APPENDIX XXIIIa

SAMPLE INFORMED CONSENT

ACTG 185 Version 5.0: "A Phase III Randomized, Double-blind, Controlled Study of Hyperimmune Anti-HIV Intravenous Immune Globulin (HIVIG) in Prevention of Maternal-Fetal Transmission in Women and Newborns Receiving Zidovudine (ZDV)"

You are being asked to take part in a research study entitled "Use of HIVIG in Prevention of Maternal/Fetal HIV Transmission in Seropositive Pregnant Women Receiving Zidovudine." To decide whether or not you wish to take part in this study, you need to understand enough about the risks and benefits to make an informed decision. This process is called informed consent.

This consent form gives you detailed information about the research study which your doctor will discuss with you. Once you understand the study and if you agree to take part, you will be asked to sign this consent form and you will be given a copy to keep. The father of your baby will also be asked to sign a consent form if, in your opinion, he is reasonably available.

It is really important that you understand the following:

1. Your participation in the study is entirely voluntary.

2. You may refuse to take part in the study or drop out of the study at any time without penalty or loss of benefits to which you are otherwise entitled.

3. A decision to withdraw from the study will not affect your future medical care or possible participation in future research studies.

4. The father of the baby may refuse to give consent and this would prevent the mother's participation in the study.

Nature of the Study:

Women in this study are all pregnant and all infected with the Human Immunodeficiency Virus (HIV or AIDS Virus). HIV can be passed to your baby during your pregnancy, during birth, or after birth through breast milk. It is estimated that for every 100 babies born to HIV-infected mothers, some 15 to 32 of them will become infected with the HIV virus. If infected, the babies are at risk of dying from AIDS during the first years of life. It is not known exactly when the virus can infect an unborn baby or why some babies are infected and others are not.

All of the women in the study are taking Zidovudine (ZDV or AZT) by mouth during pregnancy. The decision about your taking ZDV (AZT) during pregnancy has already been made by you and your doctor prior to this study. The dose of ZDV (AZT) you are taking is set by your doctor, and will be checked by your doctor and changed if needed. The ZDV (AZT) you are taking is not part of the study, and is not supplied as part of the study.

All women in the study will receive ZDV (AZT) intravenously during labor. The intravenous ZDV (AZT) is supplied as part of the study. After your delivery, the decision about continuation of your oral ZDV (AZT) regimen will be made by you and your doctor; your oral ZDV (AZT) is not supplied as part of this study.

In addition, about half of the women in the study will take hyperimmune intravenous immune globulin (HIVIG), a drug containing concentrated antibodies to HIV, and the other half will take intravenous immune globulin (IVIG), a drug without specific antibodies to HIV. The study drug assignment will be done randomly (like flipping a coin) and neither you nor your doctor will know which drug you are taking.

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After your baby is born, your baby will also receive a dose of HIVIG or IVIG (whichever you were receiving) and also will receive ZDV (AZT) for 6 weeks after birth. About half of the infants will take HIVIG and half will take IVIG (whichever you were receiving). All infants will receive ZDV (AZT) for 6 weeks, which is supplied as part of the study, and your infant will be closely monitored for any side effects of the ZDV (AZT).

The purpose of the study is to see if giving HIVIG to women who are taking ZDV (AZT) can lower the chance that a baby will get HIV from his/her mother. Therefore, the group taking HIVIG will be compared to the group taking regular IVIG control to see if there is any difference in the number of babies who become infected from their mothers in these two groups. This is not known at this time.

HIVIG (HIV hyperimmune intravenous immune globulin) is the experimental treatment that is being tested in this study. It is made from the blood of people who have HIV infection but are not sick. Their blood contains substances called antibodies that fight HIV by attaching to it and keeping it from infecting blood cells. The HIV antibodies from this blood are concentrated and treated so that HIVIG contains specific antibodies to HIV, but no live HIV virus and is non-infectious.

IVIG (intravenous immune globulin) is being used as a control drug. It is made from the blood of people who do not have HIV infection, so it has antibodies to some illnesses, but not the HIV virus. It is also concentrated and prepared so that it contains no live HIV virus and is non-infectious.

You are taking a drug called Zidovudine, or ZDV (previously called AZT) because your doctor has decided that it is medically necessary for your own health, based on laboratory tests and your general medical condition. ZDV (AZT) is an antiretroviral drug (a drug that slows or prevents the HIV virus from multiplying). It has been shown to prevent the growth of HIV in non-pregnant adults and children infected with the AIDS virus.

Study Procedures:

If you agree to take part in the study, you will first have some tests to see if you qualify to take part in the study. These tests include a history and physical examination, laboratory tests (including blood tests), and a sonogram (an ultrasound examination of your baby).

During the study, you will be seen by your doctor every 4 weeks for a physical examination and blood tests, through the time of delivery, and at 6, 12, 26, 48 and 78 weeks afterwards. The total amount of blood to be drawn for blood tests during the study will not be more than 153 cc (which is about 5 fluid ounces). Some of the blood will be saved and stored for further testing. A sample of the placenta may also be saved for testing.

You will receive the study medication (either HIVIG or IVIG) intravenously (into your vein) every 4 weeks until delivery. The amount of drug will vary with your weight; for example, a 130-pound woman would receive about 8 ounces (1 cup) of drug at each infusion. During your labor and delivery, you will receive ZDV (AZT) intravenously (into your vein) until your baby is born. After delivery of your baby, you and your doctor will decide about continuation of the ZDV (AZT) by mouth you were taking during your pregnancy. Your oral ZDV (AZT), during pregnancy or afterward, is not part of this study. You will not receive HIVIG or IVIG after delivery.

Your baby will be examined at birth, and if his/her medical condition indicates that he/she is eligible to continue the study, the baby will be given HIVIG or IVIG (whichever one you were given during pregnancy) by vein during the first twelve hours after birth. For example, a 7 pound baby would receive slightly less than 3 teaspoons of drug over a period of 1 1/2 hours. If the drug is given more slowly, the infusion will take longer. Your baby will also be given ZDV (AZT) every 6 hours, beginning 8 to 12 hours after birth, either by mouth (as a flavored syrup) or by vein (if your baby is not taking liquids by mouth yet). Your baby will take the ZDV (AZT) syrup every 6 hours for a total of 6 weeks. In addition to being examined at birth, blood samples will also be drawn. The blood sample will be taken from the umbilical cord and your baby's vein. After you and your baby go home from the hospital, your baby will be seen for physical examinations

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at: 1 week of age, 2 weeks, 6 weeks, and at months 3, 4, 5, 6, 9, 12 (1 year), 15, and 18. Blood tests will be taken at some of these visits to check for any side effects of the medicine or signs of HIV infection. The total amount of blood to be drawn from the baby for blood tests during the study will not be more than 80 cc's which is less than 3 fluid ounces. Some of the blood will be saved and stored for further testing.

Risks to You, the Mother:

HIVIG has not been used in HIV infected pregnant women. It has been tested in animals and a small number of adult males with HIV infection. The results suggest that HIVIG is non-toxic and as safe as IVIG, which has been used in pregnancy and in the newborn. Side effects that can occur in some people who receive HIVIG or IVIG include: fever, chills, backache, flushing, redness or swelling of hands or feet, vomiting, muscle aches, tiredness, changes in vital signs, rash and itching, and, rarely, shock. These side effects are usually related to the rate (speed) at which the medication is given. Very rare but reported side effects include hemolysis (breakdown of red blood cells), thrombosis (development of blood clots), lung or kidney abnormalities, or aseptic meningitis. Although the HIVIG or IVIG used in this study is made so as to be as sure as possible that it is safe, there is always a small but real risk that any product made from blood could transmit germs that cause infections (such as hepatitis).

The decision about you taking zidovudine (ZDV or AZT) by mouth during your pregnancy has been made by you and your doctor before this study, and is not part of this study. You and your doctor have discussed that ZDV (AZT) has not been approved for general use in pregnant women. The major side effect seen in adult patients taking ZDV (AZT) is anemia (a decrease in the number of red blood cells in your blood) that may in some instances cause premature labor. A decrease in hemoglobin (the part of the red blood cell that carries oxygen from the lungs to the tissues) and a decrease in the number of white blood cells could reduce your body's ability to fight infection. Minor side effects have included nausea, vomiting, and dizziness.

The ZDV (AZT) you receive by vein during labor is part of this study. The intravenous ZDV (AZT), like oral ZDV (AZT), is approved for use in adults who are infected with the HIV virus who are not pregnant. The side effects of intravenous ZDV (AZT) are the same as ZDV (AZT) by mouth. An IV infusion may cause some discomfort, bleeding, swelling, or bruising at the site of entry of the needle, as can drawing of blood samples. There is also a slight chance of infection.

Risks to the Fetus:

Information on the effects of HIVIG on the unborn baby is not yet known. HIVIG, in the laboratory, has been noted to increase HIV infection of cells. This effect was not present at higher concentrations of HIVIG, such as that used in humans. In tests of HIVIG in HIV-infected persons, no increase in virus multiplication has been observed, but rather a decrease in viral multiplication has been seen. The dose of HIVIG used in this study should provide antibody levels 10,000 times greater than the antibody level seen to increase infection in cell culture. However, HIVIG has not been used in pregnant women, and, while unlikely, it may be possible that HIVIG could increase the risk of HIV infection of the fetus.

However, there is significant experience with the use of IVIG in pregnant women; HIVIG and IVIG differ only in that HIVIG contains concentrated HIV antibodies. There have been no bad effects (miscarriages, fetal deaths or abnormalities) reported in pregnancies or children born to mothers who have received IVIG during pregnancy. Although the HIVIG or IVIG used in this study is made so as to be as sure as possible that it is safe, there is always a small but real risk that any product made from blood could transmit germs that cause infections (such as hepatitis).

The decision about your taking ZDV (AZT) during your pregnancy has already been made by you and your doctor. Although your unborn baby is at risk of developing anemia and a low white blood cell count from ZDV (AZT), data from earlier studies suggest that this occurs infrequently and does not harm the newborn. The long term effect ZDV (AZT) may have on your unborn baby is not known.

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Risks to Your Baby:

The major side effects of Zidovudine (ZDV or AZT) in children is anemia and low white cell count, but this usually occurs when the drug is taken for more than 6 weeks. The possible side effects of HIVIG or IVIG for a child are the same as those mentioned above for adults. In addition, protection against childhood illnesses (such as polio, diphtheria, whooping cough, tetanus, and other diseases) by vaccines (immunizations) your child receives as part of regular medical care may be reduced (that is, the risk of these illnesses may be increased by HIVIG or IVIG). HIVIG or IVIG may decrease the effect of vaccines (immunizations) your child receives. It is not known what long term effects of HIVIG in newborns there might be. Drawing of blood or an IV infusion may cause some discomfort, bleeding, swelling, or bruising at the site of entry of the needle. There is also a slight chance of infection. Although the HIVIG or IVIG used in this study is made so as to be as sure as possible that it is safe, there is always a small but real risk that any product made from blood could transmit germs that cause infections (such as hepatitis).

Benefits to You and Your Baby:

HIVIG and Zidovudine (ZDV or AZT) may help in fighting your HIV infection during pregnancy and possibly help prevent transmission of the HIV from you to your baby. At this time, it is not known if there is any benefit from the experimental treatment provided in the study. HIVIG and IVIG both contain antibodies to other infections and may help prevent or fight infections that you and your baby have or get.

Confidentiality of Records:

Research records of you and your baby's participation in the study will be kept confidential to the full extent of the law, and will not be released without your written permission. Your and your baby's research records will be identified only by a code number, and the code will be stored in a secure place with access only to clinic staff and designated staff from the Food and Drug Administration (FDA). Medical records which identify you or your baby by name may be inspected by monitoring personnel from the FDA, the National Heart, Lung, and Blood Institute (NHLBI),the National Institute of Child Health and Human Development (NICHD), the National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS (DAIDS), and the manufacturer of the study drugs, but confidentiality will be maintained to the extent permitted by law. You or your baby will not be identified by name in any publication or presentation resulting from this study.

Circumstances for Withdrawal from the Study:

You or your baby's participation in this study may end for the following reasons:

1. Voluntary withdrawal on your part.
2. Worsening health or other conditions that might make continued participation harmful to you or your baby.
3. Failure to keep appointments or take medications as instructed.
4. A serious reaction to the study drug.
5. Ending of the study by the study sponsor.
6. If the father of the baby withdraws consent for your participation in the study.

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Safeguards:

You and your baby (before and after birth) will be carefully evaluated during the study. Your doctor will carefully check all results of you and your baby's tests to ensure the safety of the study. In addition, any adverse (bad) side effects will be reported and reviewed by a panel at the National Institutes of Health (NIH).

Alternatives to Participation:

There is no known treatment available at this time that has been proven to prevent the transmission of the HIV virus from mother to infant during pregnancy and delivery in women who are receiving ZDV for their own health, who have CD4 counts 200 or below, or both. In pregnant HIV infected women who have not received antiretroviral treatment during their current pregnancy, who do not need antiretroviral treatment for their own health, and who have CD4 counts above 200, zidovudine treatment beginning after 13 weeks of pregnancy, during labor and delivery, and of the newborn for 6 weeks has been shown to reduce the risk of transmission of HIV by two-thirds (from 25.5% to 8.3%). HIVIG is an investigational new drug and is not available for general use.

Policy Regarding Research Related Injuries:

Immediate necessary care is available if you or your baby become injured due to participation in this study. However, no financial compensation will be given to you by (Name of Institution), the study drug manufacturers, NHLBI, NICHD, or NIAID. Treatment will be at your expense or the expense of your insurance carrier.

Significant New Findings:

You will be notified of any new findings or discoveries that occur during the study that could affect your willingness to take part in the study.

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Problems or Questions:

If you have any questions about this study or your rights as a participant, you should contact your doctor, who is the principal investigator responsible for safeguarding your welfare and the welfare of your baby, or the Institutional Review Board (IRB) of the hospital where the study is being conducted, at the following:

_____
(Name of Investigator)

OR

_____
(Name of Clinic Nurse or Coordinator)

Phone: _____

Address: _____

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OR

_____
(Name of IRB Contact Person)

Address: _____

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Statement of Consent:

The purpose of the study, the procedures to followed, and risks and benefits have been fully explained to me. I understand that I may withdraw my participation or my baby's participation at any time without affecting my rights or those of my baby to receive medical care.

Name* (print or type)	Signature*	Date
*Volunteer's name or that of legal representative or guardian, as appropriate.		
Witness' Name (print or type)	Witness' Signature	Date

Father* (print or type)	Father's Signature*	Date
*If reasonably available.		
Witness' Name (print or type)	Witness' Signature	Date

I have explained the purpose of this study to the patient. To the best of my knowledge, she understands the purpose, procedures, risks, and benefits to her and her baby.

Investigator Name (print or type)	Investigator Signature	Date