of the subject or the day of the procedure or any other information that may link the sample to the subject. As for the distress during the consent process, the patient will be reassured by the Planned Parenthood nurse and the physician performing the procedure that no change will be made in the standard procedure regardless of agreeing for the utilization of the tissues collected. This is absolutely voluntary and if the patient would not like to participate or even be informed of the research, she will not be asked to consent for the utilization of the tissues collected. [REDACTED] nor [REDACTED] will participate in the consenting process for the utilization of the tissues.

### 4.3 Explain why the risks to the subjects are reasonable in relation to the anticipated benefits.

\* All precautions will be followed to de-identify the samples and maintain confidentiality. The samples from the tissues will be done in a private room. The overall benefit to society from this study could result in a better understanding of the details in the metabolic pathways involved in the growth restriction. To determine which pathway and how is affected to produced the abnormal growth. This may correlate with specific gene products that may be amenable to be manipulated through pharmacologic therapies. In conclusion, it will allow a better

understanding for future research and possibly a better outcome for fetuses with aneuploidy.

#### 4.4 Describe the provisions in place to identify and address unanticipated problems or complications.

\* Weekly review of the tissue collection protocol by the PI and the Co-I. Every week the PI and the Co-I will meet and evaluate every step of the process from obtaining the consent to the processing of the samples. By doing this, unanticipated problems will be identified and properly handled in a timely fashion.

**4.5 Does this study constitute minimal risk research?** NOTE: 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.

\*  Yes  No

**4.5.1 If no, describe the data and safety monitoring plan for this study.** NOTE: If a formal Data Safety Monitoring Board or Data Monitoring Committee exists, provide a general description of the committee or board's membership (e.g., number of members, expertise, and whether members are independent of the sponsors/researchers) and the expected frequency of their meetings.

### SUBJECT POPULATION: GENERAL

**1.1 Provide the total number of subjects required from all study locations.** NOTE: You must provide an integer. If you are enrolling a range of subjects (e.g., 50 to 100 subjects), enter the larger number.

\* 40

**1.2 Provide the number of subjects that will be recruited at sites under UW-Madison purview.** NOTE: You must provide an integer. If you are enrolling a range of subjects (e.g., 50 to 100 subjects), enter the larger number.

\* 40

**1.3 Provide a formal statistical justification for sample size and analysis of results. If a formal justification does not exist, explain why and provide a rationale for the sample size.** NOTE: To supplement your response, you can upload a word document with the statistical justification at the end of this application.

\* In selecting the sample size, consideration to the novel nature of this research was acknowledged. The analysis of 40 samples would account for the intrinsic differences between hybridization samples as established by Newto et al. About 5 samples are expedted to be abnormal. For comparison of the gene expression, no ratio between normal and abnormal would be necessary since the aim of the study is to compare the presence or not of different gene expression. 35 normal samples would be enough to validate the mcroarry hybridization differences. Since aneuploidy is a rare event previous studies like the one from Newton et al have suggested that 5 samples would be acceptable.

**1.4 Describe the main inclusion criteria.**

\* Any pregnant women terminating the pregnancy between 10-19 weeks of gestation.

**1.5 Describe the main exclusion criteria.**

\* No exclusion criteria.

**1.6 If any racial/ethnic group will be targeted for or excluded from this study, identify**

**the group that will be targeted or excluded and provide justification for this. If this does not apply to your study, select Not Applicable.**

Not Applicable

**1.7 If men or women will be targeted for or excluded from this study, identify which sex will be targeted or excluded and provide justification for this. If this does not apply to your study, select Not Applicable.**

Men are excluded; only women experience pregnancy

Not Applicable

## **SUBJECT POPULATION: VULNERABLE GROUP CHECKLIST**

**2.1 If your study involves *targeted* enrollment of any of the following populations, additional information may be needed. Check all that apply. NOTE: If inclusion of any of these populations is only *incidental*, do not select that population. If none apply, check "None of the above."**

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Pregnant women/fetuses

## **SUBJECT POPULATION: VULNERABLE POPULATIONS**

**3.1 What is the justification for the inclusion of these subjects?**

\* These subjects would be pregnant patients undergoing a voluntary interruption of pregnancy from which the tissue collected would normally be discarded. Collection and analysis of such tissues from placenta and fetal at the gestational age between 10- 19 weeks would provide an understanding of the details in the metabolic pathways involved in the growth restrictions and potentially provide a better outcome for fetuses with aneuploidy.

**3.2 Describe the additional safeguards that have been included in this study to protect the rights and welfare of these subjects. Include the measures that will be taken to minimize any potential coercion or undue influence in recruitment and ongoing participation in the study.**

\* This is absolutely voluntary and if the patient would not like to participate or even be informed of the research, she will not be asked to consent for the utilization of the tissues collected. the patient will be reassured by the Planned Parenthood nurse and the physician performing the procedure that no change will be made in the standard procedure regardless of agreeing for the utilization of the tissues collected. [REDACTED] nor [REDACTED] will participate in the consenting process for the utilization of the tissues.

## **SUBJECT IDENTIFICATION AND RECRUITMENT: GENERAL**

**1.1 From what sources or by what methods will subjects be identified and/or recruited?**

\*

---

Identification in clinical practice: Other

---

Medical records

**1.1.1 If other, specify.**

## **ID RECRUITMENT: GENERAL MEDICAL RECORDS**

**1.2 If medical records are being used to identify potential subjects, do you confirm that all key personnel reviewing the records have valid clinical access?** NOTE: Valid clinical access means that all key personnel reviewing records have a clinical role, independent of this research study, for which access to patient records/data/images is already present.

Yes  No

Not Applicable

**1.2.1 If 1.2 is answered no, do you confirm that all key personnel accessing medical records have authorized access to identify subjects via these records.** NOTE:

Authorized access to identify subjects means research personnel have obtained access to patient lists or other records for the purpose of subject identification through the formal authorization process of the record holder. If access cannot be confirmed for UW Health medical records, contact UW Health-UWHC Information Technology Services to obtain access. For other health systems, contact that organization's medical records department.

Yes  No

**1.3 If medical records are being used to identify potential subjects, describe what records will be reviewed (e.g., WISCR departmental records, HealthLink, etc.).** NOTE: If medical records will not be accessed for subject recruitment, select Not Applicable.

[Healthlink](#)

Not Applicable

## RECRUITMENT METHODS

**2.1 Describe the recruitment plan for this study.** NOTE: This description should address what methods will be used, when and how often they will be used, and how many times potential subjects will be contacted.

**2.2 If any advertisements will be posted, list locations and describe what advertisements will be posted at which locations.** NOTE: Study teams must obtain permission from each location prior to posting recruitment materials.

Not Applicable

**2.3 Upload copies of recruitment flyers.** NOTE: Recruitment flyers are any advertisement that will be posted in public locations.

File

There are no items to display

Not Applicable

**2.4 Upload copies of any other recruitment materials, including scripts, brochures, or advertisements (radio, newspaper, mailed letters, etc.).**

File

There are no items to display

Not Applicable

**2.5 Are you using an IRB approved recruitment database to disseminate recruitment materials or to contact subjects?**

\*  Yes  No



**2.5.1 If yes, provide the IRB protocol number of the recruitment database.**

**2.5.2 Describe what will be disseminated to individuals who agreed to be included in the recruitment database.**

**2.5.3 If the recruitment database is not the investigator's own, upload a letter of support for the use of the database.**

File

There are no items to display

## **SUBJECT RECRUITMENT: CONTINUED**

**3.1 Will subjects be paid or offered other material inducements to participate in the study?**

\*  Yes  No

**3.2 Will subjects undergo a preliminary phone screen to determine basic eligibility?**

\*  Yes  No

## **SUBJECT SCREENING**

**4.1 Describe the procedures subjects will undergo as part of screening to determine eligibility.**

\* The study nurse, through normal clinical duties, will review the charts of scheduled termination and will notify the investigator when a termination due to chromosomal abnormalities is scheduled (since this is already recorede in the chart). This is a rare occurrence and is expected to be between 3-5 patients per year.

**4.2 Describe any study procedures that will be conducted before written informed consent is obtained from subjects (e.g., phone screening, fasting, discontinuing medications, etc.).**

\* None

## **PRIVACY AND CONFIDENTIALITY**

**1.1 Describe the precautions that will be used to ensure subject *privacy* is protected (e.g., research intervention is conducted in a private room; collection of sensitive information about subjects is limited to the amount necessary to achieve the aims of the research).**

\* Collection of the sample will be done in a private room. The sample will be completely de-identified.

**1.2 Select how subjects are identified in the research records. Check all that apply:**

\*

Indirectly: Information identifying subjects is linked to data record but stored separately

**1.3 Describe the measures that will be implemented by your research team to safeguard the identifiable subject information from unauthorized use or disclosure for both paper and electronic forms of information. Include how and where data will be stored.**

\* The samples will be labeled with a number which is linked to the gestational age. This information will be kept in a separate database. The rare nature of terminations due to chromosomal abnormalities could theoretically lead to identification of subjects in the study arm, but this would be extremely difficult. We will not be recording dates of sample collection and the sample itself will not be labeled with the chromosomal abnormality; this will be on the data collection sheet only and will be stored separately.

**1.4 Are you planning to retain data collected for this study for purposes not described in this application (e.g., future unrelated research project)?**

\*  Yes  No

**1.4.1 If yes, do you confirm that any future uses not described in this application will be submitted separately for IRB review?**

Yes  No

**PRIVACY AND CONFIDENTIALITY: CONTINUED**

**2.1 Will data be stored on laptops or portable devices?**

\*  Yes  No

**2.1.1 If yes, what additional safeguards have been put in place (e.g., link for coded data will be stored separately, data will be deidentified) to protect these data from risk of breach of confidentiality (e.g., theft of laptop, loss of portable device)?**

NOTE: Consult with your IT department about security of data storage on laptops or portable devices.

The data will be de-identified, coded and kept on a secured password protected computer.

**2.2 Will subject data, specimens, or images be shared outside the UW-Madison, the Madison VA (Wm. S. Middleton VA Hospital), or UWHC (including UWMF clinics)?**

NOTE: This is not referring to industry-sponsored clinical trials or cooperative group studies. For such studies, select Not Applicable.

Yes  No  
 Not Applicable

**INFORMED CONSENT: GENERAL**

**1.1 What consent process or waivers of consent are you requesting for this study?**

\*

Consent process with signed consent documentation

**INFORMED CONSENT: OVERVIEW**

**6.1 Describe when the consent process will occur.**

\* The consent process will be done at Madison Planned Parenthood on the day of the procedure. The study nurse will speak privately with the subject and explain the aims of this study. The subject would be able to ask questions and express concerns. Planned Parenthood mandates the use of a specific consent form for the disposal of products of conception which will be used. (form is attached). If the patient agrees to participate, she will sign the consent, the procedure will be done as scheduled that day per Planned Parenthood, and the sample will be taken to [REDACTED] as explained previously. Distress in the process of obtaining the consent will be addressed by first allowing the patient to decide if she even wants to consider

participating in the study. IF the patient does not want to hear about it, she will NOT be given any additional information and the study nurse will leave the room immediately. If the patient is comfortable being informed of the study, then she again will be reassured that in no manner will her procedure be affected in any way by participating in this study or not.

## 6.2 Describe where the consent process will occur.

- \* The consent process will occur in a private room at Madison Planned Parenthood.

## 6.3 Describe how you will ensure potential subjects are given sufficient time to consider participation.

\* In order to minimize what could already be a distressful situation, the patient will first be asked if she would like to hear about the study and then will be provided ample time to decide. IF the patient does not want to hear about it, she will NOT be given any additional information and the study nurse will leave the room immediately.

As explained previously, if the patient is interested in hearing about the study, the study will be fully explained, and the patient will be reassured her procedure will not change in any manner based on her decision. When and if she feels comfortable with participating, she will be asked to sign the consent form and the procedure will continue as planned.

## 6.4 Do you confirm that all study personnel responsible for obtaining informed consent have the following qualifications:

- Are familiar with the details of the study;
- Will ensure subjects are provided with sufficient information to make an informed and voluntary decision about study participation;
- Are familiar with UW-Madison policies regarding informed consent.

\*  Yes  No

## 6.5 Upload all consent documents and, if applicable, information sheets (e.g., consent form, assent form, translated consent documents). NOTE: If the main consent document for this study is over 5 pages long and/or if the CTCRC will be used for this study, an information sheet MUST also be uploaded.

\*

File

Planned Parenthood Consent Form

## HIPAA: GENERAL

NOTE: For guidance on the HIPAA privacy rule, including what constitutes individually identifiable information and Protected Health Information (PHI), refer to the HIPAA website. If the purpose of this study or project is to create a database or registry, contact the HIPAA Privacy Officer to determine whether it needs to be registered.

## 1.1 Will the research involve the access, collection, use, or disclosure of individually identifiable information?

\*  Yes  No

**1.1.1 If yes, are you or any member of the study team conducting the study under a Madison VA (Wm. S. Middleton VA Hospital), UWHC, or UW Medical Foundation appointment or an appointment that is within the UW-Madison Health Care Component (HCC)?** NOTE: The HCC of the UW-Madison currently includes SMPH clinical departments; School of Pharmacy (clinical units only); School of Nursing; University Health Services (non-student records only); State Laboratory of Hygiene; and Waisman Center

(clinical units only).

Yes  No

## COLLECTION AND/OR USE OF BIOLOGICAL SPECIMENS: GENERAL

**1.1 Select the types of biological specimens to be used for this study. Select all that apply.**

\*

Other \_\_\_\_\_

**1.1.1 If tissue or other, specify.**

collection of fetal and placental tissue

**1.2 Select from where you are obtaining the biological specimens. Select all that apply.**

\*

Residual (to be discarded) biological specimens from a clinical or research procedure (i.e., prospectively obtained)

**1.3 Are you banking specimens for future research purposes (i.e., research beyond the scope of the current study)?**

\*

Yes  No

**1.3.1 If no, describe when and how specimens will be destroyed.**

**1.4 Will results of any testing performed on the samples be released to subjects?**

\*

Yes  No

**1.5 Are you performing genetic analysis on specimens?**

\*

Yes  No

**1.6 Are you testing for HIV or other infectious diseases (e.g., hepatitis) and/or screening for illegal drug use?**

\*

Yes  No

**1.7 Does this study involve collection and/or use of fetal tissue?**

\*

Yes  No

## COLLECTION AND/OR USE OF BIOLOGICAL SPECIMENS: GENERAL, CONTINUED

**2.1 Describe the purpose of collecting the specimens.**

\* To perform gene expression profile on the samples collected. The fetal tissues, including the placenta, are processed to obtain RNA that would allow for the determination of the activity of specific genes according to the RAN present. This information is obtained through microarray analysis. Microarray analysis allows for the determination of gene activity in terms of upregulation or downregulation meaning very active or not active genes. There is no difference in the handling and processing of the placental tissue compared to the rest of the fetal tissue sample.

**2.2 Describe the information that will be associated with the specimens (e.g., clinical information such as diagnosis, date of collection, lab results).**

\* The samples will be labeled with a number that is linked to the gestational age and will be kept in a separate database.

**2.3 Describe how specimens will be labeled (e.g., name, initials, coded ID number linked to identifiers, anonymous).**

\* The research scientist, the PI and the Co-investigator will have access to the samples.

**RESIDUAL BIOLOGICAL SPECIMENS**

**4.1 Describe the source of the residual specimens (e.g., surgical pathology).**

\* The samples will be obtained at the time of termination of pregnancy. These tissues are never submitted to pathology.

**4.2 Describe the study team's arrangements for obtaining the samples and ensuring that a sufficient sample has been secured to fulfill any non-research objectives for collection (e.g., clinical testing). NOTE: Any samples obtained during surgery that will not be first processed by pathology will require special permission from pathology.**

\* The research fellow or research coordinator will contact Planned Parenthood in advance to know which day will be appropriate to collect samples.

The research fellow or research coordinator will have Planned Parenthood consent for the disposal of the tissue. The patient will be approached before the procedure and before any sedatives have been given.

If the patient decides to participate in the study by allowing the tissue collection, the consent will be signed and put into the consent folder.

Once the procedure is done and the fetal tissue is out of the room and inspected by the physician performing the procedure the research fellow will collect the sample and put it in the lab tubes he will carry with him. The research fellow will use the homogenizer in every tube. Before using it, the homogenizer must be cleaned by submerging it into pure water. After this it should be sprayed with ARNase and then used. Repeating this process for every tube.

The tubes will have written on them, a number linked to the gestational age and the name of the specimen (i.e. brain, liver, placenta, etc.).

Each number will be logged into a database.

At the end of the day, after all tissue have been collected, the tubes will be brought to [REDACTED] and stored in the -80C freezer. A collection box/ladder will be set aside for these samples; one row per patient. Example:

Patient #1 Brain Heart Kidney Liver Bone Muscle Placenta  
Patient #2 Brain Heart Kidney Liver Bone Muscle Placenta

One single tube for every patient will contain a different media. This is the Karyotype tube. The tissue sample would be placed in cold RNase free, transport media to preserve the the RNA and then be transported to the laboratory. Total RNA will be extracted with RNA STAT-60 following the manufacturer's directions (Tel-Test Inc., Friendswood, TX), and mRNA will be isolated and purified using the Micro-FastTrack 2.0 kit (Invitrogen, Carlsbad, CA). RNA integrity will be tested at the [REDACTED].

The deidentified RNA samples will be placed on RNA microarray chips, targeted to specific genes encoding for metabolic receptors and transporters. Specific software exists to analyze the results as down or up regulated. The data are expressed in units measured by the color pattern (red-green). Means are defined for every gene expression with the appropriate +/- SD. Significance will be determined by a p value of <0.05. T test would be appropriate to compare different gene expression. Cluster analysis would be done for hierarchical clustering (average linkage) and indicated systematic differences among the various experiments, without discrimination between normal and aneuploidic subjects. Gaussian profile (Kolmogorov-Smirnov test) will be obtained using the genes set on which the statistical analysis was performed. In addition, due to the fact that the low number of samples may question the assumption of a parametric distribution of the variable "spot intensity," a nonparametric test (rank analysis) for significance of overexpression, with similar results will be perform.

#### 4.3 Indicate any vulnerable groups whose residual biological specimens will be targeted for collection, if applicable.

\*

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Pregnant women/fetuses

### GENETIC ANALYSIS

#### 8.1 Is this component optional for some or all subjects?

\*  Yes  No

8.1.1 If yes, describe the optional components (e.g., genetic testing is optional for controls only, for parents of minor subjects, for all subjects, etc.).

genetic testing is optional for controls only.

### COLLECTION AND/OR USE OF FETAL TISSUE

GUIDANCE: Human fetal tissue means tissue or cells obtained from a dead human fetus after a spontaneous or induced abortion, or after a stillbirth. The woman donating this tissue must be informed (e.g., in the informed consent document) of any known medical risks to her or risks to her privacy that might be associated with the donation of the tissue and that are in addition to risks of such type that are associated with the woman's medical care. If the woman's attending physician who will be obtaining the tissue is involved in the research, his/her interest in the research to be conducted with the tissue must also be disclosed.

In the case of fetal tissue obtained for research purposes pursuant to an induced abortion:

- The consent for donation of the tissue for research must occur after the consent for the abortion,
- No alteration in the timing, method, or procedures used to terminate the pregnancy may be made solely for the purposes of obtaining the tissue for research, and
- The abortion must be performed in accordance with applicable state law.

### SUPPLEMENTAL INFORMATION

#### 1.1 Does this submission represent a replacement of a protocol previously approved by a UW-Madison IRB (e.g., one closed under the campus Five Year Renewal Policy)?

\*  Yes  No

Not applicable

1.1.1 If yes, please provide the reason for the replacement (e.g., IRB required closure due to Five Year Renewal Policy):

**1.1.2 If yes, provide the previous number assigned to this protocol by the UW-Madison IRB that approved the study:**

**2.1 Provide any additional relevant documents (e.g., supplemental statistical justification information), if applicable.**

File

Data Sheet

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**2.2 Describe what additional documents were added in 2.1.**

Data Collection Sheet

## **FINAL PAGE**

**1.1 Do you certify that (1) the information presented in this application is accurate; and (2) if the application is being submitted on behalf of the Principal Investigator (PI) rather than by the PI, the information presented was done so with the PI's agreement?**

\*  Yes  No

To complete and submit this application to the IRB office, please follow the steps below:

1. Select Hide/Show Errors at the top of this page to identify any omissions in the application;
  2. Select Finish or Exit on this page to return to the study workspace;
  3. To submit this application to the IRB office, click the Submit activity in the study workspace.
- NOTE: The Submit activity is only available to certain study team members.

## **STUDENT/TRAINEE DETAIL**

**Student/Trainee:**

\* JESUS IRURETAGOYENA

**Indicate the category of the student/trainee.**

\* Fellow

**If other, specify.**

**Course of program for which this project is being completed.**

\* Endocrinology Reproductive Physiology Program

## Meeting Minutes

Protocol Number:	H-2009-0071
P.I.:	Dr. Dinesh M Shah
Protocol Title:	Metabolic Gene Profile on Aneuploidy Relevant to Fetal Growth Abnormalities
Meeting Date:	5/26/2009
Submission Type:	Initial
Staff Reviewer:	[REDACTED]

### Summary:

#### IRB Determination:

The IRB determined that the study was approvable as submitted.

#### IRB Discussion:

The primary reviewer summarized the study and noted that while there are no concerns with the safety or ethics of the study, the scientific design is flawed such that resulting data may not be meaningful. For example, there were concerns that the design does not account for the fact that many things can affect abnormal fetal growth, not just aneuploidy, that gestational age is notoriously inaccurate, and that there was no consideration of chromosomal mosaicism, or when the number of chromosomes in the placenta is different than in the fetus.

The secondary reviewer agreed, but felt that because the study was minimal risk, it was ultimately approvable. The IRB agreed and determined that the study is approvable, but that suggestions to improve design will be outlined for the investigator.

The committee moved to approve the study upon resolution of modifications.

Risk/Benefit Ratio: The IRB determined that this study is minimal risk pursuant to 45 CFR 46.102(i). The abortion procedure will not be impacted in any way by the collection of the fetal tissue and all tissue samples will be anonymized. No safety and/or ethical concerns were raised.

Special Populations: N/A

Recruitment and Consent Process: The recruitment process was found to be acceptable. However, given the potential for emotional distress in this subject group, particularly for those terminating due to chromosomal abnormalities, the IRB considered the possibility of a feeling of coercion in women if the physician performing the abortion was also obtaining consent to obtain the fetal tissue for research purposes. Thus, the investigator will be asked to confirm the [REDACTED] will not be involved in the consent process OR, if she will obtain informed consent, that this will be done *after* the procedure has been completed. The IRB determined that it was acceptable for the research nurse to obtain consent prior to the procedure.

The consent form, while not consistent with the standard UW template, was found to be adequate in informing women of the option of donating tissue for research purposes. Because the women themselves are not considered to be subjects pursuant to 45 CFR 46.102(f) as no procedures are being performed for research purposes and no PHI is being collected, this consent form was found to be acceptable.

HIPAA Requirements: No PHI is being collected. The tissue will be anonymous.

Conflict of Interest: The IRB noted that the investigator has submitted an Outside Activities Disclosure



form, and that no apparent financial conflicts of interest exist.

Oversight: Study procedures involving subjects will take place at Planned Parenthood. While the investigators involved in obtaining consent and collecting the tissue are performing these procedures for Planned Parenthood, they are UW employees ( [REDACTED] and a TBD study nurse), and have completed UW training requirements. A letter of support has been provided from Planned Parenthood. Because this is not a federally-funded study recommend that no formal IRB Authorization Agreement is necessary.

FDA: N/A

VA: N/A

Other: N/A

Review Period Assigned: **INSERT** months

Notes to the Investigator:

1. Given the potential for emotional distress in this subject group, particularly for those terminating due to chromosomal abnormalities, the IRB considered the possibility of a feeling of coercion in women if the physician performing the abortion was also obtaining consent to obtain the fetal tissue for research purposes. Thus, please confirm the [REDACTED] will not obtained informed consent OR, if she will obtain informed consent, that this will be done *after* the termination procedure has been completed. [The IRB determined that it was acceptable for the research nurse to obtain consent prior to the procedure.]
2. Please be reminded that once the research nurse is identified, this person must be added to the protocol via the Personnel Change form, prior to engaging in study activities.
3. The IRB had concerns that there were several factors which may confound results, or at the least, make data interpretation difficult, that had not been considered. Please note that no changes are required in light of these and that they are merely suggestions for consideration. Should you chose to make any revisions to the study based on these suggestions, please indicate that and revise materials accordingly:
  - a. The IRB noted that there are many factors that can affect abnormal fetal growth, not just aneuploidy, and that this might be an important confounding factor.
  - b. Conversely, not all individuals with aneuploidy have growth retardation, for example, in the case of sex chromosomal aneuploidy, and are thus likely to have very different gene activity.
  - c. Gestational age is known to an inaccurate and ambiguous parameter, particularly in abnormal fetuses. This could be another confounding factor.
  - d. Finally, placental mosaicism, or when the number of chromosomes in the placenta is different than in the fetus, could also confuse resulting data.

Action: Req Mods

Votes:

For: 18	Against: 0	Abstained: 0	Total:18
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## Meeting Minutes

Protocol Number:	2009-0071
P.I.:	Dinesh M. Shah, MD
Protocol Title:	Metabolic Gene Profile on Aneuploidy Relevant to Fetal Growth Abnormalities
Meeting Date:	06.08.2010
Submission Type:	Continuing
Review Type:	Full
Staff Reviewer:	

**IRB Discussion and Determination:**

The progress report was summarized and the IRB determined that the study could be re-approved for a period of 12 months. The progress report did not raise any concerns and the risk/benefit ratio for the study is unchanged. The IRB determined the study continues to meet the requirements of 45 CFR 46.111.

Conflicted IRB member, Dinesh Shah, left the room for the final discussion and vote on this protocol.

Study status:

The study continues to collect post-mortem fetal tissue.

Consent materials:

The Planned Parenthood consent documents submitted are unchanged from those previously approved. The IRB did not request any changes in light of the progress report and the documents were re-approved as submitted.

Adverse events, unanticipated problems, other incidents reported:

No adverse events, unanticipated problems, patient complaints, or other incidents were reported.

New information reported:

The investigator indicates that no new information regarding risks, benefits, or alternatives to study participation has emerged since last continuing review/initial review.

Other:

N/A

Changes of protocol:

Additional staff have been added to study personnel. The IRB found these changes to be unproblematic.

Review period assigned:

The study has been re-approved for a period of 12 months.

Action: Approval

Votes:

For: 17	Against: 0	Abstained: 0	Total: 17
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Change: CP001 for IRB Study H-2009-0071 ( H-2009-0071-CP001 )

Abstained: 0, For: 10, Against: 0 - Updated minutes: IRB Determination and Discussion: The IRB determined that the change of protocol was approvable as submitted and agreed the study continues to meet the criteria for IRB approval pursuant to 45 CFR 46.111 and 21 CFR 56.111 or 38 CFR 16.111, if applicable.

Risk/Benefit Ratio: The IRB found that the changes do not significantly affect the risk/benefit ratio of the study, which remains acceptable. The risks of participation remain adequately minimized in relation to the potential benefits of the study.

Subject Selection, Recruitment, and Consent Process: The change did not alter subject selection, subject recruitment, or the consent process or documents previously approved by the IRB.

Special Populations: This study does not include any apparent special populations and the change did not alter the subject populations previously approved for enrollment in this study.

Privacy and Confidentiality, including HIPAA Requirements: The change did not alter the privacy and confidentiality protections previously approved by the IRB.

Conflict of Interest (Study Team Members): None identified

Conflict of Interest (IRB Members): None identified

Funding: There were no changes to funding as a result of this change of protocol.

IRB-of-Record Issues: There were no IRB-of-record issues raised by this change of protocol.

FDA: This study is not FDA-regulated.

VA: This study does not fall under VA purview.

Scientific Review and Ancillary Committees: This change does not trigger any ancillary committee reviews.

Other Regulatory Issues: No other regulatory issues were identified for this change of protocol.

Review of Study Team Response to Modifications: No modifications were requested.

Review Period: The change of protocol did not alter the review period for the study.



THE UNIVERSITY  
of  
**WISCONSIN**  
MADISON

Health Sciences IRB  
**NOTICE OF ACTION**  
**Modifications Requested**  
Date of Correspondence: 6/1/2009

Principal Investigator: Dinesh M Shah, M.D.  
Obstetrics and Gynecology, 6C Meriter-Park, 202 South Park St., Madison,  
WI

Point of Contact: J I Iruretagoyena  
Maternal Fetal Medicine, 6C Meriter, 202 S. Park St.

Protocol: H-2009-0071 "Metabolic Gene Profile on Aneuploidy Relevant to Fetal  
Growth Abnormalities"

IRB Staff Contact: [REDACTED]

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Your Initial Review Application, including the supporting materials you submitted with your application, was reviewed by the full Health Sciences IRB at its May 26, 2009 meeting and modifications and/or clarifications were requested. Please submit a written, point-by-point response to the following and provide any additional documents cited:

1. Given the potential for emotional distress in this subject group, particularly for those terminating due to chromosomal abnormalities, the IRB considered the possibility of a feeling of coercion in women if the physician performing the abortion was also obtaining consent to obtain the fetal tissue for research purposes. Thus, please confirm the [REDACTED] will not be obtained informed consent OR, if she will obtain informed consent, that this will be done *after* the termination procedure has been completed. [The IRB determined that it was acceptable for the research nurse to obtain consent prior to the procedure.]
2. Please be reminded that once the research nurse is identified, this person must be added to the protocol via the Personnel Change form, prior to engaging in study activities.
3. The IRB had concerns that there were several factors which may confound results, or at the least, make data interpretation difficult, that had not been considered. Please note that no changes are required in light of these and that they are merely suggestions for consideration. Should you choose to make any revisions to the study based on these suggestions, please indicate that and revise materials accordingly:
  - a. The IRB noted that there are many factors that can affect abnormal fetal growth, not just aneuploidy, and that this might be an important confounding factor.
  - b. Conversely, not all individuals with aneuploidy have growth retardation, for example, in the case of sex chromosomal aneuploidy, and are thus likely to have very different gene activity.
  - c. Gestational age is known to be an inaccurate and ambiguous parameter, particularly in abnormal fetuses. This could be another confounding factor.

- d. Finally, placental mosaicism, or when the number of chromosomes in the placenta is different than in the fetus, could also confuse resulting data.

Please be sure to do the following:

- For modifications that involve the research protocol itself, please provide one copy of the revised protocol with the changes identified (e.g., highlighted or underlined) with a version number and date.
- For revisions that involve the consent or assent document(s), please provide two copies of these forms (one with the revisions highlighted, and one unmarked copy). Please include a version number and date in the header or footer and leave sufficient space for the IRB approval stamp (2" circle) in the upper right corner.
- For revisions that involve the authorization form, please provide one copy of these documents with the revisions highlighted.
- For modifications to recruitment materials, please highlight any revisions and include a version date on the document(s).

**You may not begin your research or recruit subjects until you receive written notice of IRB approval and a stamped consent form to use (if you are required to obtain informed consent from subjects).**

If you have any questions, feel free to contact me.

Sincerely,



Staff Reviewer, Health Sciences IRB Office



THE UNIVERSITY  
of  
**WISCONSIN**  
MADISON

**Health Sciences IRB  
NOTICE OF ACTION  
Approval**

Principal Investigator: Dinesh M Shah, M.D.  
Obstetrics and Gynecology, 6C Meriter-Park, 202 South Park St., Madison, WI  
Point of Contact: Jesus I Iruretagoyena  
Maternal Fetal Medicine, 6C Meriter 202 South Park St., Madison, WI 53715-1599  
Protocol: **H-2009-0071** "Metabolic Gene Profile on Aneuploidy Relevant to Fetal Growth Abnormalities"  
Review Period: 12 months  
Approval Expires: 5/25/2010  
IRB Staff Contact: [REDACTED]

Your Initial Review Application, including the supporting materials you submitted with your application, was reviewed by the full Health Sciences IRB at its 5/26/2009 meeting and modifications or clarifications were requested. Your response letter dated 6/2/2009 has addressed the IRB's concerns. You may now begin your above-referenced research and enroll subjects, using the standard Planned Parenthood consent documents. The review period and expiration date of your approval are indicated above.

Please be sure to do the following:

- Use your Health Sciences IRB protocol number (listed above) on any documents or correspondence with us concerning your protocol.
- Keep a copy of this approval letter with your files.
- Use only copies of the enclosed consent forms or information sheets, which have the IRB approval and expiration date-stamp, to obtain informed consent; give all subjects a copy of the consent document.
- If applicable, use only copies of the approved authorization form or altered authorization form to obtain subjects' permission to access, use, or disclose their protected health information.
- Comply with all requirements described in the **Investigator Responsibilities Related to the Protection of Human Subjects** attachment.

If you have any questions, please contact the staff person listed above.

Sincerely,

[REDACTED]

[REDACTED]

Health Sciences IRB Office

Enclosure(s):  
Investigator Responsibilities Related to the Protection of Human Subjects



THE UNIVERSITY  
of  
**WISCONSIN**  
MADISON

Health Sciences IRB  
**NOTICE OF ACTION**  
**Approval**

Date of Correspondence: 6/9/2010

Principal Investigator: Dinesh M Shah, M.D.  
Obstetrics and Gynecology, 6C Meriter-Park, 202 South Park St., Madison,  
WI

Point of Contact: [REDACTED]  
Obstetrics and Gynecology, Suite 555, One South Park St., Madison, WI  
53715

Protocol: **H-2009-0071 "Metabolic Gene Profile on Aneuploidy Relevant to Fetal  
Growth Abnormalities"**

Review Period: 12 months

Approval Expires: June 07, 2011

IRB Staff Contact: [REDACTED]

Your Continuing Review Protocol Progress Report and Change of Protocol were reviewed and approved by the full Health Sciences IRB at its June 08, 2010 meeting. The following changes are now approved:

Personnel changes.

You may continue your research. The review period and expiration date of your approval are listed above.

Please be sure to do the following:

- Use your Health Sciences IRB protocol number (listed above) on any documents or correspondence with us concerning your protocol.
- Keep a copy of this approval letter with your files.
- Comply with all requirements described in the **Investigator Responsibilities Related to the Protection of Human Subjects** attachment.

Sincerely,

[REDACTED]

Staff Reviewer, Health Sciences IRB Office

Enclosure(s):

Investigator Responsibilities Related to the Protection of Human Subjects

UW-Madison Health Sciences Institutional  
Review Boards Mail Code #9425  
800 University Bay Dr. (UBOB), Ste. 105  
Madison, WI 53705  
Phone: 608-263-2362 FAX: 608-265-5811

University of Wisconsin

Health Sciences IRB  
Review Boards

2500 Overlook Terrace Madison, Wisconsin 53705  
www.medicine.wisc.edu/irb/



**Health Sciences IRB**  
4/26/2011

**Submission ID number:** [H-2009-0071-CR001](#)

**Title:** Metabolic Gene Profile on Aneuploidy Relevant to Fetal Growth Abnormalities

**Principal Investigator:** DINESH SHAH

**Point-of-contact:** [REDACTED]

**IRB Staff Reviewer:** [REDACTED]

A designated HS IRB member conducted an expedited review of the above-referenced continuing review progress report form. The study was approved by the IRB member for the period of 12 months with the expiration date of 4/25/2012. The study qualified for expedited review pursuant to 45 CFR 46.110 and, if applicable, 21 CFR 56.110 and 38 CFR 16.110 in that the study presents no more than minimal risk and involves:

**Category 5:** Use of materials (data, documents, records, or specimens) that have been or will be collected solely for nonresearch purposes

To access the materials approved by the IRB, including any stamped consent forms and recruitment materials, please log in to your ARROW account and view the documents tab in the submission's workspace.

Please review the Investigator's Responsibility guidance, which includes a description of IRB requirements for submitting continuing review progress reports, changes of protocol and reportable events:

<http://arrowhelp.hsirbs.wisc.edu/content/investigator-responsibilities>.

Please contact the IRB office at 608-263-2362 with general questions. For questions related to this submission, contact the assigned staff reviewer.





**Submission ID number:** [H-2009-0071-CR002](#)

**Title:** Metabolic Gene Profile on Aneuploidy Relevant to Fetal Growth Abnormalities

**Principal Investigator:** DINESH SHAH

**Point-of-contact:** [REDACTED]

**IRB Staff Reviewer:** [REDACTED]

A designated HS IRB member conducted an expedited review of the above-referenced continuing review progress report form. The study was approved by the IRB member for the period of 12 months with the expiration date of 4/9/2013. The study qualified for expedited review pursuant to 45 CFR 46.110 and, if applicable, 21 CFR 56.110 and 38 CFR 16.110:

**Category 5:** Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis)

Please note, **the IRB recommends submitting a continuing review six weeks prior to expiration.** Please follow this guidance in the future, in order to help prevent expiration of your study: <http://kb.wisc.edu/hsirbs/page.php?id=17713>

Please review the Investigator Responsibilities guidance ( <http://go.wisc.edu/m0lovn> ), which includes a description of IRB requirements for submitting continuing review progress reports, changes of protocol and reportable events.

Please contact the appropriate IRB office with general questions: Health Sciences IRBs at 608-263-2362 or Education Research and Social & Behavioral Science IRBs at 608-263-2320. For questions related to this submission, contact the assigned staff reviewer.



**Submission ID number:** [H-2009-0071-CR003](#)

**Title:** Metabolic Gene Profile on Aneuploidy Relevant to Fetal Growth Abnormalities

**Principal Investigator:** DINESH SHAH

**Point-of-contact:** [REDACTED]

**IRB Staff Reviewer:** [REDACTED]

A designated HS IRB member conducted an expedited review of the above-referenced continuing review progress report form. The study was approved by the IRB member for the period of with the expiration date of 2/13/2014. The study qualified for expedited review pursuant to 45 CFR 46.110 and, if applicable, 21 CFR 56.110 and 38 CFR 16.110:

**Category 5:** Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis)

To access the materials approved by the IRB, including any stamped consent forms and recruitment materials, please log in to your ARROW account and view the documents tab in the submission's workspace.

Please review the Investigator Responsibilities guidance ( <http://go.wisc.edu/m0lovn> ), which includes a description of IRB requirements for submitting continuing review progress reports, changes of protocol and reportable events.

Please contact the appropriate IRB office with general questions: Health Sciences IRBs at 608-263-2362 or Education Research and Social & Behavioral Science IRBs at 608-263-2320. For questions related to this submission, contact the assigned staff reviewer.



**Submission ID number:** [H-2009-0071-CP001](#)

**Title:** Metabolic Gene Profile on Aneuploidy Relevant to Fetal Growth Abnormalities

**Principal Investigator:** [JESUS IRURETAGOYENA](#)

**Point-of-Contact:**

**IRB Staff Reviewer:**

The convened HS IRB conducted a full review of the above-referenced change of protocol application. The change of protocol was approved for the remainder of the approval period. This study expires on 2/13/2014. You must log into your ARROW account in order to view the specific changes approved by the IRB.

To access the materials approved by the IRB, including any stamped consent forms, recruitment materials and the approved protocol, if applicable, please log in to your ARROW account and view the documents tab in the submission's workspace.

If you requested a HIPAA waiver of authorization, altered authorization and/or partial authorization, please log in to your ARROW account and view the history tab in the submission's workspace for approval details.

Please review the Investigator Responsibilities guidance ( <http://go.wisc.edu/m0lovn> ), which includes a description of IRB requirements for submitting continuing review progress reports, changes of protocol and reportable events.

Please contact the appropriate IRB office with general questions: Health Sciences IRBs at 608-263-2362 or Education Research and Social & Behavioral Science IRBs at 608-263-2320. For questions related to this submission, contact the assigned staff reviewer.

 **Planned Parenthood**  
of Wisconsin, Inc.  
302 North Jackson Street, Milwaukee, WI 53202  
1-800-230-PLAN

Patient Name: \_\_\_\_\_  
Date of Birth: \_\_\_\_\_  
Chart Number: \_\_\_\_\_

**Client Information for Informed Consent  
DONATION OF ABORTED PREGNANCY TISSUE FOR MEDICAL  
RESEARCH, EDUCATION, OR TREATMENT**

Recent advances in medical science have been developed through research using tissue that has been aborted. This research is being done to treat and find a cure for such diseases as diabetes, Parkinson's disease, Alzheimer's disease, cancer, and AIDS.

Tissue can be obtained as a result of donation of pregnancy tissue after an abortion. Before you give your consent to donate pregnancy tissue, **read each of the following statements and initial the line to the right.** If there is any statement you do not understand, or if you have any questions, someone will discuss them with you.

Before this consent was ever offered to me, I had previously decided to have an abortion and signed an informed consent document. \_\_\_\_\_

I agree to donate the tissue from the abortion and/or miscarriage as a bodily gift to be used for education, research, treatment or the advancement of medical science. \_\_\_\_\_

I understand the donation is made without any restriction regarding who might receive the donated tissue or for what purpose it might be used. \_\_\_\_\_

I have not been informed of the identity of any individual who will receive the tissue that I am donating. \_\_\_\_\_

I understand the method, timing or procedure of abortion cannot and will not be substantively altered for the purpose of obtaining the tissue. \_\_\_\_\_

I understand there will be no payment to me for the donated tissue or for any product, process or service that may result from this donation. \_\_\_\_\_

I understand that I may refuse to donate pregnancy tissue, and this will not affect my current medical care or my ability to get any future medical services at Planned Parenthood of Wisconsin, Inc. \_\_\_\_\_

Signature: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_

Witness: \_\_\_\_\_ Date: \_\_\_\_\_

**Planned Parenthood of Wisconsin  
Ste 23  
111 King St, Madison, WI 53703  
(608) 256-7549**

**Metabolic Gene Profile in Fetuses affected by Aneuploidy**

**DONATION OF ABORTED PREGNANCY TISSUE FOR MEDICAL  
RESEARCH, EDUCATION, OR TREATMENT**

Recent advances in medical science have been developed through research using tissue that has been aborted. This research is being done to treat and find a cure for such diseases as diabetes, Parkinson's disease, Alzheimer's disease, cancer, and AIDS.

Tissue can be obtained as a result of donation of pregnancy tissue after an abortion. Before you give your consent to donate pregnancy tissue, **read each of the following statements and initial the line to the right.** If there is any statement you do not understand, or if you have any questions, someone will discuss them with you.

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I understand there will be no payment to me for the donated tissue or for any product, process or service that may result from this donation. \_\_\_\_\_

I understand that I may refuse to donate pregnancy tissue, and this will not affect my current medical care or my ability to get any future medical services at Planned Parenthood of Wisconsin \_\_\_\_\_

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

Witness: \_\_\_\_\_

Date: \_\_\_\_\_