AN EVALUATION OF FALSE POSITIVE HIV RESULTS DUE TO TESTING ERRORS

City Health department
Harare, Zimbabwe

Médecins sans Frontières
Harare, Zimbabwe

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CONTENTS

1.0 SUMMARY

1.1 TITLE

Evaluation of false positive HIV results due to testing errors

1.2 BACKGROUND

An unacceptably high frequency of false positive HIV test results has been reported in various settings. Given the severity and implications of an HIV+ diagnosis, a false positive result is likely to be psychologically traumatic and may result in inappropriate and potentially harmful treatment. The current HIV testing algorithm being used in Zimbabwe does not include repeat testing for HIV positive results, and it is not currently known whether testing errors are leading to false positive diagnoses at a significant rate. WHO recommends that an additional specimen for testing be collected at some point after the initial diagnosis is made. This procedure aims to rule out possible technical or clerical errors including specimen mislabelling and transcription errors[1].

1.3 STUDY OBJECTIVE

To evaluate the number of false positive HIV results due to testing errors, using the WHO retesting recommendations, in 6 clinics in Harare, Zimbabwe.

1.4 RATIONALE

The study will determine the accuracy of using 2 rapid diagnostic tests only for the diagnosis of HIV infection in an adult population in Harare. The study will directly benefit the study participants as the WHO HIV testing algorithm aims to reduce the number of false positive results. The results of this study can be used to advocate for the revision of the current national HIV testing algorithm, if required by the findings.

1.5 DESIGN

This is a prospective observational cohort study. All participants who test HIV positive at all the study sites will be invited to participate in the study. Repeat testing is done at a central laboratory by a laboratory technician using the same tests used by the primary sites. The participants are then referred appropriately as per standard of care after receiving the laboratory results. Those confirmed to be HIV positive in the laboratory are referred to the

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1 'It is usual best practice to obtain an additional specimen after a time interval (i.e. not the same day) to retest all newly diagnosed individuals. Retesting is usually performed as part of the clinical and laboratory-based assessment of treatment eligibility and entry to care. This procedure aims to rule out possible technical or clerical errors including specimen mislabelling and transcription errors'. Service delivery approaches to HIV testing and counselling (HTC): a strategic HTC policy framework. WHO, 2012.

OIC as per standard of care. Those found to be HIV negative are counselled and referred to have another testing after 3 months as per standard of care.

1.6 DURATION

Recruitment of participants is expected to last 6 months. Data analysis will last 4 weeks. The dissemination of results is expected to take 4 weeks at most.

1.7 SAMPLE SIZE

3,500participants will be recruited, which will confirm a positive predictive value of using the 2 rapid tests of 99.99%.

1.8 POPULATION

All clients attending the clinics for PITC services at the 6 primary sites who test HIV positive using the serial testing algorithm.

1.9 RISKS AND BENEFITS

The chances of being given a false positive result are reduced. The same sample which is used for baseline tests (e.g. CD4 count) will be used for confirmation; therefore there is no need for an extra sample to be collected. The results of this study can benefit other people in future being tested for HIV, as the results can be used to lobby that HIV results be repeated in the laboratory, if this is reflected in the study findings.
There are no risks additional from the study. The HIV retesting will be done on the same sample collected for CD4 count as per standard of care.

1.9.1 DISSEMINATION OF RESULTS

The results will be disseminated locally and internationally. The purpose is to improve the quality of HIV results being disseminated to the clients

2**. 0 PROTOCOL TEAM ROSTER**

2.1 Principal Investigators

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3.0 PROTOCOL SPECIFIC GLOSSARY OF TERMS

3.1 ABBREVIATIONS

AIDS Aquired Immune Deficiency Syndrome
ART Anti-Retroviral Treatment
CI Confidence Intervals
CT Counselling and testing
EIA Enzyme Immunoassay
ELISA Enzyme Linked Immuno Sorbent Assay
ERB Ethics Review Board
HIV Human Immunodeficiency Virus
LIA Line Immunoassay
MoHCW Ministry of Health and Child Welfare
MSF Médecins sans Frontières
MRCZ- Medical research Council of Zimbabwe.
OCA Operational Centre Amsterdam
PMTCT Prevention of Mother to Child Transmission
PPV Positive Predictive Value
RDT Rapid diagnostic test
VCT Voluntary Counselling and Testing
WB Western Blot
WHO World Health Organization

4.0 SITES PARTICIPATING IN THE STUDY

6 PITC centres located in Harare

1. Rutsanana Polyclinic
2. Mabvuku Polyclinic
3. Hatcliffe Polyclinic
4. Hatfield clinic
5. Budiriro Polyclinic
6. Mbare Polyclinic

5.0. STUDY OBJECTIVES

5.1 Overall Study Objective

To quantify false positive HIV results due to testing and recording errors, using the WHO retesting recommendations, in 6 clinics in Harare, Zimbabwe.

6.0 INTRODUCTION

6.1 Background and Literature Review

RDTs for the detection of HIV antibodies are mostly used in counselling and testing (CT) services, PITC services, prevention of mother-to-child-transmission (PMTCT) initiatives and nowadays also in mobile units [1]. RDTs are simple in that they need little or no equipment, and fast in that results are mostly available within 15-20 minutes. Most RDTs have very few manipulation steps, can be read visually and be carried out at ambient temperature. Often kits can be stored between 2 °C and 30 °C. These characteristics make RDTs the ideal assay in resource- limited settings where the infrastructure and human resources do not support the use of more complex techniques such as ELISA or confirmation test (i.e. Western Blot and line immunoassay).

The development of RDTs that can detect HIV antibodies in whole blood in addition to serum and plasma has allowed the use of these assays in situations where the necessities such as electricity, equipment (e.g. centrifuge) and skilled personnel (e.g. nurses, laboratory technicians, doctors) are lacking (2).In Zimbabwe, HIV testing is done largely by VCT and PITC institutions using RDTs. The algorithm for testing is defined as serial testing using Determine HIV 1 /2 as the first test and First Response HIV 1-2 as the second test (14). By 2011, a total of 1390 testing sites had been established; these sites performed a total of 1,832,222 tests in the same year (12).

Although HIV RDTs are regularly evaluated by the WHO, with highly sensitive and specific results (e.g. Determine, First Response on whole blood specimens with final sensitivity of 100.0% for both tests and a specificity of 99.4% for Determine® and 98.8 First Response [2], a frequency of false positive test results as high as 10.6% has been reported within some MSF missions [3]. In Uganda in another study, specificity as low as 94.1% and positive predictive value as low as 74.0% were encountered[4], and in the same country in another

study, out of a total of 507 positives, 33 where found to be false positive. [8]. In Tanzania, Determine was found to exhibit low specificity (for blood) giving rise to a high level of false positives (11). Given the severity and implications of an HIV+ diagnosis, a false positive result is likely to be psychologically traumatic and may result in inappropriate and potentially harmful treatment.

Zimbabwe uses a serial testing algorithm which includes Determine as the first test and First Response as the second test. These can be interchanged depending on clinic stock status. The tie breaker in either case is Insti or Combior. This algorithm does not include repeat testing for HIV positive results (14). In addition, an evaluation of the counseling and testing (CT) false positive rates in primary care polyclinics has never been undertaken in Zimbabwe.

WHO in 2012 recommended a testing strategy in high prevalence settings (prevalence above 5%): "All specimens are first tested with one assay, and specimens that are non-reactive (A1−) are considered HIV-negative and reported as such. Any specimens that are reactive on the first assay (A1+) should be tested again using a different assay. For specimens that are reactive on both the first and the second assays (A1+; A2+), the result should be reported as HIV+ positive. These individuals should be referred for assessment of their eligibility for treatment and entry to care, if these services are not available at the testing site".
WHO further recommends that "It is usual best practice to obtain an additional specimen after a time interval (i.e. not the same day) to retest all newly diagnosed individuals. Retesting is usually performed as part of the clinical and laboratory-based assessment of treatment eligibility and entry to care. This procedure aims to rule out possible technical or clerical errors including specimen mislabelling and transcription errors" (13).

6.2 STUDY RATIONALE

Zimbabwe is a high prevalence setting as the current HIV prevalence is 14.90% among adults aged 15-49 years (12). WHO recommends that it is good practice that HIV retesting be done on all newly diagnosed patients. Retesting is usually performed as part of the clinical and laboratory-based assessment of treatment eligibility and entry to care. This procedure aims to rule out possible technical or clerical errors including specimen mislabelling and transcription errors. This study aims to quantify false positive results arising from the 6 PITC centres and hence define the benefit of the new WHO guidelines.

The study will directly benefit the study participants as the WHO HIV testing algorithm aims to reduce the number of false positive results.
The results of this study can be used to inform policy.

7.0 Methodology

All clients participating in the study will be receiving HIV testing and counselling services according to the national algorithm currently being used. The study protocol will not change

the testing protocol used by the site for routine PITC. However, each client will be offered re-testing which will be done on blood collected for CD4.

7.1 Study Design

This is a prospective observational cohort study to establish the occurrence of false positive results in 6 clinics of the Harare City Council.

7.2 Sample Size

The sample size is projected to be 3,500, which will confirm a positive predictive value of the serial testing algorithm of 99.9% (95% CI 99.80-100.0%). It is foreseen that recruitment of this quantity of patients will be done over a 6-month period.

7.3 Study Duration

The recruitment is expected to run from June 2013to Dec 2013. Data analysis will take place from the end of recruitment up to March 2014. Dissemination of study results will be from Apr 2014 to May 2014. The study results will be disseminated to all the study sites that participated in the study, Harare City Health, Ministry of Health and Child Welfare, MSF-OCA, as well as for potential publication in international journals.

7.3 Study population

All clients above 18 months of age attending the CT programme at the 6 primary sites that test HIV positive using the serial testing algorithm.

7.3.1 Inclusion criteria

All of the following should be met:

1. Clients above 18 months testing HIV positive on Determine and First Response performed at any of the primary sites
2. Written informed consent by the by the client and/or guardian

7.3.2 Exclusion criteria

The following reasons are considered reasons for exclusion:

1. Lack of informed consent provision.
2. Clients testing negative or indeterminate result

7.3.3 Sampling

All clients attending the 6 participating sites who meet the inclusion criteria.

7.4 Study procedures

7.4.1. Study primary site procedures

All clients will be tested according to the national algorithm by a nurse counsellor, the primary care counsellor, or a microscopist. The testing person will follow instructions from the manufacturer. All clients meeting the inclusion criteria will be sensitized about the study

during their post test counselling session. The client is booked for CD4 count sample collection at a later date, within 14 days of an initial HIV positive result. On the appointed date, the client is referred to the study nurse, who will explain the purpose of the study and will ask for a written consent (Annex1). The clients are registered under care and assigned an OI number as per standard of care. The participants are now entered into the enrolment register, using the OIC number. Approximately 4 ml of venous blood will be collected into a 4 ml EDTA tube for routine CD4 as per standard of care. Information recorded on the tube will include OI number, clinic, age, sex and a large R to each sample as a marker to the lab that the sample needs be re tested for HIV. In addition a request form for retesting accompanies each sample. A sheet register will accompany each daily shipment of participants' samples to the lab for each participating clinic. Nurses at the primary study sites will be responsible for sample collection, storage shipment, and receiving and entering of results from the central laboratory into the enrolment register

7.4.2. Procedures and analysis at BRIDH laboratory

All samples will first be assayed for CD4 count as per standard of care. All samples from the clinic marked R will be used to test for HIV using Determine and First Response following the manufacturer's instructions. The technician will record the results in the sheet register from each clinic and file it. In addition the technician will record the result into each accompanying HIV re testing form and send it back to the clinic.

7.5 Outcomes, data entry and analysis Data

Results from the laboratory will be sent back to the primary sites, the data entry clerk will visit all the primary sites once in 2 weeks to collect the data from the sites.
Outcomes, data entry and analysis data will be double-entered using Excel 2007 data management software. Analysis will be carried out using Excel 2007 and EpiInfo data analysis software.

7.6 Formal and ethical approval

The study will be implemented after approval by the City of Harare, MSF and MRCZ Ethics Review Boards. The study will be carried out in accordance with the Declaration of Helsinki concerning medical research in humans. All study staff will undertake ethics training, in collaboration with MRCZ. All enrolled participants will sign or fingerprint the informed consent. Provision of informed consent for this study is a pre-requisite of MRCZ.
Adult Consent: *To the adult prospective client, an explanation of the study will be given and an invitation to participate is extended. Upon agreeing to be part of the study, the adult will be given an adult consent form to sign.*

Adolescent Consent*: For the adolescent, an explanation of the study will be given. Upon agreeing to be part of the study it will be explained to the adolescent that it is a requirement for his/her parent or guardian to give consent. It will be explained that for this to happen, the client should be willing to share his/her status with the guardian or parent concerned. If the*

adolescent agrees then the guardian/parental consent is sought after. In this case, the adolescent signs the assent form and the guardian/parent signs the consent form. If agreement is not secured, then on the basis of failure to secure the necessary consent documents, the candidate is excluded. Provision of informed consent for this study is a pre-requisite of MRCZ.

***Child Consent**: The parent or guardian is given an explanation of the study and consent is sought. After the parent or guardian agrees to participate, a simple explanation is given to the child. If the child agrees to participate he/she is included into the study, if not he/she is excluded from the study.*

7.6.1 Risks: The only risk associated directly with the study is handling of differing results between the clinic and the laboratory. If the laboratory result is negative, the patient is counselled and requested to come for another test after 3 months as per standard of care. If the laboratory result is indeterminate (Determine Pos, First Response Neg), a third test, Insti is used as a tie breaker.)

7.6.2 Benefits: Each participant will receive the retesting results from the laboratory, thereby reducing the chances for a participant to receive false positive results. The results from this study will be used to lobby for the implementation of the WHO 2012 recommendations of laboratory retesting for all HIV positive results in Zimbabwe, if appropriate.

7.7 Financing of the study

The study has been granted funding by Médecins sans Frontières, which will pay for all material and personnel required in the field and for additional tests and costs as required.

8.0 References

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12.UNAIDS 2012: Zimbabwe Country Report, Global AIDS Response Progress Report 2012
13.WHO: Service Delivery Approaches To Hiv Testing And Counselling (Htc): A Strategic Htc Programme Framework 2012
14. Brigadier General Gwinji(Secretary For Health and Child Welfare): New Rapid Test Algorithm For HIV Screening in Zimbabwe Circular: 7 August 2012

9. Annexes

9. 1. Informed Consent (English)

ADULT INFORMED CONSENT FORM

[**U*se appropriate Institutional letterhead***]

EVALUATION OF RATES OF FALSE POSITIVE HIV RESULTS DUE TO COUNSELLING AND TESTING ERRORS (ECATE)

Principal Investigator: Tatenda Maparo, [*QUALIFICATIONS*]
Phone number(s):0775 228 502/0712347662

What you should know about this research study:

- We give you this consent so that you may read about the purpose, risks, and benefits of this research study.
- Routine care is based upon the best known treatment and is provided with the main goal of helping the individual patient. The main goal of research studies is to gain knowledge that may help future patients.
- We cannot promise that this research will benefit you. Just like regular care, this research can have side effects that can be serious or minor.
- You have the right to refuse to take part, or agree to take part now and change your mind later.
- Whatever you decide, it will not affect your regular care.
- Please review this consent form carefully. Ask any questions before you make a decision.
- Your participation is voluntary.

PURPOSE

You are being asked to participate in a research study of HIV repeat testing in the laboratory. The HIV test kits being used detect antibodies to HIV, not the virus itself. Antibodies are the body's reaction to the virus. A POSITIVE test usually means that a person is infected with HIV and can pass it to others. By itself, a positive test does not mean that a person has AIDS, which is the most advanced stage of HIV infection. A NEGATIVE test means that antibodies to HIV were not detected. This usually means that the person is not infected with HIV. In some cases, however, the infection may have happened too recently for the test to show a positive result. The blood usually turns positive within 1 month after infection and in almost all cases within 3 months. Therefore, if you were infected very recently, a negative result could be wrong.

Some recent studies show that some patients who initially test positive are not actually infected with HIV. When those who initially test positive are tested again, the second/repeat test sometimes (but very rarely) reveals that the initial (positive) test result was inaccurate. Repeat testing of those who initially test positive thus leads to fewer patients being wrongly diagnosed with HIV. .In order to ensure accurate testing results we want to determine with this study whether repeat testing in the laboratory is required on all clients receiving HIV testing in Zimbabwe. We do not know the number of people in our setting that initially test positive, and then turn out to be negative in the laboratory. However, almost all of participants who tested positive in the initial testing will remain positive.

The purpose of the study is to see the proportion of people being tested positive in our clinics, who continue to be HIV positive after being tested in the laboratory. All people participating in the study will be asked to allow some additional HIV tests to be performed in the laboratory.

You were selected as a possible participant in this study because you tested HIV positive at this clinic. 3 500 clients in Harare who are over 18 months will be enrolled into the study.

PROCEDURES AND DURATION

If you decide to participate, you will undergo a process to enable you to have another HIV test in the laboratory. On the blood sample that will be collected from you for CD4 testing, a repeat testing of HIV will be done in the laboratory. You will be given a date to come for your CD4 results, on that same day, you will also receive the results of HIV retesting.

If your result remains positive, you will be referred to the local OI clinic to receive standard of care medication. If your result is negative however you will be referred to the local PITC centre where you will receive the standard medical care for clients with a negative HIV result

. This will be your last contact with the study, as you will then continue to receive your usual medical care from the clinic. If you do not attend an appointment, a member from the polyclinic will remind you to come to the clinic by telephone or by a visit to your home, if you give us permission to contact you in this way.

RISKS AND DISCOMFORTS

There are no additional risks caused by the study. We will use the blood sample that will be taken anyway for the other tests that need to be done as per standard of care.

BENEFITS AND/OR COMPENSATION

Participation in this research will confirm (or possibly, but unlikely, disconfirm) your previous HIV test results. Participation is this research will increase chances that you ultimately receive an accurate diagnosis of your HIV status

. Other basic tests that need to be done before one is commenced on drugs are also done during the same visit that your results will be confirmed in the laboratory. . There will be refreshments offered in the form of drinks and biscuits. The results of this study can benefit other people in future being tested for HIV, as the results can be used to improve testing practices.

ALTERNATIVE PROCEDURES OR TREATMENTS

It is not known yet the number of people that are receiving false positive results. Whatever your choice, you will receive the standard medical care today and in the future. You will receive care for your health whether you participate in the study or not.

Also, if you choose to participate, you can decide to withdraw from the study at any time and for any reason, with no consequences for you and your future treatment in the clinic.

CONFIDENTIALITY

If you indicate your willingness to participate in this study by signing this document, we plan to disclose the results only to health staff involved with your care. We will not put your name or address in the electronic data base. Any information that is obtained in connection with this study that can be identified with you will remain confidential and will be disclosed only

with your permission. The combined information on all participants will be used for further analysis and publication in an international medical journal that is published on the internet. No personal or individual patient information will be included in any such publications. Publication of study results will allow other similar clinics to learn from the results of this study.

ADDITIONAL COSTS

It will not cost you anything to be in the study. The study will not pay for the regular medical care provided to you.

VOLUNTARY PARTICIPATION

Participation in this study is voluntary. If you decide not to participate in this study, your decision will not affect your future relations with the polyclinic, its personnel, and associated government hospitals. If you decide to participate, you are free to withdraw your consent and to discontinue participation at any time without penalty.

OFFER TO ANSWER QUESTIONS

Before you sign this form, please ask any questions on any aspect of this study that is unclear to you. You may take as much time as necessary to think it over.

AUTHORIZATION

You are making a decision whether or not to participate in this study. Your signature indicates that you have read and understood the information provided above, have had all your questions answered, and have decided to participate.

The date you sign this document to enrol in this study, that is, today's date, MUST fall between the dates indicated on the approval stamp affixed to each page. These dates indicate that this form is valid when you enrol in the study but do not reflect how long you may participate in the study. Each page of this Informed Consent Form is stamped to indicate the form's validity as approved by the MRCZ.

_____ _____

Name of Research Participant (please print) Date

_____ _____

Signature of Participant Time

_____ _____

Signature of Witness Signature of Staff Obtaining Consent

(*Optional*)

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

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; or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team, please feel free to contact the Medical Research Council of Zimbabwe on telephone 791792 or 791193 and cell phone lines (insert physical location).

ADOLESCENT INFORMED CONSENT FORM
(For children above 13 years to 17 years)
Date: 02 April 2013
[U*se appropriate Institutional letterhead*]
EVALUATION OF RATES OF FALSE POSITIVE HIV RESULTS DUE TO COUNSELLING AND TESTING ERRORS (ECATE)

Principal Investigator: Tatenda Maparo, [*QUALIFICATIONS*]
Phone number(s):0775 228 502/0712347662

What is this all about?
This is a study on HIV. I am being asked if I want to be in this study. This assent form is a form I sign to show that I agree to take part in the study and that I understand what I am supposed to do in the study.
Some recent studies show that some patients who initially test positive are not actually infected with HIV. When those who initially test positive are tested again, the second/repeat test sometimes (but very rarely) reveals that the initial (positive) test result was inaccurate. Repeat testing of those who initially test positive thus leads to fewer patients being wrongly diagnosed with HIV. The study aims to see the number of people being tested HIV positive in our clinics who continue to be HIV positive after being tested again in the laboratory. All people taking part in the study will be asked to allow repeat/second HIV tests to be done on their blood collected for CD4 count test.
So I am being asked if I am willing to allow my blood taken for the CD4 count test to be retested in the laboratory for HIV.

PROCEDURES AND DURATION
If I agree to be in the study, I will be asked to sign this consent form to show that I agree to take part and to have a second HIV test done on my blood collected for CD4 count. For this

to happen, I need my parent/guardian to allow me to participate. This means that I should be willing to allow you to tell my parent or guardian my HIV results and get their approval for me to participate in the study. If my result remains positive, I will be referred to the local OI clinic to receive my treatment. If my result is negative however I will be referred to the local PITC centre where I will receive instructions and information necessary for clients with a negative HIV result.

This will be my last contact with the study, as I will then continue to receive my usual medical care from the clinic. If I do not attend an appointment, a member from the polyclinic will remind me to come to the clinic by telephone or by a visit to my home, if I give you permission to contact me in this way.

Will this hurt me?

What is done in this study will not hurt me. The repeat/second HIV testing in the laboratory will use the blood that is collected for the CD4 count test.

BENEFITS AND/OR COMPENSATION

Participation in this research will confirm (or possibly, but unlikely, disconfirm) my previous HIV test results. Participation is this research will increase chances that I will get an accurate diagnosis of my HIV status. Other basic tests that need to be done before one is started on treatment are done during the same time that my blood will be re-tested in the laboratory. There will be refreshments offered in the form of drinks and biscuits. The results of this study can benefit other people in future being tested for HIV, as the results can be used to improve testing processes.

ALTERNATIVE PROCEDURES OR TREATMENTS

The number of people receiving inaccurate positive results is not known yet. Whatever my choice: to participate in this study or not to, I will receive my medical treatment today and in the future. I understand that I will receive care for my health whether I participate in the study or not.

CONFIDENTIALITY

If I agree to take part in this study by signing this consent form, you can only disclose my results to healthy staff involved with my care and to none else without my agreement

VOLUNTARY PARTICIPATION

Participation in this study is voluntary. If I decide not to participate in this study, my decision will not affect my future relations with the polyclinic, its personnel, and associated government hospitals. If I decide to participate, I am free to withdraw my consent and to discontinue participation at any time without penalty.

AUTHORIZATION

My participation in this research study is voluntary. I have read and understood the above information, asked any questions I may have and have agreed to participate. I will be given a copy of this form to keep.

_____ _____

Name of Participant Date

_____ _____

Signature of Participant Time

_____

Name of Parent/Guardian

_____

Signature of Parent/Guardian

_____

Signature of Staff Obtaining Consent

PARENT/GUADIAN INFORMED CONSENT FORM

FOR CHILD PARTICIPATION

Date: 02 April 2013

[**U*se appropriate institutional Ohio letterhead***]

EVALUATION OF RATES OF FALSE POSITIVE HIV RESULTS DUE TO COUNSELLING AND TESTING ERRORS (ECATE)

Principal Investigator: Tatenda Maparo, [*QUALIFICATIONS*]

Phone number(s):0775 228 502/0712347662

Co-Investigator(s) _____ [*if applicable*]

Phone number(s)_____

ADD THE FOLLOWING PARAGRAPH TO ALL CONSENT FORMS

MORE THAN TWO (2) PAGES LONG (BEFORE ADDITION OF THIS PARAGRAPH)

What you should know about this research study:

- We give you this consent so that you may read about the purpose, risks, and benefits of this research study.
- Routine care is based upon the best known treatment and is provided with the main goal of helping the individual patient. The main goal of research studies is to gain knowledge that may help future patients.
- We cannot promise that this research will benefit your child. Just like regular care, this research can have side effects that can be serious or minor.
- You have the right to refuse to allow your child to take part, or agree for your child to take part now and change your mind later.
- Whatever you decide, it will not affect your child's regular care.
- Please review this consent form carefully. Ask any questions before you make a decision.
- Your choice to allow your child to participate is voluntary.

PURPOSE

The HIV test kits being used detect antibodies to HIV, not the virus itself. Antibodies are the body's reaction to the virus. A POSITIVE test usually means that a person is infected with HIV and can pass it to others. By itself, a positive test does not mean that a person has AIDS, which is the most advanced stage of HIV infection. A NEGATIVE test means that antibodies to HIV were not detected. This usually means that the person is not infected with HIV. In some cases, however, the infection may have happened too recently for the test to show a positive result.The blood usually turns positive within 1 month after infection and in almost all cases within 3 months. Therefore, if you were infected very recently, a negative result could be wrong.

Some recent studies show that some patients who initially test positive are not actually infected with HIV. When those who initially test positive are tested again, the second/repeat test sometimes (but very rarely) reveals that the initial (positive) test result was inaccurate. Repeat testing of those who initially test positive thus leads to fewer patients being wrongly diagnosed with HIV In order to ensure accurate testing results we want to determine with this study whether repeat testing in the laboratory is required on all clients receiving HIV testing in Zimbabwe. We do not know the number of people in our setting that initially test positive, and then turn out to be negative in the laboratory. However, almost all of participants who tested positive in the initial testing will remain positive.

The purpose of the study is to see the proportion of people being tested positive in our clinics, who continue to be HIV positive after being tested in the laboratory. All people participating in the study will be asked to allow some additional HIV tests to be performed in the laboratory.

Your child was selected as a possible participant in this study because the child has tested HIV positive at this clinic. 3 500 adults in Harare at least 18 months old will be enrolled into the study.

PROCEDURES AND DURATION

If you decide to allow your child to participate, your child will undergo a process to enable you to have another HIV test in the laboratory. On the blood sample that will be collected from you for CD4 testing, a repeat testing of HIV will be done in the laboratory. You will be given a date to come for your CD4 results, on that same day, you will also receive the results of HIV retesting. If your result remains positive, you will be referred to the local OI clinic to receive standard of care medication. If your result is negative however you will be referred to the local PITC centre where you will receive the standard medical care for clients with a negative HIV result.

. This will be your last contact with the study, as you will then continue to receive your usual medical care from the clinic. If you do not attend an appointment, a member from the polyclinic will remind you to come to the clinic by telephone or by a visit to your home, if you give us permission to contact you in this way.

RISKS AND DISCOMFORTS

There are no additional risks caused by the study. We will use the blood sample that will be taken for the other tests that need to be done as per standard of care.

BENEFITS AND/OR COMPENSATION

Participation in this research will confirm (or possibly, but unlikely, disconfirm) your previous HIV test results. Participation is this research will increase chances that you ultimately receive an accurate diagnosis of your HIV status

- . There will be refreshments offered in the form of drinks and biscuits. The results of this study can benefit other people in future being tested for HIV, as the results can be used to
- improve testing practices".

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ALTERNATIVE PROCEDURES OR TREATMENTS

It is not known yet the number of people that are receiving false positive results. Your child will receive care for the health whether you decide for the child to participate or not to participate in the study.

CONFIDENTIALITY

If you indicate your willingness for your child to participate in this study by signing this document, we plan to disclose the results only to healthy staff involved with your care. We

will not put your name or address in the electronic data base. Any information that is obtained in connection with this study that can be identified with your child will remain confidential and will be disclosed only with your, and when appropriate, your child's permission. The combined information on all participants will be used for further analysis and publication in an international medical journal that is published on the internet. No personal or individual patient information will be included in any such publications. Publication of study results will allow other similar clinics to learn from the results of this study. Under some circumstances, the MRCZ and the local Institutional Review Board may need to review patient records for compliance audits.

ADDITIONAL COSTS

It will not cost you or your child anything to be in the study. The study will not pay for the regular medical care provided to you.

VOLUNTARY PARTICIPATION

Participation in this study is voluntary. If you decide not to allow your child to participate in this study, your decision will not affect your or your child's future relations with this institution, its personnel, and associated government hospitals**.** If you decide to allow your child to participate, you and your child are free to withdraw your consent and assent and discontinue participation at any time without penalty.

OFFER TO ANSWER QUESTIONS

Before you sign this form, please ask any questions on any aspect of this study that is unclear to you. You may take as much time as necessary to think it over.

AUTHORIZATION

YOU ARE MAKING A DECISION WHETHER OR NOT TO ALLOW YOUR CHILD TO PARTICIPATE IN THIS STUDY. YOUR SIGNATURE INDICATES THAT YOU HAVE READ AND UNDERSTOOD THE INFORMATION PROVIDED ABOVE, HAVE HAD ALL YOUR QUESTIONS ANSWERED, AND HAVE DECIDED TO ALLOW YOUR CHILD TO PARTICIPATE.

The date you sign this document to enrol your child in this study, that is, today's date, MUST fall between the dates indicated on the approval stamp affixed to each page. These dates indicate that this form is valid when you enrol your child in the study but do not reflect how long your child may participate in the study. Each page of this Informed Consent Form is stamped to indicate the form's validity as approved by the MRCZ.

_____ _____

Name of Parent (please print) Date

_____ _____

Signature of Parent Guardian Time

_____

Relationship to the Participant

_____ _____

Signature of Witness (optional) Signature of Staff obtaining consent

YOU WILL BE GIVEN A COPY OF THIS CONSENT FORM TO KEEP.

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; or if you feel that you have been treated unfairly and would like to talk to someone other than a member of the research team, please feel free to contact the Medical Research Council of Zimbabwe on telephone 791792 or 791193.

INFORMED ASSENT FORM
(For children 7 to 12 years old)

Date: 02 April 2013

[U*se appropriate Institutional letterhead*]

EVALUATION OF RATES OF FALSE POSITIVE HIV RESULTS DUE TO COUNSELLING AND TESTING ERRORS (ECATE)

Principal Investigator: Tatenda Maparo, [*QUALIFICATIONS*]
Phone number(s):0775 228 502/0712347662

What is this study about?

I am being asked if I want to be in this study. The goal of the study is to see the number of people being tested HIV positive in our clinics, who continue to be HIV positive after being tested again in the laboratory. All people participating in the study will be asked to allow some additional HIV tests to be performed on their blood collected for other tests.

What do I have to do?

If I am in the study, I will be asked to sign this assent form and to have extra HIV test to be performed on my blood collected for other tests.

Will this hurt me?

Procedures in this study should not hurt

Do I get anything for being in the study?

I will not get anything for bring in the study

Can I ask questions?

All the questions that I asked about the study were answered. I know that I can still ask if I have questions later. I can call Mr Tatenda Maparo on 0775 228 502/0712347662.

Do I have to do this?

I know that I do not have to be in the study if I am not interested. No one will be angry at me if I say no. I will continue to get treatment.

I want to be in the study at this time yes ☐ no ☐

_____

Child's printed name: _____ _____

Child's signature: Date:

I have explained the research at a level that is understandable by the child and believe that the child understands what is expected during this study

_____ _____

Signature of person obtaining assent: Date: