

INDEPTH EFFECTIVENESS AND SAFETY STUDIES OF ANTIMALARIALS IN AFRICA (INESS)

INDEPTH Network Effectiveness and Safety Studies of Antimalarials in Africa (INESS) is a platform with a goal to provide safety and effectiveness information on antimalarials and vaccines to enable African countries to make rational and timely policies on drugs and vaccines.

The INESS platform works in seven sites in four African countries (Ghana, Tanzania, Mozambique and Burkina Faso) and covers Anglophone, francophone and Lusophone Africa. It therefore has the potential to provide national, regional and international health decision makers with independent and objective evidence on the safety and effectiveness of new antimalarial drugs as a basis for malaria treatment policy in Africa.

In the year 2011, the project made significant progress towards achieving its key objectives which are:

- To develop and maintain Phase IV - Effectiveness Studies of Antimalarials in Africa
- To assess effectiveness of new malaria treatments and its determinants in real life
- To evaluate the safety of new treatments through a comprehensive pharmacovigilance in a health system context

Driving the INESS project are its Principal Investigator, Prof Fred Binka, Clinical Trialists Dr. Bernhards Ogutu and Dr. Mrs. Rita Baiden, Statistician Martin Adjuik and Dan Kajungu, Finance Officer Raymond Akparibo and Administrative Officer Mrs. Margaret Bugase, alongside a host of researchers and data managers from the participating field sites in the selected countries across Africa.

Despite a few challenges, the project remained very much on course in 2011 giving every indication that its completion will greatly enhance Africa's capacity to monitor local health systems in order to track costs, effective coverage and effects of new or alternative post-registration antimalarial treatments. A number of innovative activities were pursued from the INESS platform including accelerated data collection for all the different modules, tools and SOPs development and deployment, review meetings and stakeholder consultations.

INESS works through task teams from three collaborative sub-partners namely: the School of Public Health, University of Ghana, the Swiss Tropical and Public Health Institute (Swiss TPH) and the US Centers for Disease Control and Prevention (CDC). These task teams have successfully developed, trained and conducted field tests of both tools and SOPs for the different modules prior to adaptation and use. Each task team was assigned a specific role with the School of Public Health being in charge of data analysis and synthesis under the supervision of a full time in country statistician.

In the course of the year module specific protocols were developed for System Effectiveness, Community Compliance, Cost and Cost-effectiveness, Impact and Context, Safety, Drug Efficacy, Data Linkage and Data synthesis.

Some key activities were a Data Synthesis and Review meeting held in Dar es Salaam, Tanzania from 16th – 18th February. This meeting was attended by representatives from the participating HDSSs, (Ifakara and Rufiji in Tanzania, Nouna in Burkina Faso, Manhica in Mozambique and Navrongo, Kintampo and Dodowa in Ghana). There were also stakeholders including School of Public Health, University of Ghana, Ifakara Health Institute, US Centers for Disease Control, Atlanta, Swiss Tropical and Public Health Institute, Tanzania Food and Drug Administration, National Malaria Control Programmes, Tanzania and Nigeria, GSK, PATH/MVI, Medicine for Malaria Venture (MMV) and Novartis. The objectives were to:

- update and review activities of the INESS project
- present interim analysis results after 1 year of data collection in the INESS sites in Tanzania and Ghana.

In the month of March, there was a follow up meeting with MMV and Gates Foundation in Geneva to discuss and agree on modalities relating to implementation of a Phase IV study for Eurartesim. The meeting also discussed registration prospects for Eurartesim, drug donation and funding and procurement and distribution processes at country levels.

The INESS Governance Council held a meeting also in March in Accra at which preliminary results on system effectiveness (access, population parasite prevalence, targeting accuracy, provider compliance, patient adherence, costing) and safety were presented by two participating sites from Tanzania (Rufiji and Ifakara HDSS). While the Council generally expressed satisfaction with the progress of enrolment it was also concerned about the Safety module (Cohort Event Monitoring) which was lagging behind. To address this, the Council agreed to a suggestion from the sites and the Secretariat to: (i) increase the number of field staff for the safety module and (ii) use phone calls to increase follow up rates.

The month of June was quite eventful for INESS in that during this period the task teams worked closely with the sites and country statisticians to develop an analysis plan. Additionally a number of activities were carried out to facilitate the implementation of new ACTs. It was also in the month of June that the European Medicines Agency (EMA) recommended the approval of Eurartesim (DHA+PQP) from Sigma-Tau for the treatment of uncomplicated *Plasmodium falciparum* malaria. Further interactions were also held with stakeholders such as regulatory authorities and policy makers in Burkina Faso, Mozambique, Ghana and Tanzania in preparation for smooth drug deployment.

A significant achievement at the end of June was the completion of data collection as well as the start of deployment of the data linkage module in Mozambique and Burkina Faso. Also noteworthy is the fact that the module on therapeutic efficacy of the first line treatment was initiated in Ifakara and Rufiji, (Tanzania) in April, Kintampo and Navrongo, (Ghana) in June and Dodowa in July. Burkina Faso started enrolment in late July and Mozambique at the end of August 2011.

Prior to the INESS project the DSS-Health Facility software in use had a number of challenges such as non conformity of photos to the format required for the ID card software. To overcome

this problem, in April, new software which was successfully developed and implemented in Kintampo was deployed in Dodowa and Navrongo. Subsequently it was extended to Rufiji and Ifakara in Tanzania in June.

In September, a critical meeting was held in Accra from 15th – 16th to provide an opportunity for all participating sites to share experiences and consider various publications that would emanate from the studies.

In October, at the INDEPTH Scientific conference in Maputo, Mozambique the progress of work and the key findings were presented to an audience of over 300 scientists, researchers and policy makers. Before the year ended, the INESS project convened its second Ghana stakeholder consultative meeting in Accra on November 21st. The meeting assembled national, regional and district representatives from the Ghana Health Service, Ministry of Health, the Food and Drugs Board and other collaborators to discuss issues related to the preliminary findings of the project.

By the end of the year INESS activities had been successfully integrated into (i) routine HDSS activities and (ii) district health management thereby marking an important step towards building district health observatories. It was clearly established that the INESS platform can be used to determine effectiveness and safety of other interventions.

“SMS for Life” was also made operational in all INESS districts in Tanzania and Ghana while through the INESS platform also it has become possible to monitor stock levels of ACTs on a weekly basis with the resultant improvement in supply chain management.

Overall INESS has gained outstanding recognition for its ability to recruit and follow-up large cohorts of patients for safety evaluation in real-life settings. In each country, 10,000 patients with suspected uncomplicated malaria were followed up.

Furthermore the project has demonstrated an ability to detect, record and report several different adverse events in patients including using cell phones to do follow-up. This is very important as it gives the possibility to carry out large scale real-life phase IV studies without the need for follow-up of patients at home. Going forward it should be entirely possible to use newer cell phone based technologies to automatically send SMS to patients to encourage them to report any adverse events post-drug exposure as well as to remind them to undertake specified actions.

Considering the fact that the WHO database of adverse drug reactions (Vigibase) contains only 464 reports to all ACTs, the INESS sample size makes them one of the biggest post-marketing safety studies of antimalarials ever conducted. After case causality assessment by the INESS Safety Monitoring Panel, those reports deemed to be causally related to ACT intake would be contributed to the WHO database raising the possibility that INESS would contribute the highest proportion of Adverse Drug Reactions to ACTs in the global database, some of which will relate to pregnancy exposure to ACTs.

An important 2011 INESS take home message for policy makers and researchers is that Cohort Event Monitoring as a methodology for phase IV data collection, should be instituted in all INDEPTH sites whenever new medicinal products, new combinations of existing products or new vaccines are introduced in order to provide timely information of the safety of the product in the immediate period following introduction. This would be useful also for patients to enable early detection of any safety signals for quick correction.