

Project name: HPLC Laboratory Network

Monitoring of safety of drugs and human use of drugs in Africa using liquid chromatography and mass spectrometry in African laboratories

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Objectives

1. Multistudy of drug quality and monitoring of human drug use in Africa
2. Establishment of e-network of drug analytical laboratories in Africa in collaboration with Karolinska Instiut .

Technology used, standards and services employed

The key laboratory is situated in Kampala. This department has presently access to 3 HPLCs (High Performance Liquid Chromatography (<http://en.wikipedia.org/wiki/HPLC>) machines. The drug analytical laboratory is headed by a recently graduated chemist from Karolinska Institutet- Dr Muhammad Ntale. The laboratory can run either pharmaceutical products as such or blood/urine from patients undergoing drug treatment. Our counterpart institutions is continuously support by a team of researchers and developers at Karolinska Instituee in drug analysis (Olof Beck), in medicine and clinical pharmacology (Lars L Gustafsson) and in development work of drug analyses and in support locally in Kampala or in Stockholm (Margarita Mahindi).

Drugs in developing countries are often of low quality or even faked. Specific drug analytical methods such as HPLC can be used to measure the contents of the drug in specific preparations or the the concentrations of drugs and its metabolites in patients. Low concentrations can be measured and in Stockholm we have more advanced techniques called LCMS (Liquid Chromatography Mass Spectrometry) that allows even lower measurements, have higher speed and can be next to completely automated. We plan to transfer also LCMS technique to our African Counterpart in Kampala allowing this laboratory to set up critical methods to monitor the concentrations of artemisinin and its derivatives. In order to maintain high quality of drugs and monitor drug levels in humans we can safeguard this drug from development of resistance.

Analysis of the drug contents in pharmaceutical products and drug concentrations are in particular

important to measure in drugs against HIV/AIDS, malaria, tbc and for antibiotics.

Our laboratories have developed several field-adapted methods to collect, distribute and monitor drug levels by application of small capillary volumes (50-100 ul) on filter papers. When the filter paper sample is dried in can easily be transported to the laboratory for analysis.

Laboratories equipped for analysis of drugs and concentration of drug ingredients and rest products in blood have been established at university hospitals in East Africa (Tanzania and Uganda), associated with research groups at their faculties of medicine. The liquid chromatography equipment is sensitive and requires a specific competence to use. Pioneers at the African university hospitals need to support each other and to work with experts with more experience elsewhere in the world to tune the methods to set up and run tests and to interpret the results.



Figure: High Performance Liquid Chromatography Laboratory in Department of Pharmacology & Therapeutics in Kampala, Uganda.

Research activities carried out and scientific data generated

Primarily we aim to systematically monitor the quality of available drugs by epidemiological random sampling of pharmaceutical products in initially Uganda and then in up to 5 more African countries. The focus to assess the quality of drugs will be on drugs to control malaria and on antibiotics.

We will develop methods by a joint effort between laboratories to establish a multidrug analytical methods of HIV-drugs to be used to monitor the adherence to long-term treatment.

Our project will gain data on:

- quality of drugs (i.e. contents) and uptake in humans (bioavailability) randomly collected from randomly selected regions in first Uganda and then later in more countries.
- data on variability in drugs concentrations in chronic diseases like HIV/AIDS and thereby increasing our understanding on variability in drug disposition in Africans. The variability of these drug concentrations can be related to the occurrence of different type genes controlling drug metabolism.
- experience on establishment, development and maintenance of 6-country based capacity building

program allowing on-line connections etc.

Principal outcomes and documentation (plus link to case studies)

1. Number of peer-reviewed publications
2. Number of PhDs that will be graduated during this program
3. Number of trained scientific, management and technical staff
4. Establishment of an e-network for drug analytical laboratory in Africa.

Other potential application areas/ actual spillovers

By establishment of this e-network for drug analytical laboratories in Africa with continuous support from Karolinska Institutet we assume that commercial laboratories will be developed. Such laboratories for drug analyses can provide services to drug industries in each countries. Presently local production of drugs are increasingly seen in a number of African studies. We also foresee that commercial drug analytical laboratories can be developed for provision of services to understaffed and poorly trained laboratories at drug regulatory authorities.

Financing

Sida funding about to expire

Finance amount over what time

This project should be extended another three years to consolidate the results achieved since it will take time to expand connections between laboratories in Africa where the focus initially is to connect drug analytical laboratories in Uganda, Tanzania, Nigeria and Ghana. In particular it will take time to provide capacity building.

Annual costs:

Staff: Uganda 0.5 position for coordination and research (PhD) equivalent to 8000 Euro. Other African partners 0.5 for postdoc equivalent to 8000 Euro. Sweden 0.5 position as researcher (PhD) equivalent to 38000 Euro.

Traveling: 9000 Euro, Computers and other costs: 5000 Euro

Access to high-performance networks 2000 Euro

Total Annual costs 70000 Euro

Resources employed (people, systems, software, etc.)

This project already has access to an established rather well-functioning academic environment in Kampala where 7 PhDs will be graduated within a Swedish/Ugandan joint PhD-program. The Swedish team is supporting the laboratory, students and supervisors continuously by frequent travels and by stay of one coordinator/senior laboratory engineer in Kampala for 2-3 months twice a year.

The research groups in Africa and Sweden have access to research and development groups in about 5 countries in Africa.

By the connection and collaboration with the prequalification program (a type of drug registration) at WHO Headquarter we will get support to identify collaborating partners for the future in Africa and elsewhere. The collaboration with WHO Geneva will help to identify drugs with poor quality where drug analytical methods should be established.

Cost-Benefit analysis of increased access to e-infrastructure resources

1. Possibility to manage drug analyses that otherwise could not be carried because of lack of tools or competence
2. Continuous access to foreign (Africa or globally) experts will provide effective learning of staff and thereby make the laboratory more sustainable
3. The few trained specialists in the field can be easily connected and thereby stimulate each other and organize effective competence-sharing and specialization.
4. University laboratories can more easily be informed on potential collaborative projects and can provide rapid drug analytical services by easy access to customers.

Economic efficiency

Increased revenues and decreased costs

Operational efficiency

Reduction of human resources, equipment, space requirements and access to distance high-speed computers for evaluation of laboratory results.

Time saving

Drug costs account for 20-60% of health care budgets in poor African countries. Faked drugs are common. It has been estimated that in many East-African countries every fifth patients treated with anti-malaria drugs may be given faked drugs. An establishment of control laboratory of the drugs and of laboratories that can measure drug levels in humans are needed. The Kamplala laboratory is one of the few drug analytical laboratories in Africa.

This project can speed-up capacity building that is absolutely necessary in order to get tools- drug analytical laboratories- that can monitor the quality of drugs and the use of drugs in humans. High speed connections over the net provide improved chances of sustainability of laboratories due to easy access to global support. E-learning run by distance- from Kampala to other countries- and from Stockholm to several unites in Africa will shorten the training period of professionals including scientists, chemists and technical staff.

Accessibility

By connecting the HPLC-laboratories to a high-performance broadband network in African countries the development and research institutions would be able to speed up the development of the methods by on-line collaboration. These laboratories can be connected to senior advisers and laboratories in Karolinska Institutet and around the globe for guidance in the development, problem solving and also for distance technical service and support. The necessary capacity building can be accelerated by e-learning and the e-network can share processing computer capacity that in particular can help to establish LCMS equipped laboratories in Africa.

Environmental impact

This project will diminish the environmental impact of traveling since support of the HPLC equipment can easily be provided over the network. A proper handling of the equipment will diminish the risks of unsafe use of chemical substances and solutions.

e-Infrastructure potential

Available infrastructure includes computers connected to the locally installed HPLCs. Variable access to low-speed Internet connects.

Access to high-speed networks will facilitate a common database, discussions about results and methodologies, capacity building, etc.

Interview data

Multiple interviews with our own trained scientists and in particular Dr Muhammad Ntale. This application builds on discussion over the past 2 years with experts in the area of quality of drugs in Africa including professor Lembit Rägo and the previous head of Pre-qualification Program at WHO-professor Raul Kiivet (presently head of Department of Public Health, Tartu University, Estonia).