CONSENT FORM COVER SHEET

Study title: The Effect of Antibiotics on Latency in Previable Prelabor Rupture of Membranes between 18 0/7 and 22 6/7 Weeks Gestational Age

NCT ID: Not yet assigned

Unique Protocol ID: RP-19-001

WH IRB Approval Date: 04/2019

Principal investigator: R. Clifton Moore, MD

You may be eligible to take part in a research study. Taking part in this study is *completely voluntary.* It is up to you whether or not to take part in this research study. Even if you decide to join the study today, you are free to leave at any time if you change your mind.

This form contains information to help you make a decision about whether or not to take part in this study. All of this information is important, but here are some key points to help you make a decision:

- This is research. Medical scientists do research to learn about diseases and how to treat them. Research can be different than regular medical care. The purpose of this study is to determine if a course of antibiotics will help to prolong pregnancy after rupture of membranes (after your water breaks).

- Your time in this study will depend on when your water broke. The maximum time involved with this study would be 5 weeks if your water breaks at 18 weeks of your pregnancy and a minimum of 1 day if your water breaks at 22 weeks of your pregnancy.

- If your doctor finds that your membranes ruptured (your water broke), you will be admitted to the hospital for a 24-hr observation period. If no signs of labor, infection, or vaginal bleeding are noted then you will be discharged with antibiotics (azithromycin and amoxicillin) to take at home. You will be followed very closely with weekly visits in the Maternal-Fetal Medicine office until either you reach 23 weeks of pregnancy or there are no signs of labor, infection, or complications.

- If there are signs of labor or complications, then you will be admitted to the hospital for delivery. If you reach 23 weeks of pregnancy without signs of labor or complications, then you will be further managed by your doctor.

- The main risks for taking part in this study are: reactions to the antibiotic course, risk of infection, risk of the placenta separating from the uterine wall, or risk of problems for your baby.

- The main benefits you may receive if you decide to take part are: opportunity to prolong your pregnancy .

- The other options for you if you decide not to take part are: inducing labor when your water breaks or other management of your pregnancy by your doctor.

Please take the time to read this entire form. Please ask any questions you have about the study. You may also wish to discuss this study with your family, friends, and doctor to help you make a decision about taking part. If you decide to take part in the study, you will be asked to sign this form.

Informed Consent Form

The Effect of Antibiotics on Latency in Previable Prelabor Rupture of Membranes between 18 0/7 and 22 6/7 Weeks Gestational Age

1. **Performance Sites:** Woman's Hospital, 100 Woman's Way, Baton Rouge, LA 70817
2. **Investigators:** Robert Clifton Moore, MS, MD
Primary Investigator
100 Woman's Way
Suite 100
Baton Rouge, LA 70817
(225) 924- 8338

Felicia LeMoine, MD
Co-Investigator
500 Rue de la Vie
Suite 402
Baton Rouge, LA 70817
(225) 215-7960

In case of research injury contact: Felicia LeMoine or R. Clifton Moore
Phone: (225) 924-8338, (225) 215-7960, respectively.

INTRODUCTION
This research is being done on the effects of antibiotics during early pregnancy after your water breaks. Before you decide to take part in the study, please speak with your doctor or the researchers about any questions you have.

3. **Purpose of Study:**

The purpose of this research study is to see if antibiotics, given after your water breaks, before the baby is capable of survival outside of the womb, will increase the number of days that you will remain pregnant before delivery. Secondly, we will see if antibiotics increase the chances that your pregnancy will continue to the gestational age at which the baby can survive outside of the womb. Though we know that antibiotics help increase the chance that a baby will survive once a pregnancy is at a certain point (usually 24 weeks of pregnancy) there are no prior studies that prove antibiotics are, or are not, helpful before this time. Our goal is to see whether or not antibiotics are helpful for women whose water breaks early.

4. **What are the study procedures?**

Your doctor will do an exam to see if your water bag has broken. If your water bag has broken, and you have no signs of vaginal bleeding, infection or contractions and you want to continue with the pregnancy, then you will be admitted to the hospital for overnight observation.

When you are in the hospital, lab work will be done (blood work, urine samples, and vaginal swabs) to see if there is an infection. An ultrasound will also be done to measure the fluid around your baby.

During the 24-hour observation period we will continue to monitor your vital signs (temperature, blood pressure, heart rate, respiratory rate). We will also monitor you for signs of vaginal bleeding, labor (contractions), and/or infection. If you have any problems while you are in the hospital, such as fever or cramping, your doctor will examine you. If your doctor is concerned by any complications, your doctor may induce labor.

If no signs of vaginal bleeding, labor, or infection are noted over the 24-hour observation period, then you will be offered to take part in this research study.

If you consent to take part in this research study, then you will be randomly placed in one of two groups. This placement is done at random, like flipping a coin.

The first group (the control group) will be given the regular treatment for pregnant women whose water has broken.

Those women in the second group (the treatment group) will receive antibiotics. The first dose will be given in the hospital. Then, when you are discharged from the hospital, you will take the antibiotics at home. We will monitor you following your first dose for any reactions to the antibiotics. The antibiotics given in this study are Azithromycin and Amoxicillin.

<u>What are the Possible Side Effects?</u>

The most common side effects of azithromycin are loose stools, diarrhea, and abdominal pain. Other side effects could include, but are not limited to, allergic reaction, heart beat irregularities, liver problems, and renal (kidney) problems. These risks are less common.

The most common side effects of amoxicillin include allergic reactions, skin conditions, and gastrointestinal conditions (nausea, vomiting, *Clostridium difficile* with prolonged use). *Clostridium difficile* is a bacterium that can cause symptoms that range from diarrhea to life-threatening inflammation of the colon.

Other risks include decreased lung development, abnormal facial appearance, and arm/leg/skeletal deformities of the baby if pregnancy is extended for a long period of time before delivery. Also, there is an increased risk of placental separation from the uterus, increased risk of placental pieces remaining inside the uterus after delivery and increased risk of infection inside the uterus when pregnancy is continued for longer periods of time after the water breaking.

<u>Other Study Procedures:</u>

All participants of the study, in both the treatment and control groups, will be given a Patient Information Pamphlet. You will use this pamphlet to track your body temperature. If your temperature is greater than 100.4 degrees at any point, you should go to the Woman's Hospital Assessment Center immediately. Emergency contact information will also be provided in this pamphlet.

If you are placed into the control group (the group not receiving antibiotics), you will also receive the patient pamphlet. You, too, will be expected to monitor daily body temperature and record it into the chart.

Both groups in the study will have weekly follow-up appointments in the Maternal-Fetal Medicine clinic. At these appointments, the clinic staff will record your vital signs (temperature, weight, blood pressure, heart rate, respiratory rate). The doctors will do an exam along with an ultrasound to monitor you and your baby. Fluid around the baby will also be measured at each follow up visit.

If at any point during the study there are signs of infection, vaginal bleeding, or labor, or if the baby appears distressed as seen during monitoring, then you will be admitted to Woman's Hospital Labor and Delivery Unit for further management.

If you remain without any signs of labor or infection, and do not experience any serious side effects during the study, you will be readmitted to Woman's Hospital Labor and Delivery unit at 23 weeks of pregnancy. This will be done for both groups. After you are re-admitted to the hospital, the regular treatment for early rupture of membranes will be given.

Once admitted to the hospital you will stay in the hospital until the time of delivery.

During your time in this study, you will continue to receive routine care from your doctor in addition to your follow up with the Maternal Fetal Specialists as recommended by your doctor.

5. **Benefits to Subjects:**

Possible benefits of this study include prolonging the time before delivery, prevention of intrauterine infections during the period between your water breaking and delivery, and possible improvement in baby outcomes if the pregnancy is able to continue.

6. **Risks to Subjects:**

Possible risks with being in this study include side effects with antibiotic use, including, but not limited to, allergic reactions, cardiovascular (heart) toxicity, liver toxicity, renal (kidney) toxicity, or most commonly gastrointestinal side effects (like diarrhea, nausea, and vomiting).

Other risks include bleeding after placental abruption (when the placenta comes away from the inner wall of the uterus) or bleeding that comes from the placenta staying in place after delivery, which may require surgery. Risks also include infection of the mother and the baby. There is a risk of preterm delivery, which can lead to life-threatening medical problems. Some of these possible problems are serious intestinal disease, bleeding in the brain, sepsis (a dangerous response from your body to infection), eye disease, severe lung conditions, poor lung development, or skeletal deformities.

Psychological risks from being in this study may include distress from preterm delivery, despite trying to prevent early delivery. Referral to appropriate social workers will be part of routine orders at the time of that you are admitted to the hospital. This will be done because there is concern for possible early delivery of your baby when your water breaks early. The doctor can also refer you for more counseling if you show signs of distress, or if you request it.

7. **Alternatives to Participation in the Study:**

The alternative is not to take part in this study.

Doctors do not know which is the best way to treat early rupture of membranes between 18 and 22 weeks. The way this is usually treated is either induction of labor or keeping the woman in the hospital for observation (with or without antibiotics). An alternative to this study is either induction of labor or having your doctor monitor your pregnancy.

8. **Subject Removal:**

The researcher may stop you from taking part in this study if at any time it is believed to be in your best interest, if you do not follow the study procedures, or if the study is stopped. You could be taken off the study if your health worsens, if another treatment option appears to be appropriate, or for any other cause which prevents your continuing in the study.

9. Subject's Right to Refuse to Participate or Withdraw:

Participation is voluntary. Refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. You may withdraw at any time without penalty or loss of benefits to which you are otherwise entitled. If you do not want to take part or you later change your mind and want to withdraw, it will not affect your medical care. Tell the researcher if you are thinking about withdrawing from the study so that you may do so safely. If you decide to withdraw, you should seek medical advice for alternatives. We will give you any new information that might affect your willingness to take part in this study.

10. Release of Information/ Confidentiality:

Organizations that may inspect and/or copy your study-related medical records include: the LSUHSC-NO Institutional Review Board, the Woman's Hospital Institutional Review Board, and the doctors listed on page 1 of this consent form and their staff. While every effort will be made to maintain your privacy, absolute confidentiality cannot be guaranteed. Records will be kept private to the extent allowed by law. There is a risk that someone could trace the information back to you. The researchers believe the chance that someone will identify you is very small, but the risk may change in the future as people come up with new ways of tracing information.

If the results of this study are published, you will not be identified in any way. Your personal information may be disclosed if required by law. We will keep your study records for 10 years and they will be stored in a medical file (marked by your unique patient identifier). The records will be stored within a locked office drawer within a locked medical office. You will be identified by a unique code including the acronym "OAPPPROM patient", your initials, and a unique, randomly generated number. Any data collected from you as part of the research from which identifiers have been removed will not be used or distributed for future research studies.

Some entities may view or copy your study-related information. These entities include: Woman's Hospital Foundation Institutional Review Board, Woman's Hospital Research Department, Woman's Hospital Research and Development Committee, LSUHSC Institutional Review Board, and federal agencies as required by law.

11. Financial Information:

The costs of all drugs and medical supplies will be provided by the Maternal Fetal Medicine Department of Woman's Hospital. The cost of office visits, hospitalization, and complications will be

the responsibility of the participant and the participant's health insurer. The treatment required is felt to be part of good medical care and are, for the most part, covered by most insurance companies. Participation in this study will not result in any extra charges above and beyond those routinely incurred by patients with similar conditions. You will not be paid for your participation as reimbursement for your time and travel.

CONTACTS OF INTEREST

If concerns arise during non-business hours (outside the hours of 8:00 AM and 5:00 PM) please contact the on-call provider associated with your primary obstetrician. If concerns or questions about the study, the terms of enrollment, or any other information regarding the study please contact one of the following:

Dr. Robert Clifton Moore, Maternal-Fetal Medicine Specialist
Primary Investigator
100 Woman's Way
Suite 100 (first floor)
Baton Rouge, LA 70817
(225) 924- 8338

Dr. Felicia LeMoine, LSU OBGYN Resident
Co-Investigator
500 Rue de la Vie
Suite 402
Baton Rouge, LA 70817
(225) 215-7960

For questions about your rights as a research subject, contact Ericka Seidemann, Human Protections Administrator, at (225) 231-5296.

CERTIFICATE OF CONSENT

This study will involve a 24-hour, inpatient observation period at Woman's Hospital followed by daily self-monitoring and weekly Maternal-Fetal Medicine follow-up visits. I am aware that there may be no benefit to me or my baby and that I will not be compensated for my involvement in this study.

I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions that I have asked have been answered to my satisfaction. I have been provided with the name of a researcher who can be easily contacted should question, concerns, or issues arise. Additional questions regarding the study should be directed to the investigators listed on page 1 of this consent form. If I have questions about subject's rights, or want to discuss problems, concerns or questions, or obtain information or offer input, I can contact the Chancellor of the LSU Health Sciences Center New Orleans at (504) 568-4801 and/or Ericka Seidemann, Human Protections Administrator, at (225) 231-5296. I consent voluntarily to participate in this study. I have the right to

withdraw from the research at any time without it in any way affecting my medical care. I acknowledge I have been given a copy of the consent form. I have not waived any of my legal rights by signing this consent form.

_____	_____	_____
Signature of Patient	Date	Time
_____	_____	_____
Signature of Legal Representative	Date	Time
_____	_____	_____
Signature of Witness	Date	Time
_____	_____	_____
Signature of Primary Investigator	Date	Time

The study subject has indicated to me that the subject is unable to read. I certify that I have read this consent form to the subject and explained that by completing the signature line above the subject as agreed to take part.

_____	_____	_____
Signature of Reader	Date	Time
_____	_____	_____
Signature of Witness	Date	Time

A copy of this Informed Consent Form has been provided to participant _____
Investigator Initials

LSU Health Sciences Center

Número de Protocolo/ Protocol Number/Title:
Investigador Principal/Principal Investigator:

Consentimiento para Participar en un Estudio de Investigación Médica:
Consent to Participate in a Clinical Research Study - Spanish

En el presente documento se ha usado "usted" para referirnos al paciente o sujeto de la investigación. Con ello también nos referimos a la persona autorizada para dar consentimiento en relación a la participación del paciente en dicha investigación.

A usted se le ha ofrecido participar en un estudio médico(un tipo de investigación experimental). Solo aquellos pacientes que decidan participar formarán parte de dicho estudio. Le rogamos que se tome el tiempo necesario para decidir y consulte su decisión con familiares y amigos.

Antes de dar su consentimiento, el investigador debe informarle sobre lo siguiente:
1) el objetivo del estudio que se va a realizar;
2) cuántas personas participarán en el;
3) los procedimientos a seguir en la investigación y cuales son experimentales;
4) el tiempo que Ud. va a formar parte de la investigación;
5) los posibles riesgos y molestias;
6) posibles beneficios para Ud.;
7) otras alternativas y opciones;
8) la confidencialidad de la investigación;
9) los gastos que conllevará la participación en el estudio;
10) sus derechos como sujeto/paciente del estudio.
11) personal que puede contactar en caso de tener alguna pregunta o algún problema;
12) la posibilidad de recibir remuneración económica o el debido tratamiento medico, si ocurriera una lesión;
13) posibles circumstancias por las que el investigador pudiera suspender su participación y qué sucede si Ud. decide retirarse del estudio;
14) cuándo se le informaría sobre nuevos resultados que podrian hacerle cambiar de idea sobre su permanencia en el estudio.

En caso de que Ud. accediera a participar, se le daría una copia firmada de este documento y una copia en inglés de su consentimiento para el estudio.

Para cualquier pregunta sobre la investigación o para casos de lesión como resultado de un estudio, póngase en contacto con (nombre) _____ en el (número) _____.
(contact name) (telephone)

Para preguntas sobre sus derechos como paciente en un estudio médico puede ponerse en contacto con el comité examinador institucional de LSUHSC Institutional Review Board, al teléfono 504-568-4060, o al rector de LSUHSC al teléfono 504-568-4801.

Su participación en esta investigación es voluntaria. Si no accediera a participar o se retirara del estudio, la asistencia médica que pueda recibir ahora o en el futuro no se vería afectada, así como tampoco sus beneficios médicos.

La firma en este documento indica que el proceso de la investigación, incluyendo la información anterior, le ha sido presentado oralmente, y que Ud., por su propia voluntad, accede a participar.

_____	_____
Firma del sujeto/paciente Signature of subject/patient	Fecha Date
_____	_____
Firma del testigo Signature of witness	Fecha Date