VHFMoDRAD
Viral Haemorrhagic Fever Modern Approaches for developing bedside Rapid Diagnostics

Welcome to the VHFMoDRAD newsletter

Visit our website at https://vhfmodrad.eu/

Contact the VHFMoDRAD team https://vhfmodrad.eu/contact-us/

Follow us on twitter @VHFMoDRAD_eu

View our project flyer here

VHFMoDRAD

Modern Approaches for developing bedside Rapid Diagnostics for Viral Haemorrhagic Fever diseases

VHFMoDRAD is a four-year European project and is part of IMI's EBOLA+ programme that was launched in 2014 to respond to the Ebola epidemic by accelerating all aspects of vaccine development and diagnostics.

The project has started in January 2019 and is **coordinated by Folkhälsomyndigheten** (the Public Health Agency of Sweden, FoHM) represented by **Professor Ali Mirazimi**. VHFMoDRAD brings together 13 cutting-edge complementary partners:

- Folkhälsomyndigheten (FoHM), Sweden
- Inserm Transfert (IT), France
- University of Stirling (UoS), United Kingdom
- Department of Health, Public Health England (DH-PHE), United Kingdom
- Coris BioConcept SPRL (CORIS), Belgium
- Institut national de la Santé et de la recherche médicale (INSERM), France
- University of Copenhagen (UCPH), Denmark
- Istituto Nazionale per le Malattie Infettive "L. Spallanzani" I.R.C.C.S (INMI), Italy
- Institut Pasteur de Dakar (IPD), Senegal
- RD-Biotech (RD-B), France
- CEPHEID, France
- Aix-Marseille University (AMU), France
- Emergency (EMR), Italy

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement N° 823666. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA and CEPHEID Europe SAS.

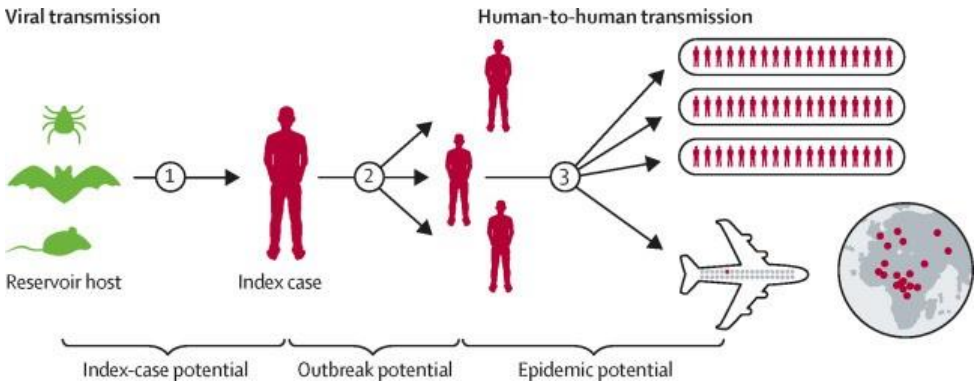
The project is supported by the **EU's research and innovation programme** and **CEPHEID Europe SAS through the Innovative Medicines Initiative (IMI)**. Two companies and consortium partners, Coris BioConcept and RD Biotech, also provide financial support to the project.

View an interview with coordinator Ali Mirazimi here, IMI, Brussels 26th September 2019.

VHFMoDRAD: why?

Natural epidemics and outbreaks of emerging infectious diseases are growing international problems spreading everywhere. For decades, Africa has faced sporadic outbreaks of **viral haemorrhagic fevers (VHFs)**, which result in deaths and widespread fear.

Some examples of VHF diseases are Lassa Fever, Crimean Congo Hemorrhagic Fever, Rift Valley fever, Ebola, Marburg, Yellow fever and Dengue fever.
Human cases or outbreaks of haemorrhagic fevers caused by these viruses occur sporadically and irregularly and the occurrence of outbreaks cannot be easily predicted.



Conceptual progression of a viral hemorrhagic fever from animal reservoir to global pandemic

One of the most important key actions to limit and stop the spread of VHF diseases is to identify acute patients and index cases and to trace their contacts. Consequently, rapid and accurate diagnosis at the point-of-care is essential for **better preparedness for a future outbreak.**

As there is no cure or established drug treatment, VHFs remain a major threat to public health. Vaccinations exist for only a few types of VHFs. Until additional vaccines are developed, the best approach is prevention.

VHFMoDRAD: what for?

The overall aim of VHFMoDRAD is to **develop and deliver rapid and Point-of-Care (POC) diagnostic tools** that will significantly increase the capacity to handle outbreaks of filoviruses, other VHF diseases in Africa and other highly pathogenic emerging viruses. VHFMoDRAD will

bring the outcome of the recently-ended successful IMI project EbolaMoDRAD project to the next level.

VHFMoDRAD set out the following specific objectives for the duration of the project:

- to develop **rapid molecular** and **serological antigen/antibody detection methods** for use as POC and surveillance tools in endemic and non-endemic areas;
- to validate the diagnostic tools;
- to increase preparedness through a **capacity-building programme 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.

VHFMoDRAD 1st year: what has been done?

Development of diagnostic tools in endemic and non-endemic areas

Significant progress has been made during the first year with regard to the development of:
- molecular detection methods at the level of clinical diagnostic laboratories and at healthcare centers in endemic countries.
- serological antigen/antibody detection methods for point-of-care and routine laboratories at very early diagnosis stage.

The VHFMoDRAD partners have received the **specific equipment and tools** to carry out their work. CEPHEID provided training on its equipment to other partners. The reference material and reagents are now listed and currently under production. In order to develop lateral flow diagnostic tools, already initiated protocols and reagents for Crimean Congo hemorrhagic fever from a previously available platform have been used. The protocol to produce the protein has been optimized for efficiency and protein purity. The protein has been distributed to VHFMoDRAD partners for developing antibodies. New batches of Ebola lateral flow tests (both antigen and antibody detection) have been produced.

Validation of newly developed diagnostic tools

The validation of the new diagnostic methods developed in VHFMoDRAD will be performed at different levels:
- Preclinical validation by using pertinent and available animal models as well as archived animal and human samples (serum samples) in high containment laboratories in Europe.
- Field validation that will be carried out in African settings, both in an advanced laboratory (Senegal) and in a field primary care hospital (Sierra Leone).

The **first step of the preclinical validation** was performed during this first year of the project. VHFMoDRAD has been successful in setting up the list of archived human and animal samples available at each facility obtained in the framework of past outbreaks and/or animal experimentations, which will be used for the validation of newly developed assays.

Implementation of a capacity-building programme in West Africa

In order to increase preparedness, a strong and effective capacity-building programme in Africa will be implemented during VHFMoDRAD. It will be addressed through:

- a training and exchange programme to ensure correct registration, containment and treatment of VHFs,
- a pilot study, through a twinning approach, to transfer the production capacity for lateral flow strip and POC tests to a technical campus in Senegal, with the objective to pave the way for a biotech start-up venture in West Africa.

Planning of the **twinning training activities** started and a training session will be scheduled in the next months. Work has begun to identify and initiate contact with other initiatives.
A **market analysis** to study the market potential and regulatory situation for POC test production in West Africa has been conducted during this first year.

Communication and dissemination of the results

In order to ensure the dissemination of important information (scientific research, data and tools) generated during VHFMoDRAD, the consortium will:
- focus on transfer of knowledge and technology between the partners and the countries in West Africa though public health bodies, outbreak management teams and local hospitals and via the EBOLA+ Central Information Repository (CIR) where relevant.
- establish links with the national and international organisations, institutions and laboratories located in different areas.

All **communication tools** were prepared and distributed among consortium partners and made available on the project website during first year of the project. A plan to **engage with related initiatives** was prepared and is starting to be implemented.
INMI submitted an abstract to the International Conference on (re-)Emerging Infectious Diseases (ICREID, program) in Addis Abbaba, Ethiopia in October 2020 presenting project activities and goals. The abstract has been accepted as a poster.

In the first year of the project, the consortium succeeded in completing the first steps required to set up the tools which are necessary to achieve the goal set out in VHFMoDRAD.

Professor Ali Mirazimi, coordinator of VHFMoDRAD, commented *"I believe the current the outbreak of SARS-CoV2 demonstrate clearly, the importance of to have a reliable, sensitive and easily accessible diagnostic to fight against infectious disease".*

VHFMoDRAD: expected results and impacts?

The major expected results and potential impacts of the VHFMoDRAD project are as follows:

Development of innovative and novel diagnostic tools for haemorrhagic fever virus diseases

- Sensitive and rapid Polymerase Chain Reaction (PCR)-based assays,
- Development of a **novel low-cost high-performance molecular POC In Vitro Diagnostic (IVD)** test using Recombinase Polymerase Amplification (RPA),
- **Sensitive lateral flow POC tests for detection of antigens and antibodies** against haemorrhagic fever virus for POC diagnostic: requires no/little equipment, delivers data

less than 30 minutes, and is user-friendly to general health care workers, technicians and nurses.

The project will demonstrate that the transfer of a TaqMan assay needing specific environment and expertise into an assay that can be operated closer to patients with little specific expertise can be operated in weeks because of the stability of the Lyoph-P&P and the capacity to produce Armored (encapsidated) synthetic RNA acting as viral particles. This has been demonstrated in the case of the Covid-19 crisis with the availability of such reagents in the European Virus Archive catalogue less than 3 weeks after the TaqMan protocol was released.

The field testing of the new diagnostic tools developed within the project will be the final step of the validation process and will allow to fully assess the performance of the novel assays in field settings where the VHFs circulate. The successful assays will benefit from Cepheid's existing installed base of instruments, "sample-to-answer" ease of use, and ability to generate results that have a public health impact.

Reinforcement of capacity building

- Increased preparedness for future epidemics through **training in field diagnostics in the West African region,**
- Transferring the **production capacity** for lateral flow strip production to a local African site
- **Consolidation of the network** to World Health Organisation, Collaborating Centres and reference laboratories for emerging viral diseases, and to develop biosafety and biosecurity behaviours and attitudes.

Several of the outcomes of VHFMoDRAD can be applied in the context outbreak of the viruses targeted by VHFMoDRAD. The diagnostic tools developed will significantly increase capacity to handle outbreaks and preparedness allowing **quick identification of viruses before the epidemic spreads**. The results of the VHFMoDRAD project will also assess the possibility and the impact of the deployment of these diagnostic tools in the field and in laboratories with no or little equipment in a future outbreak scenario. The project will also **build a platform** which can be adapted to new outbreak situations. In the first year of the project, there have been several interactions between partners in response to the outbreak of SARS-CoV2, which demonstrate the capacity of VHFMoDRAD to contribute to increased preparedness. Partner 5 (CORIS) and partner 1 (FoHM) could develop the COVID-19 Ag Respi-Strip rapid antigen test against SARS-CoV-2, validated it and bring it to the market (https://www.corisbio.com/Products/Human-Field/Covid-19.php). Another example is partner 3 (UoS) who could rapidly develop an RPA assay against SARS-CoV2. The dissemination of data and tools developed during the project will very likely be useful and constructive in the long-term for **supporting preparedness campaigns of new outbreaks**, further research and public health strategies.

News from VHFMoDRAD

Consortium meetings

December 13th, 2019: 3rd Executive Committee Meeting (Paris, France):
This meeting gathered the leaders of the different work packages of the VHFMoDRAD project, progress and updates have been discussed.

Relevant publications, abstracts, conferences

"Lyophilized Matrix Containing Ready-to-Use Primers and Probe Solution for Standardization of Real-Time PCR and RT-qPCR Diagnostics in Virology" (*Charrel et Al., Viruses. 2020 Jan 30;12(2). pii: E159. doi: 10.3390/v12020159*) https://www.mdpi.com/1999-4915/12/2/159

November 21st, 2019: MEDICA (Dusseldorf, Germany)
Participation of partner CORIS, VHFMoDRAD project leaflet presented.

June 14-16th, 2019: 7th European seminar in Virology (Padova, Italy)
Presentation by partner UCPH (O. Blixt) – "Efficient identification of immunodominant (glycol) peptides for type-specific serology and monoclonal antibody developments" EuSeV 2019

April 15-16th, 2019: European Congress of Clinical Microbiology and Infectious Diseases (Amsterdam, The Netherland)
Poster presentation by CORIS: "Evaluation of new rapid diagnostic tests for Ebola virus disease"
ESCMID eLIbrary

October, 2020: International Conference on (re-)Emerging Infectious Diseases (Addis Abbaba, Ethiopia) ICREID Program
Poster to be presented by Partner INMI: "Full-Length Genome Sequence of a Dengue serotype 1 virus isolate from a traveler returning from Democratic Republic of Congo to Italy", July 2019, Francesco Vairo

Useful Links

VHFMoDRAD
https://vhfmodrad.eu/
https://www.imi.europa.eu/projects-results/project-factsheets/vhfmodrad

IMI Ebola+ programme
https://www.imi.europa.eu/projects-results/project-factsheets/ebola

EbolaMoDRAD
http://www.ebolamodrad.eu/
https://www.imi.europa.eu/projects-results/project-factsheets/ebolamodrad

This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement N° 823666. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation programme and EFPIA and CEPHEID Europe SAS.