



# A Coordinated Research Roadmap for Rift Valley Fever Virus (RVF):

Immediate Steps for implementation in the 2025 Outbreak





# **Meeting Overview**

The Phenuiviridae CORC (Collaborative Open Research Consortium) Scientific Consultation on Research Priorities for Rift Valley Fever Medical Countermeasures was convened virtually on 14 October 2025. This expert consultation brought together international researchers, national authorities from affected countries, regulatory agencies, and global health partners to establish a coordinated research agenda in response to ongoing RVF outbreaks in West Africa and for use in future RVF outbreaks.

The consultation was structured around seven thematic sessions covering epidemiological updates, outbreak response plans, transmission dynamics, diagnostics, therapeutics, vaccines, and research prioritization. Leading experts participated in panel discussions to identify critical research gaps and actionable next steps.

## **Key Principles Guiding the Roadmap**

- 1. <u>Scientific Approach to R&D Preparedness:</u> Building on pathogen family approaches within the Phenuiviridae CORC framework to inform pandemic preparedness, systematically addressing scientific uncertainty, viral evolution patterns, amid changing availability of approaches, technologies and candidate medical countermeasures.
- Country-Led Leadership: Centering national expertise and researchers from affected regions, particularly Senegal and Mauritania, in shaping research priorities.
- 3. <u>One Health Integration:</u> Coordinating human, animal, and environmental health perspectives to understand transmission dynamics and intervention opportunities.
- 4. <u>Rapid Translation</u>: Aligning research design, delivery, and outputs with immediate outbreak response needs and long-term preparedness goals.
- 5. <u>Equitable Access:</u> Ensuring interventions generated from the coordinated research roadmap are available, affordable, and accessible at the point of need for the affected countries.

This coordinated research roadmap emphasizes the critical importance of global collaboration, country leadership, and One Health approaches to address Rift Valley Fever outbreaks. The integration of immediate research priorities with long-term pandemic preparedness goals will contribute to controlling current outbreaks while building resilience against future RVF emergence.

#### **Current Outbreak Situation**

**Senegal** – As of 20 October 2025, Senegal reported 260 laboratory confirmed human RVF cases with 2,102 suspected cases, resulting in 21 deaths (case fatality rate 8.1%), and 36 clinically severe cases. Six (Saint-Louis, Mat am, Louga, Dakar, Fatick and Kaolack) out the 14 regions have reported human cases. Highest risk is considered to have been among individuals with occupational animal exposure. RVF-positive mosquitoes were also detected in 3 mosquitoes species (Cx. tritaeniorhynchus, Cx. antennatus and a pool of fed female An. gambiae) in 3 regions. Both species are species widespread in northern Senegal and southern Mauritania. Six regions confirmed animal infections across ovine, caprine, and bovine populations. Ongoing viral sequencing to characterize circulating strains showed the reemergence of the lineage H with non-conservative polymerase substitutions that may influence viral fitness.

**Mauritania** – Within the same time period, Mauritania documented 35 laboratory confirmed human cases with 13 deaths near the Senegalese border, continuing a pattern of seasonal RVF recurrence in the region with cross-border transmission. Concurrent flooding has complicated response efforts.

**Regional Context** – WHO AFRO provided epidemiological surveillance data highlighting the broader regional implications and cross-border transmission risks, emphasizing the need for coordinated multinational research and response strategies

## Main Research Priorities by Thematic Area

#### **Animal Health and Transmission Dynamics**

#### Reservoir Ecology:

Defining animal reservoirs and transmission routes that enable RVFV maintenance during inter-epidemic periods, with particular focus on wildlife reservoirs (e.g., deer, Oryx, Dorca Gazalle), domestic livestock populations (sheep, cattle, goats, camels), and emerging evidence for bat or rodent involvement in viral maintenance and dissemination.

#### **Ecological Drivers:**

Understanding how rainfall patterns, animal movements, and mosquito dynamics drive spillover risk from livestock to humans.

#### Transmission Pathways:

Quantifying the relative contributions of direct contact, vector-mediated transmission, and food/animal product practices to human infection risk and potentially to disease severity, across different settings. While certain behaviours and practices are known to increase risk of RVF infection, the relative contribution of these to human infections in different geographical contexts is poorly understood.

Adaptative changes. Investigating adaptive changes in the vector and virus within the environment that could lead to a permissive nature of the vector.

#### Early Warning Systems:

Evaluating whether livestock infection and abortion reporting can serve as an effective early warning system for human cases and assessing current surveillance system efficacy in heathcare and household settings. Evaluating enhanced vector surveillance (and diversity of vectors) and wildlife mortality, as effective early warning system indicators, particularly in high-risk outbreak settings. Assess whether integration of data with ecological drivers can serve as an effective early warning system.

#### Animal Interventions:

Identifying additional interventions in animal populations to reduce transmission likelihood to other animals and humans, including optimized vaccine programs and enhanced import/export systems to better understand movement of animals. Modelling efforts indicate potential benefit of animal vaccination on human case numbers but this requires validation. A One Health Vaccination Strategy (OHVS) for RVF, which considers optimal use of human and livestock vaccines needs to be developed.

#### Vector control intervention:

Characterizing the newly identify vectors and identifying innovative or evidence-based vector control strategies

#### **Diagnostics**

#### Molecular and Serological Tools:

- o Baseline seroprevalence studies in nationally representative samples and among high-risk groups with regular follow up.
- Developing robust molecular and serological diagnostic platforms for comprehensive monitoring of RVF spread in animal populations, addressing current limitations in field-deployable technologies
- o Improving diagnostic tools, and their availibitlity and access, for RVFV detection at point-of-care, especially in resource-limited settings, according to the ASSURED criteria.
- Advancing multiplex and broad-spectrum assays to distinguish RVF from other febrile illnesses
- Leveraging metagenomics approaches, for broad, unbiased detection of RVFV and co-infecting pathogens from complex clinical and environmental samples, enabling comprehensive pathogen surveillance.

### Technical Challenges:

- Lack of data on the evolution and persistence of viral markers in blood and other biological fluids to support diagnostic development
- Overcoming biosafety challenges for sample handling and increasing laboratory capacity in endemic regions.
- Addressing affordability and practical limitations of current molecular methods (RT-PCR, RT-LAMP, RPA) and developing novel platforms for in-field testing.
- Defining product characteristics (eg. desirable and essential assay performance) in the absence of official target product profile for rapid diagnostics.
- Lack of strong data on RVFV viral RNA and antigens persistence duration in body fluids to guide diagnostics development.
- Ensuring DIVA assays are available for post vaccination surveillance and outbreak tracing.

#### **Therapeutics**

#### <u>Antiviral Development:</u>

- Identifying the most promising approaches for RVFV-specific antivirals, targeting viral or host factors that inhibit replication or block entry
- Developing small molecules and antibody cocktails that provide protection at minimal doses through simultaneous blocking of attachment and fusion processes and that can overcome barriers such as the blood-brain barrier to treat neurological complications
- Evaluating supportive care strategies including immunomodulators, broadspectrum antivirals, and novel compounds showing efficacy in animal models through clinical trials.

#### Clinical Trial Design:

- Establishing appropriate trial designs (CORE protocols), endpoints, and standardized outcome measures for clinical efficacy studies, incorporating lessons learned from other viral hemorrhagic fever therapeutic trials for clinical efficacy studies.
- Developing assessment protocols that extend beyond short viremia periods to capture long-term outcomes, neurological sequelae, and quality of life measures.

#### Clinical and Supportive Care:

o To investigate optimal supportive care and post-infection needs and make available appropriate standards of clinical care guidelines.

#### **Vaccines**

## <u>Vaccine Development Priorities:</u>

- Develop and agree clinical case definition to support vaccine efficacy studies.
- Defining immediate RVF vaccine(s) research priorities that can be meaningfully advanced during the current outbreak window, leveraging ongoing transmission for efficacy evaluation.
- Establishing ideal immunological correlates of protection, including how neutralizing antibody and cellular responses relate to real-world immunity
- Systematically comparing (via independent WHO Vaccines Prioritization Expert Group) vaccine candidate platforms (live-attenuated, nucleic acid, viral vector, inactivated, virus-like particles, RNA and DNA) for breadth and durability of protection against circulating RVFV variants, incorporating safety profiles particularly for high-risk groups including pregnant women.
- Validation of DIVA assays and approaches to support assessment of efficacy against infection.

#### Clinical Trial Considerations:

- Determining appropriate trial designs (CORE protocols) incorporating appropriate endpoints (infection, disease severity, transmission reduction) and study populations (occupational risk groups, pregnant women, adolescents) for vaccine policy and licensure, including for DIVA approach.
- Designing CORE protocols that use innovative approaches, using seamless strategies and that can simultaneously meet needs for clinical efficacy assessment when possible, and for alternative licensure pathways to be explored, including defining essential data elements.
- Addressing challenges of evaluating efficacy in contexts of short viremia windows and variable clinical presentations.
- Building capacity and innovative approaches to simplify and facilitate implementation of high quality simple and large-scale efficacy trials in hyperendemic regions, including outbreak unpredictability, local

infrastructure challenges, and requirements for robust long-term surveillance and participant follow-up.

# One Health Integration:

 Develop and validate One Health Vaccination Strategies (OHVS) for RVF which consider integrating animal and human vaccine programs while recognizing differences in dose, formulation, safety, and regulatory oversight for cross-species vaccination.

## **Cross-Cutting Recommendations**

**Standardization:** Harmonize case definitions, laboratory assays, and clinical endpoints across research sites and countries. Establish reference standards and quality control measures for diagnostic assays, therapeutic efficacy assessment, and vaccine immunogenicity evaluation. An international antibody standard is available that should be used by developers and regulators.

Capacity Building: Strengthen capacity to conduct clinical trials integrated into the outbreak response, national laboratory capacity to support diagnostics and trials, in a collaborative maneer, and regional research infrastructure. Expand access to mobile diagnostic innovations and capabilities and integrate innovative laboratory platforms within existing public health surveillance networks and ensure use of available international antibody standard in assessments.

**Data Sharing:** Promote open data sharing through CORC networks and align with WHO R&D Blueprint for Epidemics frameworks for rapid research mobilization during health emergencies. Establish secure, interoperable data platforms that facilitate real-time information exchange while protecting participant confidentiality and intellectual property rights.

**Regulatory Alignment:** Coordinate with national ethics committees and regulatory agencies using AVAREF platform and other platforms (e.g., AMAR/AMA, EMA, national authorities and ethics committees) for streamlined clinical trial pre-approval and efficacy evidence generation pathways. Develop clear regulatory guidance for combination therapies, dual-use vaccines, and emergency use authorization procedures, and licensure.

**Funding Coordination:** Engage and collaborate with funding agencies to align international funding mechanisms to support multi-country platform trials and sustained research networks. Ensure funding available for research in outbreak context.

**Equitable Access:** Ensure interventions developed through the collaborative research roadmap are available, affordable and accessible for affected regions. Enable regional stockpiling of effective interventions and production of regionally-relevant interventions (particularly those tested in populations.

# **Immediate Next Steps**

Based on the consultation outcomes, priority actions include:

- 1. Merge and align scientific and partnership processes to support efforts for unified outbreak research response. Foster ongoing collaboration for research priorities and community-driven response strategies.
- 2. Create OPEN scientific informal working groups under the CORC to address and follow up with the implementation of each of the identified research priorities, ensuring strong participation from scientists from countries at risk of RVF outbreaks. Invite funders and donors to accompanny the scientific deliberations and use their outcomes to inform decisions on funding prospectively and to avoid unnecessary competion and duplication of efforts.
- 3. Strengthen Surveillance: Advance integrated animal-human surveillance systems and ecological forecasting capabilities
- Accelerate Diagnostic Development: Fast-track validation and deployment of point-of-care diagnostics and centralized immune assays.
- 5. Develop Target Product Profiles for diagnostics to prepare for future outbreaks and enable access and consider using enhanced sampling methods to streamline centralized testing in the current and nearterm outbreaks
- 6. Conduct sero-epidemiology studies during and after outbreaks to inform biomarker research and candidate MCMs efficacy endpoints development, and to inform target population identification for efficacy trials.
- 7. Optimize clinical care pathways to support both research objectives and outbreak response requirements. Scale up isolation facilities.
- 8. Launch Clinical Protocols: Implement RVF clinical characterization protocols to standardize case definitions and optimize care for research and response. Develop and validate DIVA assays that distinguish immune responses between infections and vaccine candidates
- 9. Enable Platform Trials: Establish multi-country, multi-outbreak clinical trial platforms (CORE protocols) for therapeutics and vaccines. Establish secure, interoperable data platforms that facilitate real-time information exchange while protecting participant confidentiality and intellectual property rights.
- 10. Vaccine Access: Facilitate access to candidate vaccines, evaluate supply logistics, and develop strategies for broader immunization coverage in atrisk populations. Provide guidance to affected countries on evidence justifying use of available animal vaccines.
- 11. Accelerate candidate vaccine production (with doses available in weeks for possible field deployment in a clinical trial). Note importance of equitable access to ensure stockpiles in region affected and a plan for transfer to regional production for future outbreak control.
- 12. Assure adherence to Good Participatory Practices (GPP) to assure ethical, inclusive and scientific outcomes in RVF research.

## Annex I

# **Background documents**

Efficacy trials of Rift Valley Fever vaccines and therapeutics: Guidance on

clinical trial design

Rift Valley Fever Research and Development (R&D) Roadmap

Rift Valley Fever WHO Webpage

Rift Valley Fever WHO Fact Sheets

Time	Topic	Speakers			
16:00 – 16:10	Introduction and welcome remarks	Yper Hall (UKHSA) Ibrahima Soce Fall (IPD, Senegal)			
16:10 – 16:15	A scientific approach to R&D preparedness and response	Ana Maria Henao Restrepo (WHO)			
Session 1: Ove	Session 1: Overview of the epidemiological Situation				
16:15 – 16:20	Outbreak situation in Senegal	Boly Diop (Senegal MOH)			
16:20 – 16:25	Outbreak situation in Mauritania	Mohamed Lemine Diakite (Mauritania MOH)			
16:25 – 16:30	Overview of regional epidemiological situation	Esther Muwanguzi (WHO AFRO)			
Session 2: Outbreak Response and Plans					
16:30 – 16:35	WHO Incident Management Response	Esther Muwanguzi (WHO AFRO)			
Session 3: Animal health and transmission dynamics Understanding how the virus moves between animal reservoirs, vectors, and humans, and identifying intervention points to prevent outbreaks					
16:35 – 16:55	<ul> <li>Panel discussion</li> <li>What are the animal reservoirs and transmission routes enabling RVF virus maintenance between outbreaks, particularly during interepidemic periods?</li> <li>Which ecological and behavioral factors (such as rainfall, animal movements, and mosquito dynamics) drive the risk of spillover from livestock to humans?</li> <li>How do direct contact, vectormediated transmission, and food/animal product practices</li> </ul>	Moderaror: Yper Hall (UKHSA)  Kariuki Njenga (Center for Research in Emerging Infectious Diseases-East and Central Africa, Nairobi, Kenya)  Mawlouth Diallo (IPD, Senegal)  Representative Institute Pasteur France (TBC)			

- contribute relatively to human infection risk in various settings?
- Can livestock infection reporting act as an early warning for human cases, and what is the efficacy of current surveillance systems for predicting and managing outbreaks?
- What further interventions in animals could be considered to reduce likelihood of transmission to other animals or humans?

Pierre-Yves Lozach, (IVPC UMR754, INRAE, Université Claude Bernard Lyon 1, EPHE, PSL Research University, Lyon, France)

Friedemann Weber (Institute for Virology, Justus-Liebig University, Giessen, Germany).

Francis Maluki Mutuku -TBC (Department of Environment and Health Sciences, Technical University of Mombasa, Mombasa, Kenya)

# Session 4: Rift Valley fever (RVF) diagnostics

Do we have the necessary diagnostic tools?

#### 16:55 – 17:15

#### **Panel discussion**

- Do we have solid serological and molecular diagnostic tools to monitor RVF spread in animals?
- How can diagnostic techniques be improved for rapid, specific, and sensitive RVFV detection at pointof-care, especially in resourcelimited and outbreak-prone settings?
- What are the best approaches to distinguish RVF from other similar febrile illnesses, using multiplex or broad-spectrum assays?
- How do we overcome biosafety challenges for sample handling and increase laboratory capacity in endemic regions?
- What are the needs and limitations of current molecular methods (RT-PCR, RT-LAMP, RPA), and how can novel platforms improve speed and practicality for in-field testing?
- How can Metagenomics enable broad, unbiased detection of RVFV and co-infecting pathogens from

Moderator: Emmanuel Agogo (FIND)

Stephen Balinandi (UVRI, Uganda)

Julius Lutwama, (UVRI Uganda)

Moussa Moise Diagne, (IPD, Senegal)

Lorenzo Subissi, (WHO) Christian Drosten - TBC (Institute of Virology, Charité-Universitätsmedizin Berlin, Freie Universität Berlin,

Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Institute of Virology, Berlin, Germany)

Catherine Cêtre-Sossah – TBC (ASTRE, University of

	complex clinical or environmental samples?	Montpellier, CIRAD, INRAe, Montpellier, France)			
		W. Ian Lipkin (Center for Infection and Immunity Mailman School of Public Health, Columbia Univ, USA)			
Session 5: Therapeutics for Rift Valley fever (RVF)  Concerning specific antivirals, supportive treatments, and strategies to prevent severe complications and deaths					
17:15 – 17:20	Landscape of existing candidate therapeutics	Julia Tree (UKHSA)			
17:20 – 17:40	<ul> <li>Panel discussion</li> <li>What are the most promising approaches for developing RVFV-specific antivirals, and which viral or host targets offer the best prospects for inhibiting replication</li> </ul>	Moderator: Cristina Cassetti (WHO/CEPI)			
		Placide Mbala, (INRB, DRC)			
	<ul><li>or blocking entry?</li><li>How can small molecules and antibody cocktails overcome</li></ul>	Laura Merson - TBC (IPD Senegal)			
	barriers such as the blood-brain barrier to treat neurological complications?	Mahaman Doutchi (Zender and Niamey University/ALIMA)			
	What supportive care strategies and adjuncts (immunomodulators, broad-spectrum antivirals, or novel)	Marco Cavaleri (EMA)			
	compounds) show efficacy in animal models and could translate to improved outcomes in humans?	Ira Longini (U Florida, USA)			
<ul> <li>What stand used including vireminal power including including the standard including in</li></ul>	What trial designs, endpoints, and standardized outcomes should be used for clinical efficacy studies, including assessment beyond short viremia periods?	James Crowe – TBC (Vanderbilt University)			
		Jim Demarest (INTREPID Alliance)			
	molecular diagnostic tools to monitor RVF spread in animals?	Janet Diaz, (WHO)			
		Julia Tree (UKHSA)			
		Ally Olotu – TBC (Ifakara Health Institute, Tanzania)			

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		Blandina Mmbaga – TBC (Kilimanjaro Clinical Research Institute, Tanzania)		
		Kariuki Njenga (Washington State University, Kenya)		
Session 6: Vaccines for Rift Valley fever (RVF) Focus on developing safe, effective vaccines for humans and animals, establishing correlates of protection, optimizing trial designs in endemic regions, and addressing One Health integration				
17:40 – 17:45	Landscape of existing candidate vaccines	Peter Hart (CEPI)		
17:45 – 18:10	<ul> <li>Panel discussion</li> <li>What are the priorities for RVF vaccine that can be addressed during this outbreak?</li> <li>What are the ideal immunological correlates of protection for RVF, and how do neutralizing antibody and cellular responses relate to real-world immunity across populations?</li> <li>Which vaccine platforms (live-attenuated, viral vector, inactivated, VLPs) provide the broadest and most rapid protection against all circulating RVFV variants, and how do these differ in terms of safety profiles, especially in high-risk groups like pregnant women?</li> <li>What endpoints (infection, severe disease, transmission reduction) and study populations (e.g. occupational risk groups, pregnant women, adolescents) are most appropriate for informing vaccine policy and licensure?</li> <li>How should efficacy be evaluated in the context of short viremia windows and variable clinical presentations, considering RT-PCR</li> </ul>	Moderator: Phil Krause (WHO)  Peter Hart (CEPI)  Daniel Wright (Oxford Vaccine Group, UK)  Kelly Lyn Warfield – TBC (Sabin Institute)  Pontiano Kalebu (UVRI, Uganda)  Brian H Bird – TBC (DDVax)  Barney Graham – TBC (Morehouse School of Medicine, USA)  Paul Wichgers Schreur (Wageningen Bioveterinary Research, Netherlands) LARISSA consortium on liveattenuated hRVFV-4s vaccine candidates		

	<ul> <li>and serology limitations for case ascertainment in field trials?</li> <li>What are the challenges for large-scale efficacy trials in hyper-endemic regions, including outbreak unpredictability, local data gaps, and logistical challenges for robust surveillance and follow-up?</li> <li>How can animal vaccines and human vaccine programs be integrated under a One Health approach, recognizing differences in dose, formulation, safety, and regulatory oversight for cross-species vaccination?</li> </ul>			
Session 7: Key priorities discussion and prioritization (20 mins).				
18:10 – 18:30	Summary of key research questions Next steps	Phil Krause (WHO)		
18:30	Adjourn			