Background Although minority HIV-1 drug-resistant HIV-1 variants may be selected under antiretroviral pressure, leading to therapy failure, their clinical significance remains controversial. This is particularly relevant in the case of prevention of mother-to-child transmission (MTCT), where transmitted drug resistance can affect treatment outcomes.

Methods An ultrasensitive HIV-1 genotyping assay based on deep sequencing (DEEPGENHIV) with a 1% mutation frequency sensitivity, was used to quantify MTCT drug-resistant variants in 38 prenatally HIV-infected children experiencing (Group I, n=27) or not (Group II, n=11) virologic failure 12 months after initiating first-line antiretroviral therapy (ART) as part of a paediatric cohort in Uganda.

Results Infants were infected with subtype A(n=20), D(n=16) or C(n=2) HIV-1 strains, distributed equally between both patients' groups. Similarly, no significant difference was observed in intra-patient HIV-1 diversity among viruses obtained from Group I or II individuals at baseline. DEEPGENHIV was able to detect all the mutations originally detected in samples obtained from four control patients in Group II, where drug resistance was identified at baseline using Sanger sequencing, e.g. K65R (78% mutation frequency), K103N (47%), or M184V (85%). More importantly, a series of low abundance (<20% detection limit of Sanger) primary and compensatory mutations associated with resistance to PIs (D30N, Q48V), NRTIs (D67N, K219Q), or NNRTIs (L100I, K103N) were identified in both groups of patients, although just a few seem to have been selected and became majority variants after 12 or 24 months of ART.

Conclusion DEEPGENHIV improves the detection of minority viral variants in infants following MTCT; however, most of the emergent HIV-1 drug resistance mutations were not present at low frequency at baseline in subjects failing ART, most likely being generated and selected following exposure to treatment. Further studies, using this or other ultrasensitive assays, are needed to better understand the transmission, dynamics and overall evolution of minority drug-resistant viruses in MTCT.

OC 8453 SCALING-UP MASS TESTING AND TREATMENT EFFECTIVELY REDUCED MALARIA ASYMPTOMATIC PARASITAEMIA IN CHILDREN UNDER 15 YEARS OF AGE IN GHANA

¹Ignatius Cheng Ndong*, ¹Collins Stephan Ahorlu, ¹Daniel Okyere, ¹Alexander A Nyarko, ²Alfred Amambua-Ngwa, ¹Kwakwo A Koram. ¹Noguchi Memorial Institute for Medical Research, University of Ghana, Accra, Ghana; ²Medical Research Council, Serrekunda, The Gambia

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Background Global efforts to scale up malaria control interventions that work, are gaining momentum. These include the use of long-lasting insecticide nets, intermittent preventive treatment and test, treat and track using artemisinin-based combination therapies. Mass testing, treatment and tracking (MTTT) of the entire populations complemented by home-based management (HBM) using volunteers could be an effective approach at lower cost. MTTT of children in Ghana has demonstrated a parasite load reduction of 90%. However, unanswered questions include – Could this be scaled-up? What proportion of the community could be covered? What do we need? Can MTTT reduce asymptomatic parasitaemia levels in under-15 children?

Methods The target population for this study was 5000 asymptomatic individuals in seven communities in the Pakro subdistrict in Ghana. A community register was developed following a census. Community volunteers conducted quarterly house-to-house testing (using RDTs) and treating positive cases with ACTs. Between interventions HBM was conducted.

Results In those tested, asymptomatic malaria parasitaemia reduced from 1795 (36.3%) in July 2017 to 942 (23.1%) in March 2018. In eight months, parasitaemia declined by 43.5% and 37.3% in children under 15 and under 5, respectively. Coverage was 98.8% in July 2017 and 81.4% in March 2018. One of the challenges that surfaced was the fact that decrease in hospital attendance had a negative effect on money generated by the health facility. The district and sub-district services, though appreciating the work, indicated that the negative effect on the health system may be serious and that measures need to be taken to address alternative financing for the health system.

Conclusion This study has demonstrated that combining MTTT and home-based management of malaria could reduce prevalence in under-15 children and that using community volunteers could ensure effective coverage at lower cost. There is need to start looking at financing of the health system without malaria.

OC 8459 ASSESSMENT OF PARASITE CLEARANCE AFTER REPEATED TREATMENT WITH ARTESUNATE AMODIAQUINE, DIHYDROARTEMISININ-PIPERAQUINE, PYRONARIDINE-ARTESUNATE IN MALARIA PATIENTS IN BURKINA FASO

Issiaka Soulama*, Sodiomon B Sirima. Centre National de Recherche et de Formation sur le Paludisme, Ouagadougou, Burkina Faso

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Background Reports from Southeast Asia showed delayed parasite clearance after treatment with known artemisinin-based combination therapies (ACTs), the first-line treatment for malaria. We then carried out a study in the framework of the WANECAM clinical trial to assess comparatively the parasite clearance time and rate from *P. falciparum* malaria patients repeatedly treated with the artesunate-amodiaquine (ASAQ), dihydroartemisinin-piperazine (DHA-PQ) and artesunate-pyronaridine (PYR).

Methods A randomised, phase III/IV comparative, multicentre, open-label, parallel 3-arms trial was conducted in Banfora Health District area comparing the efficacy of a three-day regimen of DHA-PQ, PYR with ASAQ for the treatment of children (above 6 months) and adults with uncomplicated falciparum malaria. From August 2012 to December 2013, each randomised patient was followed up for 42 days over a period of two years. Treatment was directly observed, and blood smear samples were collected twice daily (12 hour $\pm$ 2 hour) until parasite clearance.

The endpoints of the present sub-study were parasite clearance rate and time. The secondary endpoints included PCR-corrected and uncorrected cure rates.

Results Out of 2843 screened patients, 763 were recruited for parasite clearance endpoint analyses. The median parasite clearance time (PCT) was 24.1 hour (2-sided 95% CI, 24.0 to 24.2 hour), 23.9 hour (2-sided 95% CI, 23.8 to 24.0 hour) and 24.2 hour (2-sided 95% CI, 24.1 to 24.5 hour), in PYR

and DHA-PQ, respectively. The PCR-corrected efficacy rates were estimated at 99.8%; 99.7%; 99.9%, at day 28% and 99.3%; 99.7%–99.9% in PYR, ASAQ and DHA-PQ, respectively.

Conclusion The parasite clearance times were comparable among the three ACT arms of treatment and their efficacy was comparable and higher than 99%. There was no delay in parasite clearance time (PCT ≥ 72 hour).

OC 8465 THE DEVELOPMENT OF A CONJUGATE VACCINE AGAINST GROUP B STREPTOCOCCUS: AN AFRICAN PERSPECTIVE

Seanette Wilson*, Patrick Tippoo. *The Biovac Institute, Cape Town, South Africa*

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Background *Streptococcus agalactiae*, or group B streptococcus (GBS), is a gram-positive streptococcal bacterium that is well-recognised as one of the leading causes of infant death, particularly in the early neonatal period (the first week of life). An estimated one in five pregnant women around the world carries GBS bacteria in their gastrointestinal or genitourinary tracts and vertical transmission from colonised mothers can lead to invasive disease in their offspring. A recent study conservatively estimated that out of 410,000 GBS cases globally every year, there are at least 1 47 000 stillbirths and infant deaths. Despite being home to only 13% of the world's population, Africa has the highest GBS disease burden, with 54% of estimated cases and 65% of stillbirths and infant deaths.

An effective GBS vaccine, given during pregnancy, is a promising strategy to protect against GBS disease. Currently, no licensed vaccine exists to prevent it, but scientific evaluation of feasibility is favourable. The leading vaccine candidates are capsular polysaccharide-protein conjugate vaccines. Evidence suggests maternal immunisation with a safe and effective GBS vaccine may reduce the disease risk in neonates and young infants.

The Biovac Institute was established as a private-public partnership and is the only Southern African vaccine manufacturer. Located in Cape Town, South Africa, Biovac's mission is to become a leading vaccine developer and producer in South Africa to increase capacity in Africa which only has four other vaccine manufacturers.

In collaboration with PATH, an international health organisation, and other partners, Biovac is developing a multivalent conjugate vaccine against GBS. The first stage of the project involves the development of biopharmaceutical manufacturing processes and analytical tests, the preparation of clinical trial product, and execution of a first-in-human clinical trial.

This presentation will provide an overview of the project, progress to date, and the path to commercialisation.

OC 8469 REVIEWING INVESTIGATIONAL PRODUCT'S QUALITY ASSURANCE DOCUMENTATION IN MAJOR CLINICAL TRIAL REGISTRIES FOR POST-MARKETING CLINICAL TRIAL STUDIES

^{1,2}Joachim Doua, ^{1,3}Hanneke Dominicus*. ¹*Consortium for African Regulatory Expertise Development (CARED), The Hague, The Netherlands;* ²*Johnson and Johnson, Brussels, Belgium;* ³*Dominicus Medicus Consultancy, The Hague, The Netherlands*

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Background The proven worrisome quality of medicines marketed in developing countries also affects clinical trials (CTs) as they may be used as Investigational Medicinal Products (IMPs). By regulation, CT sponsors should assure IMP's quality and describe their quality measures in CT protocols that should be registered in a CT Registry (CTR). To check compliance with this regulation, we reviewed major CTRs to assess the availabilities of data fields on IMP quality for post-marketing CTs.

Methods Two reviewers independently assessed English versions of CTRs of International Committee of Medical Journal Editors (ICJME) and WHO platforms in July 2017. Each CTR was checked for availability of data fields on: brand name; manufacturer's name; regulatory approval status; approving regulator; manufacturer's compliance with Good Manufacturing Practices (cGMP); and quality testing (IMP appearance, impurities, microbial contamination, dosing). In case of discrepancy, consensus was sought.

Results Of 19 CTRs identified, 8 and 6 belonged to WHO and ICMJE, respectively, and 5 were equally part of both platforms. All CTRs had an 'intervention' data field to capture data on IMPs and IMP comparators. Unlike all others, the Canadian CTR used 'drug name' rather than 'intervention'. Only the EU CTR had data fields for 'manufacturer's name', 'product approval status', and 'approving authority'. None of the CTRs had data fields on 'cGMP' or 'quality testing'.

Conclusion None of the CTRs of ICMJE and ICTRP has adequate data fields to establish that the source of post-marketing IMPs is of assured quality. This is astonishing given the extensive requirements in WHO and ICMJE guidelines. The gap of quality assurance fields should be bridged by adding them to CTRs. Specifically, IMP quality testing should be conducted before, during, and after clinical trial completion. Until adoption of these measures, EU-CTR should be favoured for registration of CTs conducted in developing countries.

OC 8474 ASSESSMENT OF ETHICS REVIEW FRAMEWORKS FOR HEALTH RESEARCH IN EAST AFRICA FOR PURPOSES OF HARMONISATION

¹Gibson S Kibiki, ¹Novat Twungubumwe*, ²Francis Kombe, ³Carel IJsselmuiden, ⁴Prince N Bahati, ⁴Anatoli Kamali, ¹Jean De Dieu Ndirabaga. ¹*East African Health Research Commission, Burundi;* ²*Council on Health Research for Development, Kenya;* ³*Council on Health Research for Development, Geneva, Switzerland;* ⁴*International AIDS Vaccine Initiative, Nairobi, Kenya*

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Background Capacity in health research ethics review is key in Africa, given the increase in research activities, complexity, and use of advanced technologies. Harmonising ethics review frameworks can address challenges attributable to these complexities. Establishing an effective harmonised framework that is optimum or protection of the research subjects requires assessment of review capacity.

The East African Health Research Commission commissioned a study to assess the capacity of Review Ethics Committees (RECs) in the East African Community (EAC) countries, as a step towards strengthening and harmonising the regions' capacity and review frameworks.

Methods A desktop review of documentation (national and institutional guidelines, policies and SOPs) was conducted in five EAC countries. Semi-structured questionnaires were used to collect data from key informants. Qualitative interviews