ANNOUNCEMENT

Availability of Specimens from Seroconverters and HIV-negative Participants in the Randomized Controlled Trial of Male Circumcision in Kisumu, Kenya

The Chicago Developmental Center for AIDS Research (CDCFAR) has approximately 38,000 biological specimens available in its repository from men enrolled in and followed up during the randomized controlled trial (RCT) of male circumcision (MC) in Kisumu, Kenya (Bailey et al., 2007). The specimens include serum and plasma collected from 2784 men ages 18-24 years at the time of enrolment (2002-2005). There is also a nested case control sample of 123 seroconverters with two controls matched to cases on age at baseline and circumcision status. Visit-matched data on demographic characteristics, sexual behavior and laboratory results of sexually transmitted infections testing (HSV-2, N. gonorrhoeae, C. trachomatis, T. vaginalis) are also available. See below for some details on the participants and samples available.

Approval for Use of the Specimens

Approval for use of the specimens is a three step process, the first two of which can be undertaken simultaneously. First, a concept proposal must be submitted to the Executive Committee of the RCT Study Team. The concept proposal should include:

- Study objectives/specific aims
- Brief Significance/Background
- Study design
- Inclusion and exclusion criteria
- Laboratory methods
- Number and type of specimens and estimated quantities needed
- Additional data requested (e.g., specific socio-demographics, sexual behaviors, STI testing results)
- Statistical methods
- CV or biosketch of the main investigator(s); names and institutions of co-investigators to be involved
- Funding source (if any)
- Timeline for study completion and plans for dissemination

Please submit this proposal to Robert C. Bailey, PhD, Division of Epidemiology, School of Public Health, University of Illinois at Chicago, 1603 West Taylor Street, Chicago, IL 60612 or to rcbailly@uic.edu. There are no deadlines for submission. Proposals will be reviewed as they are received.

The second step in the approval process is to submit the D-CFAR Clinical Core Services Request Form to kkroc@cookcountyhhs.org. This form can be found on the CDCFAR Clinical Core website at http://www.chicagocfar.org/ClinicalCore.html. Since there is considerable overlap in the information requested by the RCT Study Team and the CDCFAR Clinical Core, these two steps may be taken simultaneously and study design and methods need not be entered twice. The concept proposal can be appended to the Clinical Core Request Form. However, approval for use of the samples is dependent on approval by both the RCT Study Team and the CDCFAR Clinical Core.
The third step is to obtain approval from all relevant Institutional Review Boards (IRB). These would include the IRB(s) of the investigators seeking to use the specimens and the Kenyan IRB that has jurisdiction over the MC RCT. This is the Kenyatta National Hospital Ethics and Research Committee (KNH ERC). RC Bailey can assist with application to the KNH ERC.

Additional Details about the Study Participants and Samples
From 2002-2005, the MC trial in Kisumu enrolled 2,784 men aged 18-24 years. For inclusion men had to be: uncircumcised, HIV-negative, sexually active in the previous 12 months, and aged 18-24 years; have a hemoglobin > 9.0 gm/dL; and reside in Kisumu District. Exclusion criteria included: foreskin covering less than half of the glans, a bleeding disorder, keloid formation, other conditions that might increase the risks of elective surgery, or a medical indication for circumcision. Participants with sexually transmitted infections (STIs) or other treatable medical conditions were deferred until treated. Trial recruitment, enrollment, reasons for refusing enrollment, and follow-up have been previously described (ref). Following written informed consent, participants were randomized 1:1 to either immediate circumcision or delayed circumcision after a two-year follow-up period (the control group).

Both groups underwent STI and HIV risk reduction counseling and were provided unlimited supplies of free condoms. Detailed evaluations were conducted at baseline, 1 month, 3 months, and every 6 months from randomization for all men. At each visit, participants underwent a standardized medical history and physical examination, blood and urine were collected for STI testing, and an extensive questionnaire was administered. Testing for HIV infection was conducted using a parallel double rapid test protocol, using Determine® HIV 1/2 (Abbott Diagnostic Division, Hoofddorp, The Netherlands), and the Uni-Gold Recombigen™ HIV Test (Trinity Biotech, Wicklow, Ireland). Men who were concordant negative were eligible for the study. Concordant positive results were confirmed by double ELISA, and men were informed of their HIV status and followed-up at the study clinic or referred to the New Nyanza Provincial Hospital. Men with discordant results were followed up with additional tests to determine their HIV status, but were not enrolled. Positive rapid test and ELISA test results were confirmed by Health Canada’s National HIV Reference Laboratory (Ottawa, Canada) by line immunoassay (INNO-LIA HIV 1/2, Immunogenetics NV, Ghent, Belgium). Specimens indeterminate by line immunoassay were tested by polymerase chain reaction (PCR) at Health Canada or the Fred Hutchinson Cancer Research Center (Seattle, WA, USA), with the PCR result deemed to be definitive. STI testing methods have been reported in detail previously. Briefly, men were tested for urogenital infection with *Neisseria gonorrhoeae, Chlamydia trachomatis*, and *Trichomonas vaginalis* at baseline and each planned 6-month study visit, and at interim visits where symptoms or signs of infection were elicited. Men were tested for HSV-2 serum antibody at baseline and at each planned 6-month study visit. Results of HPV analyses are available separately.

On the recommendation of the data monitoring and safety board, the trial was stopped at the third interim analysis on December 12, 2006. Of the 1,740 men still enrolled and eligible to participate in extended follow-up, 1,545 (89%) consented to do so. The follow-up visit schedule and procedures for these 1545 men were identical to those of the trial, with scheduled visits every 6 months that included personal interview, physical examination, and STI and HIV testing. Extended follow-up was completed on September 30, 2010, and the remaining cohort was
discharged at that time. Follow-up data and samples are available for some subjects for up to 84 months.

The following specimens are available. All specimen volumes are 1.5ml:

- Two sera and at least one plasma on all subjects for all attended visits through 24 months of follow-up
- One serum from all subjects attending visits through 84 months of follow-up
- Two sera and two plasma for all attended visits on 123 seroconverters
- Two sera and two plasma for two HIV-negative control subjects for each seroconverter. Controls are matched to seroconverters on age at baseline (18-20 years, 21-24 years), time of study visit, and circumcision status.

Acknowledgments

We ask that you acknowledge the D-CFAR in publications resulting from use of these samples. The following is a suggested acknowledgment

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In addition, we ask that you acknowledge the use of the specimens and, if appropriate, the use of any accompanying data. A suggested acknowledgement is:

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