1. General

In 2005 the HIV-research group (lead by prof Irja Lutsar) in Department of Microbiology, University of Tartu was established. Since that time the group has collected HIV related biosamples for different research projects and stored it for future studies. In 2009 the Estonian Society of Infection Diseases in collaboration with Department of Microbiology established Estonian HIV-positive persons' database (E-HIV; hiv.ut.ee). The data of adult HIV-positive patients is entered to E-HIV based on written informed consent. E-HIV is collecting demographic and HIV-related clinical data as described by Soodla et al (2015 Infect Dis). In addition, the essential task of E-HIV is also the collection, arrangement and the storage of biosamples for future research and clinical purpose.
Database has web-page in Estoinan and in English (http://hiv.ut.ee).
Person/institution who is interested in using E-HIV BIO will submit an application (overview of theme and aims) to E-HIV board. The board may ask specific questions before giving a permit and the extraction of samples and data. So far E-HIV BIO has mainly been used in variable research projects. Based on E-HIV BIO 24 articles have been published in international peer-reviewed journals, and three doctoral theses (Kristi Huik, Radko Avi and Kaja-Triin Laisaar) and six master theses have been defended (Radko Avi, Kristi Huik, Maarja Sadam, Helen Uibopuu, Merit Pauskar, Ene-Ly Jõgeda). At the moment four PhD students (Eveli Kallas, Ene-Ly Jõgeda, Pilleriin Soodla, Kerstin Kase,) are using E-HIV BIO for their doctoral theses. Collection has upgraded in collaboration with various institutions - from Estonia University of Tartu, Medicine Faculty, Department of Public Health and National Institute for Health Development, from United States of America Beth Isreal Medical Centre and Texas University and from Europe EuroCoord. In addition, E-HIV is updated in collaboration with all Estonian institutions (hospitals and prisons) which serve/manage HIV-positive patients.

2. Management and structure of collection

Biosamples (whole blood) are collected at least once a year in all Estonian institutions that are serving HIV-positive patients (hospitals and prisons). Blood plasma and peripheral mononuclear cells are extracted from whole blood and stored in Department of Microbiology, University of Tartu. As of 1st of September 2016 4667 patients were listed on E-HIV (approximately 80% of HIV positives who are visiting infection disease physician in Estonia) and samples from 1653 patients were collected on 3005 occasions. Therefore, existing scientific collection (E-HIV BIO) collects and stores biomaterial linked with clinical data of patients participating in E-HIV. These biosamples can be used to (i) describe interactions between HIV and the host and evaluate their influence on the outcome of antiretroviral therapy; (ii) determine viral and host factors that influence the development of HIV drug resistance; (iii) determine host factors (genetic, immunologic) that influence the susceptibility to HIV and disease progression; (iv) determine markers for developing prophylaxis (incl. vaccine), and (v) implement into clinical practice (for example observe patients disease on patient's graphical electronical chart (E-chart), reanalysing previous samples) etc.
There are two modules (based on software *Qure Data Management* platform) in E-HIV BIO. First, biobank module which is an electronical biobank where information of

biomaterial is administered starting with blood sent to biobank and ending with long-term stored blood components (blood plasma and peripheral blood mononuclear cells etc.). Material entry to E-HIV BIO and unique coding (referring type of biomaterial and position in collection) is done by using biobank module. This enables to link biosample to corresponding person and provide correct storing and future extraction. Second, universal biomaterial extraction module which helps users with actions related to dissension (archived all documents related to one application: application, decision, data extraction), generates and registries all operations with biomaterial (e.g. recoding the samples, extraction related laboratory protocols, positions of biosamples and corresponding position in the collection). In addition, biomaterial extraction module automatically does inventory update – calculates the remaining volume of samples and saves the melting times of specific tubes.
Data entering is performed by trained staff of hospitals and prisons (nurses and infectious diseases physicians), and HIV-research group members Merit Pauskar, Heli Rajasaar ja Dagmar Hoidmets from Department of Microbiology, Institute of Biomedicine and Translational Medicine, University of Tartu. Biomaterial processing and storing is poerformed by trained specialists Merit Pauskar, Dagmar Hoidmets and Kristi Huik. Periodically the data extraction and biomaterial is examined to control the quality of the database and biosamples.

A software platform specially created for data collection and management is used. Data is stored in the server in company QureTEC (which manages the database) located in Ülikooli 6A, Tartu. Regularly the copies of the database is produced and stored in the same building but in another room.

The head of E-HIV board Irja Lutsar is responsible for appropriate use and storage of data and biomaterial of scientific collection.

Scientific collection is located in the facilities of Department of Microbiology, Institute of Biomedicine and Translational Medicine, University of Tartu (Ravila 19, Tartu 50411).

3. Storage and viability control of the samples

Biomaterial is stored in two institutions – main collection in Department of Microbiology University of Tartu (blood plasma and PBMC) and smaller part in University of Tartu Estonian Genome Centre (rented by E-HIV). In Department of Microbiology, the collection is situated in HIV laboratory – last laboratory on hallway and used only by HIV group. Blood plasma is stored in -80 ℃ freezer and PBMC in -80 ℃ freezer as well as in vapour phase of liquid nitrogen. The temperatures of -80 ℃ freezers and the level of liquid nitrogen are supervised every day. The access to repository is limited – for entry to Department of Microbiology a permission is needed (magnetic door card).
University of Tartu Estonian Genome Centre offers a rental service for storing biosamples in liquid nitrogen. Repository is situated in the basement of Riia mnt 23b and

has restricted access (certain persons with authorisation). The level of liquid nitrogen is regulated automatically and temperature is monitored.

Biomaterial is controlled regularly – cell viability by flow-cytometry, DNA and RNA concentration and quality control by NanoDrop and qPCR.

The emergency notification of repository and course of actions is coordinated with University's security service.

4. Use and availability of biobank

The users of E-HIV data (incl. biosamples) are researchers/research institutions in Estonia as well as abroad, Estonian Ministry of Social Affairs, pharmaceutical companies and HIV treating physicians. E-HIV statute, the information about collected data, rules for application and results are presented on webpage (www.hiv.ut.ee). The application for data use (see in fail) needs to be submitted to E-HIV board (heli.rajasaar@ut.ee) which process the application, is in contact with applicant and make a decision. So far, E-HIV has been financed by different Estonian and foreign research projects. Data dispensing is free of charge for the members of Estonian Society of Infectious Diseases and persons directly related with collection of the data. Other institutions/companies will be charged according to work load. The price of the data will be determined by E-HIV board considering every application separately and based on the amount of required data, handling process and the format of data extraction. Biosamples are free of charge. Publications based on E-HIV and E-HIV BIO will be required to have at least two researchers designated by E-HIV board as co-authors of the paper/publication.

5. Scientific and development

Based on E-HIV BIO various scientific research is carried out in side institution and with international collaborators. The addition and management of biomaterial is continuous.

Scientific collection participates in European network EuroCoord which integrates the knowledge of different scientists and experts who study HIV infection including recent HIV infection. Based on E-HIV BIO articles have been published in international peer-reviewed journals and doctoral theses have been defended. Because of E-HIV Department of Microbiology has been able to participate in EU 6 frame programme project Concerted Action on SeroConversion to AIDS and Death in Europe, and EuroCoord project European Network of HIV/AIDS cohort studies to coordinate at European and International level clinical research on HIV/AIDS.
E-HIV BIO gives an opportunity to find answers to problems mentioned in section 2. In addition, E-HIV BIO is used to monitor and evaluate the HIV drug resistance. Based on that new HIV treatment guidelines for Estonia can be developed. Biobank is also used for the development of new HIV and HCV (a half of HIV-positive persons are also HCV-positive) treatment and resistance algorithms.