World Health Organization

A Coordinated Research Roadmap for Rift Valley Fever Virus (RVF): Immediate Steps for implementation in the 2025 Outbreak

A Brief overview

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October 31, 2025

R&DBlueprint

Powering research to prevent epidemics

Key Principles Guiding the Roadmap

1. **Scientific Approach to R&D Preparedness**: 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
2. **Country-Led Leadership**: Centering national expertise and researchers from affected regions, particularly Senegal and Mauritania, in shaping research priorities.
3. **One Health Integration**: Coordinating human, animal, and environmental health perspectives to understand transmission dynamics and intervention opportunities.
4. **Rapid Translation**: Aligning research design, delivery, and outputs with immediate outbreak response needs and long-term preparedness goals.
5. **Equitable Access**: Ensuring interventions generated from the coordinated research roadmap are available, affordable, and accessible at the point of need for the affected countries

Main Research Priorities by Thematic Area

- Animal Health and Transmission Dynamics
- Diagnostics
- Therapeutics
- Vaccines
- Cross-cutting recommendations
- Immediate next steps

Animal Health and Transmission Dynamics

- **Reservoir Ecology**: Defining animal reservoirs and transmission routes that enable RVFV maintenance during inter-epidemic periods
- **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.
- **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.
- **Animal Interventions**: Identifying additional interventions in animal populations to reduce transmission likelihood to other animals and humans
- **Vector control intervention:** Characterizing the newly identify vectors and identifiying innovative or evidence-based vector control strategies

Diagnostics

- **Molecular and Serological Tools**:
  - 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
  - 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
- **Technical Challenges**:
  - Lack of strong data on RVFV viral RNA and antigens persistence duration in body fluids
  - Biosafety challenges for sample handling and increasing laboratory capacity in endemic regions
  - 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
  - Ensuring DIVA assays are available for post vaccination surveillance and outbreak tracing.

Therapeutics

- **Research and Development**
  - 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
  - Evaluating supportive care strategies including immunomodulators, broad spectrum antivirals
- **Clinical Trial Design**
  - Establishing appropriate trial designs (CORE protocols), endpoints, and standardized outcome measures 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**
  - Investigate optimal supportive care and post-infection needs and make available appropriate standards of clinical care guidelines.

Vaccines- Development Priorities

- Develop and agree on 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 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) existing vaccine candidates 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.

Vaccines- Clinical Trial Considerations

- Determining appropriate trial designs (CORE protocols) incorporating appropriate endpoints and study populations for vaccine licensure, including for DIVA approach.
- Designing CORE protocols that use innovative approaches, using seamless strategies and that can simultaneously generate data for clinical efficacy assessment, when possible, and for alternative licensure pathways to be explored
- Addressing challenges of evaluating efficacy in contexts of short viremia windows and variable clinical presentations.
- Building capacity and innovative approaches to facilitate implementation of high-quality 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

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.
- **Capacity Building**: Strengthen capacity to conduct clinical trials integrated into the outbreak response, national laboratory capacity to support diagnostics and trials, in a collaborative manner, and regional research infrastructure.
- **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.
- **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.
- **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.

THANK YOU

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