CONSENT FORM

Protocol ID: MRCZ/A/1968

Brief Title: University of Zimbabwe College of Health Sciences Birth Cohort Study

Acronym: UZ-CHS-BC

Official Title: HIV Exposure, Disease Acquisition and Progression among Children: Role of Maternal Immunogenetics, Viral Genetic Diversity, HAART Exposure, Co-morbidities and Psycho-Social Status: UZ-CHS Birth Cohort.

Principal Investigator: Kerina Duri (*PhD*)
Department of Immunology
University of Zimbabwe
College of Health Sciences
Harare

INFORMED CONSENT FORM
UNIVERSITY OF ZIMBABWE COLLEGE OF HEALTH SCIENCES
DEPARTMENT OF IMMUNOLOGY

HIV EXPOSURE, DISEASE ACQUISITION AND PROGRESSION AMONG CHILDREN: ROLE OF MATERNAL IMMUNOGENETICS, VIRAL GENETIC DIVERSITY, HAART EXPOSURE, CO-MORBIDITIES AND PSYCHO-SOCIAL STATUS: THE UZ-CHS BIRTH COHORT

Principal Investigator: Kerina Duri (*PhD*)
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Purpose

This is a research project being conducted by Dr. K. Duri, a lecturer from the University of Zimbabwe, Department of Immunology, College of Health Sciences. You are being invited to take part in the above-mentioned research study because you are pregnant and registered at this clinic, which is one of our study clinics. The main aim of this study is to see how mother's illnesses such as cytomegalovirus, hepatitis B and C viruses including intestinal parasites, nutritional status, diabetes, high blood pressure, heart problems, ability to fight diseases, her general life style during pregnancy including or genetic make-up may affect her baby's growth and ability to fight diseases consequently, affecting disease acquisition and death rates. Biological specimens such as blood, cord blood, amniotic fluid, urine, stool and breast milk will be used to test for disease causing germs and ability of the body to fight diseases. Participation in the study starts at enrolment during pregnancy. Your child will be automatically recruited into the study upon delivery. You and your baby will be followed up as mother-baby pair until your baby is 24 months (2 years) old. The baby will be examined to see if he or she is growing well and blood samples will be checked for germs and the baby's body's ability to fight them.

All the laboratory tests will be done locally at the University of Zimbabwe College of Health Sciences, (UZ-CHS) laboratory except for more advanced test involving immune cells called natural killer cells and some host-viral genetics tests whose specimens will be shipped to South Africa, and Europe for further analysis due to lack of expertise and appropriate techniques locally. Genetic testing of the susceptibility genes will be done should you seroconvert during the course of the study. However, the study, with your permission will store the collected leftover mother-baby pair biological specimens namely stool, breast milk, blood and cord blood for future related sub-studies. Left over biological specimens will be disposed after testing in line with local regulations.

Several related sub-studies are anticipated from which health professional with relevant expertise will get to the bottom of these different aspects of research. Such sub-studies will be developed that will determine the role of other illnesses not covered in the main study but are known to contribute significantly to maternal and child illnesses and deaths. These include among other diseases; TB and bacterial vaginosis infections, viruses such as human simplex virus (HSV) including human papilloma virus (HPV) which is associated with cancers. In addition, studies to determine how maternal exposure to drugs such as antiretroviral drugs (ARVs) including stress and depression during pregnancy affect the child growth and development will be developed. Your permission will be sought from you for the sub studies to use your left-over specimens from this main study so that you won't be bled now and again. Permission to conduct these sub-studies will be sought from you and the local regulatory authority–Medical Research Council of Zimbabwe (MRCZ).

Findings from this study will contribute evidence based new knowledge for the better management and care of mothers and their infants at the same time building capacity among health care providers and students at the UZ-CHS and beyond.

Who Can Participate?

You can only participate in this study if you meet the inclusion criteria. Thus you qualify to participate in the study only if you:

- Are within 28-40 weeks (7-10 months) of pregnancy
- Are planning to deliver at any of the City of Harare Poly clinics
- Know your HIV status (documented HIV test)
- Give permission for your child to be enrolled in the study upon delivery.
- And your baby are willing to provide the required biological specimens, blood, cord blood, amniotic fluid, urine, breast-milk and stool which will be collected at different intervals.

How Many People Are Required?

The study will recruit 600 HIV negative pregnant mothers and 600 HIV positive pregnant mothers totalling 1200 pregnant women within the City of Harare Polyclinics. All HIV positive pregnant mothers are encouraged to participate in the study. For every HIV positive pregnant mother recruited, the 10th HIV negative mother will be enrolled into the study as it will be impossible to recruit all HIV negative mothers.

What Will I be asked to do if I Agree to Participate?

An explanation of the study and its requirements will be given after which you will make an informed decision on whether to participate or not. If you meet the inclusion criteria of the study and wish to participate, the study will commence upon your signing of the informed consent form (ICF) at enrolment which is valid up to 24 months post-delivery. Upon enrolment you will be expected to be willing to:

- Allow you and your child to participate in this study for up to 24 months after delivery
- Provide together with your baby, all the required specimens (urine, stool, blood, cord blood, amniotic fluid, breast milk) for testing of comorbidities, and immune factors,. See **Table 1** below.
- Have mother's blood specimen collected with a needle from a vein on the arm whilst from the baby, a heel prick will be done to minimise pain and discomfort at birth switching to venous blood as the child grows from two months of age.
- Collect broken waters and have midwife collect the baby's cord blood. See **Table 1** for the volumes needed. You will be given a sterile bottle where you will collect the broken waters which you will bring along to the clinic. The bottle must only be opened just before use and you will be taught by the study staff on this process.
- Have stool and urine samples mainly for examination of pathogens collected at enrolment and subsequently at every six months interval.
- Have your breast-milk collected which will be used to assess immune factors from day 10 post-natal up to weaning or last visit depending on which one comes first.
- Have you and your baby, at every visit, undergo a full physical examination by the study doctor, midwife or nurse to exclude any possible illnesses and biological samples collected.
- Make a total of 11 visits with the first one happening during pregnancy. The visits will as much as possible be designed to coincide with the routine baby clinic days depending on your date of delivery. You may be stopped from participating at any time without your consent if you consecutively fail to turn up for at least two successive scheduled study visits for any unknown reason(s).

- Have you and your baby's left-over biological specimens disposed of after testing according to local regulations.
- Spend approximately 45-60 minutes with study doctor or nurse on every visit you make to the clinic.

What will be done on every Visit?

(i) **Mother**:
- A questionnaire will be administered that includes socio-economic and dietary issues as well as history and current illnesses and past pregnancy (ies) if you had any.
- Physical examination will be done at every visit.
- From visit 2 (delivery) onwards, all HIV negative mothers will be re-tested for HIV infection on every visit up to close out.

(ii) **Baby**
- Physical examination will be done at every visit and questionnaire addressing issues to do with baby growth and development will be administered
- All negative HIV exposed babies will be re-tested for HIV infection at every visit until they are weaned or at visit 11.

Table 1. Mothers Visits, Specimens and Respective Volumes Required.

		Specimen					
Visits		**Blood**	**Cord Blood**	**Breast Milk**	**Urine**	**Amniotic Fluid**	**Stool**
1	HIV+	✓30 mL	-		✓50 mls		✓ (20 g)
	HIV-	✓25 mL			✓50 mls		✓ (20 g)
2	HIV+	✓10 mL	✓50 mls		✓50 mls	✓50 mls	✓ (20 g)
	HIV-	✓5 mL	✓50 mls		✓50 mls	✓50 mls	✓ (20 g)
3	HIV+	✓5 mL	-	✓10 mls	-	-	
	HIV-	✓5 mL					
4	HIV+	✓20 mL	-	✓20 mls	✓50 mls	-	✓ (20 g)
	HIV-	✓10 mL			✓50 mls		✓ (20 g)
5	HIV+	✓20 mL	-	✓20 mls	-	-	
	HIV-	✓10 mL					
6	HIV+	✓20 mL	-	✓20 mls	-	-	
	HIV-	✓10 mL					
7	HIV+	✓20 mL s	-	✓20 mls	✓50 mls	-	✓ (20 g)
	HIV-	✓10 mL			✓50 mls		✓ (20 g)
8	HIV+	✓20 mL	-	✓20 mls	-	-	
	HIV-	✓10 mL					
9	HIV+	✓20 mL	-	✓20 mls	✓50 mls	-	✓ (20 g)
	HIV-	✓10 mL			✓50 mls		✓ (20 g)
10	HIV+	✓20 mL	-	✓20 mls	✓50 mls	-	✓ (20 g)
	HIV-	✓10 mL			✓50 mls		✓ (20 g)
11	HIV+	✓20 mL	-	✓20 mls	✓50 mls	-	✓ (20 g)
	HIV-	✓10 mL			✓50 mls		✓ (20 g)

*Generally blood samples, amniotic fluid cord blood and breast milk will be tested for trend in immune profiles and coinfections.

**Stool samples will be tested for intestinal parasites and microbiota

*** Urine for urinalysis, microbiota

Infants' Visits, Specimens and Respective Volumes Required

Specimens					
Visits		**Blood**	**Stool**	**Urine**	PBMCs*
1	HIV+	3.5 mL	✓ (20 g)	✓20 mL	
	HIV-	2.5 mL	✓ (20 g)	✓20 mL	
2	HIV+	3.5 mL	✓ (20 g)	✓20 mL	
	HIV-	2.5 mL	✓ (20 g)	✓20 mL	
3	HIV+	3.5 mL		-	
	HIV-	2.5 mL			
4	HIV+	3.5 mL	✓ (20 g)	✓20 mL	
	HIV-	2.5 mL	✓ (20 g)	✓20 mL	
5	HIV+	3.5 mL		-	
	HIV-	2.5 mL			
6	HIV+	5 mL		-	
	HIV-	5 mL			
7	HIV+	5 mL	✓ (20 g)	✓20 mL	
	HIV-	5 mL	✓ (20 g)	✓20 mL	
8	HIV+	5 mL		-	
	HIV-	5 mL			
9	HIV+	5 mL	✓ (20 g)	✓20 mL	
	HIV-	5 mL	✓ (20 g)	✓20 mL	
10	HIV+	5 mL	✓ (20 g)	✓20 mL	
			✓ (20 g)	✓20 mL	

Generally blood samples will be tested for trend in immune profiles and coinfections.
**Stool samples will be tested for intestinal parasites
*** Urine for urinalysis
****5 mL of EDTA blood for PBMC from infants born from mothers with acute HIV infection for NK cell phenotyping, ONLY for babies of mothers will get HIV infection after enrolling into the study

WHAT ARE THE RISKS AND DISCOMFORTS OF THIS STUDY?

There may be some risks and discomforts from participating in this research study when people interact and talk about self or others carry some amount of risks.

The sensitivity of HIV and sexuality issues means that your emotional response is a potential risk. Anxiety associated with sample testing and waiting for the results may also be experienced. However, the specimen turnaround time will be minimal. Nevertheless the study will minimize such risks wherever necessary by referring you for counselling clinic including referral should need arises.

You may experience some pain and bruising from the needle prick during blood draw. However, new needles will be used for each participant so that there is no risk of transmitting diseases. Genetic test results may be another risk should they happen to be known by other third parties.

However, efforts will be put in place to avoid such mishaps. You will be told in a timely manner of any significant findings or any information that becomes available that may affect you and your baby's health. The study doctor will attend to you or refer you for further treatment if need arises. There is no anticipated risk to your pregnancy or unborn child as this is an observational study only. Nothing will be administered to you either during pregnancy and or at child birth. However, in case of death of the mother, re-consenting from the father or any family member who shall have legal responsibility for the care and custody of the baby will be done. However, in case of a child death, the mother will cease to continue participating in the study.

WHAT ARE THE BENEFITS OF THIS RESEARCH AND/OR COMPENSATION?

Participation in this study is entirely voluntary. There are no direct benefits or payment for taking part in the study. You will not be paid for participating in the study. You will however, be reimbursed for transport. A transport reimbursement amount equivalent to the value of US $5 will be given to you per clinic visit. This research is not designed to help you personally, but the results may help the investigator learn more and hope that new/alternatives for disease diagnosis and care could be established. Thus, future pregnant mothers and babies may benefit. Health education and counselling on pregnancy, delivery and childcare will be given to each mother on a continuous basis on each visit. You will be screened for many illnesses and viral load test is available for the HIV infected. The study will offer consultation and basic treatment to both the mother and child. Whenever necessary, referrals will be made through the clinic referral system.

CONFIDENTIALITY

We will do our best to keep your personal information confidential. To help protect your privacy, all records containing information about you obtained while you are in this study, as well as other related medical records will remain confidential at all times except to the study team, study monitors MRCZ and Research Council of Zimbabwe (RCZ). By signing this form you are granting the above mentioned individuals and organisations access to your personal information. No name will be written on any document. You and your baby will be identified only by a code/number. No persons other than the research staff will have access to any information that identifies you or your child individually or directly. Your name and identity will not otherwise be revealed except as may be required by laws. In addition, the findings of this study will be published for scientific purposes but your name and identity will never be revealed.

VOLUNTARY PARTICIPATION AND WITHDRAWAL FROM THE STUDY

Participation in this study is voluntary. If you decide to participate in this study, your decision will not affect you or your future treatments or consultations at this clinic and associated hospitals or relations with local health personnel. You and your child are free to withdraw your consent and discontinue participation at any time without losing any benefits to which you are otherwise entitled to. The participants will be reminded that they may not answer questions that they are not comfortable with or even terminate the interviews at any stage without having to necessarily explain such actions.

You may choose not to participate in this study or may withdraw from this study at any time for any reason without penalty or loss of benefits to which you are otherwise entitled. If you decide to withdraw from this study or you do not want your samples to be stored for future use, contact the study team. You do not necessarily have to explain why you do not wish to continue. However, if you withdraw from this study at any time, data and specimen collected prior to withdrawal may still be processed. Please note that the study personnel may remove you from the participation at any time without your consent if you consecutively fail to turn up for at least two successive scheduled study visits for any unknown reason(s).

The study is receiving funding from Wellcome Trust through the University of Zimbabwe, College of Health Sciences Research Support Centre.

WHAT IF I HAVE QUESTIONS?

If you have any questions concerning this study or consent form beyond those answered by the investigator including questions about the research, your rights as a research participant or research-related injuries; contact the Study Principal Investigator : Dr. K. Duri at the University of Zimbabwe, College of Health Sciences, Department of Immunology or telephone 04 791631 or +263772876965 or if you feel that you have been mistreated and would like to talk to someone other than a member of the research team. Please feel free to contact the MRCZ on telephone (04)791792 or (04) 791193 or cell phone number +263779 439 564. The MRCZ Offices are located at the National Institute of Health Research premises at Corner Josiah Tongogara and Mazowe Avenue, Harare.

YOU WILL BE GIVEN A COPY OF THIS PARTICIPANT INFORMATION SHEET TO KEEP.

Signature Page

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HIV EXPOSURE, DISEASE ACQUISITION AND PROGRESSION AMONG CHILDREN: ROLE OF MATERNAL IMMUNOGENETICS, VIRAL GENETIC DIVERSITY, HAART EXPOSURE, CO-MORBIDITIES AND PSYCHO-SOCIAL STATUS: THE UZ-CHS BIRTH COHORT

Principal Investigator: Kerina Duri (*PhD*)
Phone number: 791631 extension 2428
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By signing this form I am agreeing to the following:

- I have read and/ or the study has been read and explained to me in a language that I understand. All my questions pertaining the study have been answered to my satisfaction.
- I understand that participation in this study is voluntary; I may decide to participate or not participate without losing any benefits that may be entitled to me at this clinic.
- I understand that I may withdraw from the study at any time without giving a reason and without fear of negative consequences or loss of benefits.
- I have given permission to allow my unborn child to be enrolled into the study upon delivery and be followed up together as mother baby pairs for 24 months.
- I understand that some of my biological specimen blood, cord blood, amniotic fluid breast milk and stools collected will be stored for sub-sub studies and/or other future use
- I understand that some of the laboratory examination will be done in South Africa and Europe

AUTHORIZATION: I give permission for: (*Tick in the appropriate box)*

1. Myself and my baby (after delivery) to **participate** in the study; Agree☐ Disagree ☐
2. Myself and baby biological specimen such as blood, cord blood, amniotic fluid, urine, stool and breast milk to be **stored and used in sub studies** Agree☐ Disagree ☐
3. Myself and my baby's specimens such as blood, cord blood, amniotic fluid, urine, stool and breast milk to be **externally shipped to South Africa and Europe.** Agree☐ Disagree ☐
4. **Genetic testing** of my sample and those of my baby Agree☐ Disagree ☐

Name of Research Participant (please print)	Signature of Participant	Date
Illiterate Participant thumb print:		
Name of Witness / impartial witness if necessary	Signature of witness	Date
Name of Staff Obtaining Consent	Signature of staff	Date