



Summary of the context and overall objectives of the project

The COVID-19 pandemic has highlighted the critical importance of rapid and Point-of-Care (POC) diagnostics in controlling outbreaks of emerging diseases, not only in resource-limited third countries but also in developed nations. The main objective of VHF MoDRAD has been to create and deliver advanced multiplex diagnostic tools that can be used at the POC to effectively manage viral hemorrhagic fever outbreaks in Africa and potentially other regions and highly pathogenic emerging viruses. VHF MoDRAD has built on the success of the Ebola MoDRAD project, taking it to the next level.

VHF MoDRAD set out the following specific objectives for the duration of the project:

- To develop rapid molecular multiplex and serological antigen/antibody detection methods for use as Point-of-Care and surveillance tools in endemic and non-endemic areas;
- To validate the diagnostic tools;
- To increase preparedness through a capacity-building program in West Africa with focus on rapid diagnostics;
- To exploit project outputs and disseminate the results to the scientific community, public health bodies, NGOs, outbreak management teams.

Work performed from the beginning of the project to the end of the period covered by the report and main results achieved so far

VHF MoDRAD has made significant progress in the development of rapid molecular multiplex and serological antigen/antibody detection methods for use in Point-of-Care (POC) and surveillance applications. Various critical steps have been taken to validate the VHF MoDRAD-developed assays for preclinical/clinical validation and field evaluation. The project team has also successfully validated the use of Lyophilized Primers & Probes (Lyoph-P&P) on the Cepheid Flex04 cartridge for several viral hemorrhagic fevers and developed essential reagents for the optimization of Lateral Flow Device (LFD) assays. Moreover, field trials of the Crimean-Congo Haemorrhagic Fever Virus (CCHFV) molecular diagnostic assay on the Cepheid Flex04 cartridge have been conducted, yielding successful outcomes. Additionally, LFD assays for CCHFV IgM, IgG, and antigen detection have undergone validation at hospitals in Turkey during the recent outbreak.

Furthermore, we have established collaborations with various initiatives, including CCHFV vaccine. This collaboration has facilitated access to CCHFV samples for validating the developed assay at VHF MoDRAD. Additionally, we maintain a close interaction with European Virus Archives (EVA) Global, ensuring that the products of VHF MoDRAD are accessible to scientists in Europe. Our overarching objective is to strengthen the capability to manage outbreaks of filoviruses and other viral hemorrhagic fevers in Africa and other regions facing the challenges of highly pathogenic emerging viruses.

Progress beyond the state of the art, expected results until the end of the project and potential impacts (including the socio-economic impact and the wider societal implications of the project so far)

The VHF MoDRAD project has implemented a series of crucial measures to achieve the following significant results:

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- Sensitive and rapid singleplex Polymerase Chain Reaction based on the Cepheid Flex04 Cartridge technology; The CCHFV assay has been validated at field trial
- A novel, low-cost, high-performance molecular point-of-care (POC) IVD test for differential diagnosis of Ebola, Marburg, Lassa, and CCHF diseases using Recombinase Polymerase Amplification (RPA) has been explored;
- Sensitive lateral flow point-of-care tests for the detection of antigens and antibodies against hemorrhagic fever viruses for POC diagnostics. These tests require no or minimal equipment, provide results in less than 30 minutes, and are user-friendly for healthcare workers, technicians, and nurses; Several of these assays has been validated in field trials.
- Several key tools has developed such as monoclonal antibodies, antigens and also ELISA assay for several viral hemorrhagic fever,
- Improved preparedness for future epidemics through Transfer of lateral flow strip production capacity to a local African site.

These outcomes will contribute to our capacity to control filovirus and other viral hemorrhagic fever outbreaks in Africa and other regions affected by highly pathogenic emerging viruses, ultimately saving lives and mitigating the impact of such diseases.

The VHF MoDRAD project has aimed to showcase the practicality of transitioning assays that typically demand specialized environments and expertise to those that can be conducted closer to patients with minimal specific knowledge. The collaborative endeavours within VHF MoDRAD not only emphasize the project's flexibility in responding to new outbreaks and societal challenges but also showcase tangible accomplishments, including:

1. The early development of rapid antigen detection for COVID-19 (CE-IVD label in March 2020),
2. The inclusion of COVID-19 reagents in the EVA catalogue just three weeks after the release of the TaqMan protocol,
3. The inclusion of Lyoph-P&P diagnostic reagents in the EVA catalogue for several viruses causing viral haemorrhagic fevers (https://www.european-virus-archive.com/evam-portal-list/field_product_type/derived-product-10150/field_product_type/detection-kit-ruo-8022)
4. The validation of a Cepheid-based PCR for detecting Ebola Sudan virus by VHF MoDRAD partners in response to the outbreak in Uganda. These successes underscore the potential of VHF MoDRAD in delivering innovative POC tests. As demonstrated above, The VHF MoDRAD has also provided a platform that can be adapted to new outbreak situations.

