World Health Organization

UK Health Security Agency

Arenaviridae Research & Development Roadmap

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R&DBlueprint

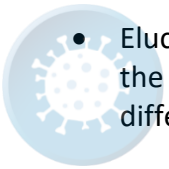
Powering research to prevent epidemics

Top 10 Research & Development Priorities

Ecology and Epidemiology

- Develop comprehensive surveillance tools that combine ecological, climatic and human behaviour to better understand transmission dynamics and spillover drivers.
- Strengthen public health detection and reporting of arenavirus infection by standardising surveillance case definitions, improving diagnostic confirmation pathways, and ensuring accurate documentation of community and home deaths.
- Establish and maintain a central, accessible repository of well-characterised arenavirus isolates with robust governance, biosafety and metadata frameworks to support global research and assay development.

Viral Family Biology



- Elucidate the virus-host interactions and immune evasions, including understanding the mechanisms of immunosuppression, and investigate the similarities and difference in the structure of viral glycoproteins for therapeutic and vaccine design.

Diagnostics

- Expand and standardise diagnostic capacity across endemic regions by improving testing capability in rural and low-resource facilities. This includes increasing workforce capacity, establishing robust referral links to higher-tier laboratories and implementing laboratory accreditation to ensure timely, accurate and comparable diagnostics and surveillance.
- Develop harmonised, evidence-based diagnostic standards and quality assurance systems (including proficiency panels, access to reference materials and standardised RT-PCR frameworks).
- Define and standardise Target Product Profiles (TPPs) for centralised and near-patient diagnostics and establish regulatory-grade validation protocols and criteria to guide manufacturers and developers.

Therapeutics and Vaccines

- Establish standardised, safe, BSL2-compatible surrogate assays and reverse-genetics systems for drug screening.
- Develop effective vaccines, especially broad-spectrum or pan-arenavirus vaccines, to identify correlates of protection for multiple arenaviruses, and develop robust animal models.
- Establish harmonised clinical trial endpoints, case definitions and diagnostic algorithms to ensure that therapeutic and vaccine studies generate comparable, high-quality data across trial sites and arenavirus-endemic regions.

Content

Abbreviations

ACEGID	Africa Center of Excellence for Genomics of Infectious Diseases
AHF	Argentinian Haemorrhagic Fever
ANLIS	Administración Nacional de Laboratorios e Institutos de Salud (Argentina)
BSL	Biosafety Level
CAB	Community Advisory Board
CDC	Centers for Disease Control and Prevention
CE/IVD	Conformité Européenne / In Vitro Diagnostic
CEPI	Coalition for Epidemic Preparedness Innovations
CHAPV	Chapare virus
CIDRAP	Center for Infectious Disease Research and Policy
CLSI	Clinical and Laboratory Standards Institute
CORC	Collaborative Open Research Consortium
CRP	C-reactive Protein
EDCTP	European & Developing Countries Clinical Trials Partnership
ELISA	Enzyme-Linked Immunosorbent Assay
EUL	Emergency Use Listing
FC	Flow Cytometry
FDA	Food and Drug Administration (USA)
GP	Glycoprotein
GTOV	Guanarito virus
IAVI	International AIDS Vaccine Initiative
IDSR	Integrated Disease Surveillance and Response
IF	Immunofluorescence
IgG	Immunoglobulin G
IgM	Immunoglobulin M
IHC	Immunohistochemistry
INEVH	Instituto Nacional de Enfermedades Virales Humanas (Argentina)
IPC	Infection Prevention and Control
IVDR	In Vitro Diagnostic Regulation
JUNV	Junín virus
LASV	Lassa virus
LCMV	Lymphocytic Choriomeningitis Virus
LDT	Laboratory-Developed Test
LUJV	Lujo virus
mAb	Monoclonal Antibody
MACV	Machupo virus

MCM	Medical Countermeasure
MIQE	Minimum Information for Publication of Quantitative Real-Time PCR Experiments
MEURI	Monitored Emergency Use of Unregistered and Investigational Interventions
mRNA	Messenger RNA
N	Nucleocapsid
NCDC	Nigeria Centre for Disease Control and Prevention
NHP	Non-human Primate
NIH	National Institute of Health
NP	Nucleoprotein
PAHO	Pan American Health Organization
PBMC	Peripheral Blood Mononuclear Cell
PCR / RT-PCR	Polymerase Chain Reaction / Reverse-Transcription Polymerase Chain Reaction
POC	Point of Care
POCT	Point-of-Care Test
PPE	Personal Protective Equipment
PRD	Product Requirements Document
PQ	Pre-Qualification (WHO)
RCT	Randomised Controlled Trials
RDT	Rapid Diagnostic Test
RNA	Ribonucleic Acid
RT-qPCR	Quantitative Reverse-Transcription PCR
RUO	Research Use Only
SABV	Sabiá virus
SBS	Social and Behavioural Science
TPP	Target Product Profile
UKHSA	UK Health Security Agency
WHO	World Health Organization
Z	Z protein (arenavirus matrix / zinc-binding protein)

Introduction

In November 2024, the World Health Organisation (WHO) launched the Collaborative Open Research Consortium (CORC) for Arenaviridae as part of the WHO R&D Blueprint for Epidemic team's global effort to improve pandemic preparedness R&D through a priority pathogen family approach. On 31st July 2025, UK Health Security Agency (UKHSA) on behalf of the WHO convened the Arenaviridae CORC to discuss research priorities related to Arenavirus medical countermeasures (MCMs) according to the following themes: epidemiology and transmission; virology and pathogenesis; diagnostics and serology; pre-clinical models, vaccine and therapeutic development. The full meeting agenda is attached (Annex I) and was attended by 170 participants.

Following the inaugural Arena CORC call, a broad literature review of three Old World Arenaviruses and five New World Arenaviruses was conducted and compiled into a matrix. This was then sent to the working group members, who were asked to highlight any challenges within these themes and state any research priorities. The information gathered during this exercise was the disseminated to the working group for two rounds of review, feedback from which was collated into this document.

This R&D roadmap outlines the priority knowledge gaps, key technological needs, and strategic goals and milestones required to advance the development of diagnostics, therapeutics, vaccines, and integrated surveillance systems for arenaviruses. By aligning stakeholders around common goals and fostering an open, collaborative research environment, it aims to reduce the time between pathogen emergence and the availability of effective countermeasures, ultimately enhancing global preparedness and health security.

Arenaviridae

Arenaviruses are a diverse group of enveloped, negative-sense RNA viruses within the family *Arenaviridae*. They are classified into four genera; *Mammarenavirus*, *Reptarenavirus*, *Hartmanivirus*, and *Antennavirus*, with human disease almost exclusively associated with mammarenaviruses. These viruses are primarily rodent borne, each species typically linked to a specific rodent reservoir, and human infection occurs through exposure to contaminated excreta or, in some rare cases, through person-to-person transmission. Mammarenaviruses include both Old World viruses (such as Lassa virus) and New World viruses (such as Junín and Sabiá viruses), several of which can cause severe viral haemorrhagic fevers.

Clinical presentation varies by virus and host factors, but human infecting mammarenaviruses commonly cause a spectrum of symptoms ranging from mild febrile illness to life-threatening disease. Early manifestations often include fever, malaise, headache, myalgia, and gastrointestinal symptoms. In severe cases, particularly with Lassa virus (LASV) and several New World mammarenaviruses, patients may progress to haemorrhage, shock, neurological involvement, and multiorgan dysfunction.

Over the past 15 years, arenaviruses have continued to cause significant public health events. Lassa fever has produced recurrent outbreaks across West Africa, with Nigeria experiencing substantial annual surges since 2018. Sporadic cases and small clusters of New World arenavirus infections have also been documented in South America, reflecting the ongoing risk posed by rodent associated spillover. In addition, recent discoveries of novel mammarenaviruses in Asia and Southeast Asia highlight the expanding ecological and geographic landscape of this viral genus and the potential for previously unrecognized species to infect humans.

Of all mammarenaviruses, Lassa virus has received the greatest scientific attention and remains the most thoroughly researched. This is largely due to the high incidence of Lassa fever (caused by LASV) across multiple West African countries where the disease is endemic, causing 100,00 - 300,000 infections and thousands of deaths each year. The WHO has identified LASV as one of its 'priority pathogens'; pathogens which have epidemic potential with few or no existing medical countermeasures available. Around 80% of LASV cases have mild or non-existent symptoms, meaning that most cases go unreported, which may contribute to the spread of the disease beyond endemic regions. The remaining 20% of cases can progress to life-threatening illnesses, often requiring hospitalisation, increasing the burden on resources.

Since the publication of the 2019 Lassa Fever Research and Development (R&D) Roadmap, significant progress has been made in several areas, however there are persistent gaps. The Research and Development Roadmap for Lassa Fever, 2024 Update published by the Center for Infectious Disease Research and Policy (CIDRAP) further highlights the progress made in the last few years, but in both reports there is a lack of emphasis on the arenavirus family as a whole, with key gaps in LASV medical countermeasure development.

One of the key gaps highlighted across both documents is the lack of a standardised point of care rapid diagnostic tool for LASV infection, which continues to persist. To progress vaccines and therapeutics, accurate reporting is essential to map disease dynamics, to track genetic changes in LASV strains and to differentiate between LASV and other circulating pathogens. Whilst there are several lab diagnostics tools for LASV, accessible point of care tools are still lacking.

Whilst several vaccine candidates have been progressed from pre-clinical stages up to and including Phase II clinical trials, there are still no licensed vaccines available. However, improvements have been made in establishing clear pathways towards regulatory approval, as well as a wider portfolio of vaccine platforms, highlighting the potential for cross-protection across LASV lineages. These are positive steps with significant implications for coverage across the wider arenavirus family.

There have been many groundbreaking developments in therapeutic clinical trial design. This includes shifting away from traditional fixed-trial design, allowing trials to continue when incidence is fluctuating, pauses dependent on outbreak intensity and dynamic

inclusion/exclusion of interventions. One major development is the re-evaluation of ribavirin as an effective therapeutic treatment for LASV infection; uncertainty over this treatment option has been reaffirmed following an observational study of ribavirin as a treatment for LASV infection. This study showed that ribavirin has a mode of action that is not antiviral and did not alleviate the concerns surrounding toxicity at high doses.

With the WHO R&D Blueprint for Epidemics shifting towards a family-centric approach, the insights gained from LASV medical countermeasure development should guide the evolution of pan-arenavirus solutions. Applying these lessons will help accelerate the development of safe, effective and equitable access to countermeasures for future outbreaks.

Current Landscape of Medical Countermeasures

Virus Common Name	Diagnostic Research	Vaccine Research	Therapeutic Research
Lassa virus	+++	++	++
LCMV	+++	+	+
Lujo virus	+	+	+
Chapare virus	+	+	+
Guanarito virus	+	+	+
Junín virus	+	+++	+
Machupo virus	+	+	+
Sabiá virus	+	+	+

+++ = licenced product

++ = significant R&D in this area, close to development/licensure of an MCM

+ = limited R&D in this area, not close to development/licensure of an MCM

Time-Phased Milestones by Thematic Area

Table 1 – Reservoirs and Transmission

Phase 1 Foundation (Years 1-2)

- Implement harmonised One Health-focused serosurveys across human populations and selected animal hosts.
- Standardise protocols for sampling, testing, and data analysis and conduct coordinated sample collection and produce comparable exposure datasets across regions.
- Integrate serological, ecological, and epidemiological data to inform surveillance and public health interventions.
- Define major zoonotic and human-to-human transmission routes.
- Identify key rodent reservoirs using molecular and ecological methods in priority regions.

Phase 2 Scale-up (Years 3-5)

- Training and harmonizing established protocols for sampling, testing, and data analysis in different settings and regions.
- Characterise effects of land use, climate, and human/animal behaviour on spillover risk.
- Predict cross-species transmission risks using receptor compatibility and restriction factor data from functional screening studies.
- Analyse rodent reservoir ecology, viral genetics, and environmental factors across high- vs low-transmission settings.
- Develop integrated transmission models incorporating identified ecological, genetic, and environmental risk factors.
- Expansion of surveillance across different habitats, spatial mapping (geospatial analysis), and identification of hotspots.
- Deliver advanced transmission models to support prevention and control strategies.

Phase 3 Consolidation and Innovation (Years 6-10)

- Maintain and update global maps of arenavirus reservoirs, transmission routes, and spillover risk, including outbreaks in humans and animal hosts.
- Operationalise integrated transmission models for routine surveillance, preparedness, and early warning.
- Validate predictive models using longitudinal ecological, environmental, and human datasets.
- Apply modelling outputs to guide targeted prevention strategies (e.g. rodent control, land-use planning, occupational risk reduction).

- Translate transmission evidence into clear, evidence-based guidance for IPC, biosafety, and post-infection counselling.
- Consolidation of integrated animal–human surveillance networks.
- Strengthen long-term One Health surveillance capacity and regional ownership in endemic countries.
- Identify and prioritise regions and viruses at highest risk of future emergence for proactive intervention.

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Table 2 – Surveillance

Phase 1 Foundation (Years 1-2)

- Establish a standardised RT-PCR diagnostic framework for New and Old World arenaviruses.
- Determine region-specific arenavirus targets to incorporate into multiplex febrile illness diagnostic panels.
- Establish community-based surveillance mechanisms for early detection of Lassa fever and other arenavirus outbreaks.
- Improve reporting of arenavirus cases and deaths as social stigma associated with these diseases may cause under reporting. Establish regionally accredited reference laboratories.

Phase 2 Scale-up (Years 3-5)

- Develop and validate point-of-collection sample inactivation and stabilization protocols for arenavirus diagnostics. At least two validated inactivation methods compatible with RT-PCR, reducing sample failure rates by ≥30% compared to current practice. Protocols validated and field-tested in ≥3 endemic countries by Year 3, with regional rollout by Year 5.
- Include arenavirus detection and reporting in regular healthcare worker training.
- Implement harmonised One Health-focused arenavirus diagnostic across accredited laboratories in endemic and non-endemic regions.

Phase 3 Consolidation and Innovation (Years 6-10)

- Integrate arenavirus surveillance into routine national disease monitoring systems.
- Keep community-based surveillance active, especially in rural and peri-urban areas.
- Combine human, animal, and environmental data to improve early warning of outbreaks.
- Keep diagnostic tests, case definitions, and reporting methods up to date and consistent.
- Use surveillance data to guide outbreak response and resource planning.
- Share data across countries to detect spread and emerging risks early.
- Implement evidence-based prevention strategies in target populations.

Table 3 – Viral Family Biology

Phase 1 Foundation (Years 1-2)

- Establish a comprehensive arenavirus reference and resource platform with standardised governance, biosafety and metadata frameworks.
- Establish a centralised arenavirus isolate repository with genetically diverse and well characterised New and Old World isolates accessible to the global research community
- Characterize the structural biology and antigenic diversity of a broader range of arenaviruses through modelling and/or structural elucidation
- Define conserved and divergent arenavirus life-cycle mechanisms, as well as a greater understanding of replication and transcription kinetic mapping.
- Compare and contrast assembly, budding and intracellular trafficking pathways across arenaviruses, and to seek to better understand viral entry mechanisms across lineages.
- Develop a pipeline for longitudinal monitoring of arenavirus–host immune interactions in animal reservoirs.

Phase 2 Scale-up (Years 3-5)

- Develop a framework for risk assessment of novel arenaviruses.
- To establish a representative arenavirus panel with harmonised experimental platforms.
- Establish and maintain an up-to-date, global repository of arenavirus host cell lines to advance research on virus–host interactions.
- Longitudinal evaluation of viral evolution in wild animal populations to monitor genetic changes over time.
- Generation and sharing of regional genomic and immunological datasets.
- Propose and validate molecular targets in arenavirus proteins for the development of disease countermeasures, based on evidence supported by structural biology.

Phase 3 Consolidation and Innovation (Years 6-10)

- Maintain an up-to-date, easily accessible global repository of arenavirus isolates and associated data.
- Pre-clinical development of candidate vaccines and antiviral treatments targeting arenavirus proteins
- Identify cross-reactive vaccines and broad-acting antivirals across different members of the arenavirus family.
- Rapidly assess biological data from newly discovered arenaviruses and prepare a risk assessment about potential for spread.
- Use improved animal models to better understand how severe disease develops in people.
- Apply knowledge about immune responses to guide vaccine and treatment design.

- Support long-term collaboration and data sharing between research groups and countries.

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Table 4 – Diagnostics

Phase 1 Foundation (Years 1-2)

- Draft target product profiles (TPPs) for arenavirus molecular diagnostic for use in centralised laboratories and near-patient testing.
- Define the specific reference protocols that will be used to validate future assays.
- Draft a Product Requirements Document (PRD) with desired performance criteria for future rapid diagnostic tests (RDTs).
- Identify/develop critical reagents, including reference material for the validation and harmonisation of the results across laboratories/methods.
- Develop RDTs to prototype and stress-test viable devices.
- Agree on data and reporting standards so diagnostic results can feed into surveillance systems.
- Identify qualified manufacturers and distributors of RDTs that meet regulatory standards for local and regional needs.

Phase 2 Scale-up (Years 3-5)

- Further develop, validate and deploy RDTs that best meet the criteria specified in the PRD, e.g. (with high sensitivity and specificity), for use in endemic areas.
- Ensure centralised testing methods have high (e.g., > 95%) capture of known lineages / variants of an arenavirus (Lassa II, III, etc.) to ensures that RDTs are not referenced against inaccurate standards.
- Establish a proficiency testing programme for centralised / reference labs.
- Test RDTs and PCR assays using samples covering low to high viral loads to understand real performance limits.
- Develop a quality management system to ISO 9001 / *in vitro* diagnostic regulation (IVDR) standards to provide a framework for the continuous monitoring and product development of selected diagnostic devices
- Strengthen the availability and distribution of assays for priority laboratories across regions and operational settings
- Enhance the accuracy, clinical validation, manufacturing scalability, and equitable distribution of RDTs and point-of-care (POC) platforms.
- Investigate and validate biomarkers to aid diagnosis and predict outcomes.

Phase 3 Consolidation and Innovation (Years 6-10)

- Ensure validated RT-qPCR assays are available for all priority arenaviruses on both open and cartridge-based platforms.
- To ensure that newly developed and existing diagnostic tools are systematically integrated into clinical algorithms and surveillance pathways to support appropriate test selection, interpretation, and reporting across different levels of care.

- Validate sample inactivation protocols (e.g., specific lysis buffers) that allow samples to be handled in Biosafety Level (BSL) 2 labs to remove the bottleneck for immediate centralised testing and enhance surveillance efforts.
- Development and validation of RDT built upon the foundation of previous phases that use the validated approaches and reference materials established in Phase II.
- Maintain quality assurance and proficiency testing to ensure long-term reliability of diagnostics.
- Ensure sustainable access to reagents, controls, and consumables, including cold-chain-free options.

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Table 5 – Therapeutics

Phase 1 Foundation (Years 1-2)

- Develop in vitro assays for assessing the efficacy of therapeutics at BSL2 using surrogate viruses or genetically reverse engineered viruses
- Establish animal models for in depth characterization of arenavirus pathogenicity and identification of mechanisms of disease development.
- *In vivo* pre-clinical testing of host-targeted therapeutic strategies and repurposed drug candidates.
- Establish harmonised clinical trial endpoints, case definitions, and diagnostic algorithms applicable across multiple arenavirus-endemic regions.
- Agree on standard measures for disease severity and major complications to support comparison across clinical trials.

Phase 2 Scale-up (Years 3-5)

- Develop and operationalise outbreak-ready therapeutic trial protocols, with pre-defined ethical provisions (including Monitored Emergency Use of Unregistered and Investigational Interventions (MEURI) where appropriate), for non-Lassa human-pathogenic arenaviruses.
- Provide scientific evidence for the use or otherwise of ribavirin for the treatment of confirmed arenavirus patients in endemic settings.
- Evaluate combination treatments (e.g. antiviral plus antibody or supportive care) using platform trial designs.

Phase 3 Consolidation and Innovation (Years 6-10)

- Make available validated, affordable therapeutics for the treatment of Lassa fever in endemic areas.
- Generate clinical efficacy data for at least one broadly active antiviral or immune-based therapeutic with applicability beyond Lassa fever.
- Ensure effective therapeutics are included in clinical guidelines and outbreak response plans in endemic regions.

Table 6 – Vaccines

Phase 1 Foundation (Years 1-2)

- To develop standardized antibody and cellular immune assays available for cross-study comparison.
- Identify/develop critical reagents, including reference material for the validation and harmonisation of the results across laboratories/methods.
- Establish & validate guinea pig and non-human primate (NHP) models for New World arenaviruses.

Phase 2 Scale-up (Years 3-5)

- Make available a safe, acceptable, accessible and effective vaccine for the prevention of Lassa fever infection/disease in endemic areas.
- Generate preclinical efficacy of vaccine candidates against individual New World arenaviruses with reported human pathogenicity.

Phase 3 Consolidation and Innovation (Years 6-10)

- Support licensure or emergency use of Lassa fever vaccines in endemic countries.
- Ensure vaccines are affordable, accessible, and suitable for use in endemic settings (e.g. stable, simple schedules).
- Integrate genomic surveillance to update vaccine targets and monitor for immune escape.
- To identify and use immune correlates and simplified assays to support vaccine evaluation where large trials are not feasible.
- Prepare and maintain ready-to-use trial designs (e.g. ring vaccination) for rapid use during outbreaks.
- Build regional capacity for vaccine delivery, monitoring, and post-licensure effectiveness studies.
- Generate evidence to support emergency use or investigational reserve vaccines for New World arenaviruses.

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Table 7 – Regulatory and Clinical Development

Phase 1 Foundation (Years 1-2)

- Prospective cohort studies established to define early symptoms and prognostic markers.
- Agree on standard case definitions and basic clinical data collection.
- Engage with the WHO on the establishment of pre-qualification (PQ) programmes for arenaviruses, with prioritisation of Lassa virus.
- To improve regional mechanism(s) for diagnostic regulatory approval in multiple countries, which would facilitate more rapid in vitro diagnostic approval, particularly in countries where the Lassa fever annual testing volumes are low.

Phase 2 Scale-up (Years 3-5)

- To have platform-based clinical trial infrastructure, trained staff, and governance systems established at priority sites.
- To have harmonised primary endpoints and outcome measures agreed across trial sites and evidence-based supportive care guidelines validated and adopted in trials.
- Establish the feasibility of multi-arm, multi-stage platform trials.
- Develop outbreak-ready clinical trial protocols and pre-review them with regulators.

Phase 3 Consolidation and Innovation (Years 6-10)

- Endemic-region sites able to rapidly initiate and run arenavirus clinical trials.
- Maintain trial-ready platforms for rapid activation during outbreaks.
- Use trial data to support regulatory decisions for vaccines and therapeutics.

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Table 8 – Social and Behavioural Science (SBS) and Community Engagement

Phase 1 Foundation (Years 1-2)

- Functional Community Advisory Boards (CABs) established in communities at highest risk.
- To increase the number of trained community health volunteers to support reporting, contact tracing and referral.
- Basic risk communication and community education approaches agreed.

Phase 2 Scale-up (Years 3-5)

- Community engagement strategies integrated into routine surveillance and outbreak response.
- Mechanisms in place to rapidly deploy supplies, diagnostics, and response teams during outbreaks.
- Community feedback used to improve surveillance, response and prevention activities.
- Improve frontline diagnostic laboratory capacity especially in rural, remote and/or under resourced health facilities.
- Provide access and training to rapid point of care diagnostics, for early detection of cases.
- Coordinate a multicentre survey assessing community-level perceptions of arenavirus disease and healthcare access barriers contributing to delayed or missed case detection across diverse regions.

Phase 3 Consolidation and Innovation (Years 6-10)

- Sustainable financing and logistics systems supporting community-level surveillance and response.
- Community engagement embedded in national preparedness and response plans.

Research and Knowledge Gaps

Reservoirs and Transmission

Primary challenges

- There is difficulty in identifying and speciating rodent species across the New and Old World Arenaviruses; for example, the reservoirs for Sabiá and Lujo viruses are currently unknown, and there is limited understanding of spillover into different rodent species.
- There is difficulty in predicting zoonotic transmission dynamics due to rodent reservoirs typically having large geographical ranges, high reproductive rates and fluctuating population dynamics, which interplay with environmental factors to influence density dependent transmission.
- Comprehensive global mapping of arenaviruses and their reservoirs is currently lacking.
- The correlation between reservoir distribution and human cases is not well characterised, and this extends to factors that underpin regional variability.
- Many arenavirus infections present with non-specific febrile symptoms, making them easily misdiagnosed as malaria, typhoid or other viral haemorrhagic fevers. There is insufficient knowledge of household-level, occupational and agricultural behaviours that drive exposure risk. Urbanisation, food storage practices and rodent control strategies very widely and are not well quantified.
- Transmission of New World Arenaviruses is not well understood. There may be sexual transmission for some Arenaviruses (such as Chapare and Lassa), which have been known to be persistent in semen. The duration and determinants of persistence differ across arenaviruses and are currently poorly mapped. These factors raise concerns for rare but possible routes of transmission.
- Viral loads in chronic infections need to be better characterised, as well as the rapid evolution of arenaviruses seen in reservoir hosts. Both factors impose challenges for case detection and the development of diagnostics.
- The risk of healthcare-associated and occupational exposure to arenaviruses remains poorly characterised, including variability in infection prevention and control (IPC) practices across endemic regions.
- There is limited understanding of viral load dynamics, duration of infectivity, and shedding of arenaviruses in different human body fluids, particularly during convalescence, and how this relates to transmission risk.

- For some arenaviruses, there is a lack of clarity between perceived versus evidence-based risk of human-to-human and nosocomial transmission, complicating risk assessment and biosafety guidance.
- Quantifying environmental and human behavioural drivers of increased human-rodent contact (e.g. land use change and agriculture), and subsequent spillover is difficult.

Key Needs/Research Priorities

- To conduct studies into rodent host species distribution and presence of arenaviruses using molecular identification processes, including co-circulation of non-pathogenic arenaviruses inside and outside endemic regions.
- To sequence arenaviruses from rodents and humans, and environmental samples, to define viral diversity, emergence hotspots and cross-species transmission networks.
- To conduct ecological studies to discover previously unidentified and/or cryptic reservoirs, particularly in under-sampled regions.
- To conduct modelling studies to predict how environmental change (e.g. land use and climate change) could alter endemicity across regions and use this information to better understand other potential exposure pathways in high-risk areas other than zoonotic transmission routes.
- To integrate surveillance combining ecological, climatic and human behavioural data for comprehensive monitoring.
- To conduct global studies to assess disease burden whilst factoring in reservoir abundance and population dynamics (especially for Lymphocytic Choriomeningitis Virus (LCMV), which has a global prevalence).
- To conduct extensive and cross-cutting transmission studies into primary (e.g. exposure to aerosolised biological waste or contaminated environmental particles) and secondary (rare human-human or healthcare exposure) routes.
- To define receptor usage, restriction factors and cross-species barriers for pan arenaviruses.
- To explore the reasons for the uneven distribution in the occurrence of Lassa fever infection/disease across different communities within an endemic area.
- To systematically characterise the risk of healthcare-associated transmission through well-designed epidemiological and clinical studies, distinguishing suspected, probable and confirmed secondary cases.
- To evaluate the effectiveness and feasibility of IPC measures and personal protective equipment (PPE) for arenaviruses in both high- and low-resource healthcare settings.
- To investigate viral persistence and shedding in humans, including sexual transmission risk, and to define evidence-based recommendations for post-infection counselling and public health guidance.

Surveillance

Primary challenges

- Surveillance of the New and Old World Arenaviruses is limited due to lack of access to reliable and accessible diagnostic tools.
- Many endemic regions have fragmented or absent surveillance, meaning outbreaks are identified only after significant spread. Surveillance is often concentrated around hotspots, leaving large areas, especially rural and peri-urban zones, poorly monitored.
- Early case detection is further constrained at the point of care, as arenaviruses (outside of Lassa fever) are infrequently encountered in routine clinical practice and are therefore not routinely recognized or considered in the initial assessment of febrile syndromes.
- Disease stigma reduces reporting, with late diagnoses contributes to poorer outcomes, particularly in pregnant women.
- There is a lack of clinically validated biomarkers to aid diagnosis and predict outcomes, which limits triage and disease management, limiting the ability to effectively stratify patients and allocate healthcare resources.
- Many arenavirus symptoms mimic dengue, malaria, typhoid, and other febrile illnesses, thus, health workers can miss or misdiagnose early cases. Healthcare workers often receive minimal training on arenavirus detection, case definitions or reporting protocols. This leads to under-recognition and inconsistent triage.
- In geographic areas with low arenavirus incidence, healthcare workers may have limited familiarity with clinical algorithms and operational pathways following a suspected case, potentially delaying appropriate notification, sample collection, and referral for diagnostic testing.

Key Needs/Research Priorities

- To define optimal sample stabilisation and inactivation protocols to underpin the development of standardised RT-PCR diagnostic tools.
- To improve reporting and diagnosis. This includes reducing inconsistencies in applying case definitions and identifying and recording deaths at home, which can often go undetected.
- To enhance clinical recognition of arenavirus-compatible syndromes at the point of care to support timely case detection and surveillance.
- To strengthen healthcare worker capacity, through targeted training, for the clinical recognition of arenavirus-compatible syndromes and for the appropriate and effective use of notification and surveillance pathways.
- To evaluate the benefit, feasibility and health economics of incorporating arenaviruses into syndromic diagnostic panels in endemic regions to improve case finding and

differential diagnosis, including strengthening clinical recognition and awareness of arenavirus infection.

- To develop point of care diagnostics for active screening at home/primary care facility use.
- To improve surveillance of potential animal reservoirs (and other important animal species) in the affected countries.
- To integrate animal and environmental data; to harmonise climate, land use, rodent population and human case data to improve prediction models and develop regional early warning tools.
- To improve certification and training of diagnostic laboratories in arenaviruses endemic and non-endemic regions by WHO.
- To improve community-based surveillance in the early detection of pan arenavirus infection.

Viral Family Biology

Primary challenges

- Generally, understanding of arenavirus biology is based largely on studies of only a few relatively well-studied members of this viral family, with the assumption that mechanisms are comparable across all other members.
- Arenaviruses mutate rapidly and show substantial genetic variation across Old and New World lineages. Their genetic diversity can complicate diagnostics development, vaccine design, and predictions about virulence or host range.
- Arenaviruses can suppress key innate immune pathways and disease severity varies across species and strains. The mechanisms resulting in severe infection (the roles of NP and Z proteins for example) are not fully understood.
- Development of animal models that accurately mimic human disease is difficult. Existing models are limited by distinct immunological variation from human disease and/or can be costly and ethically challenging.

Key Needs/Research Priorities

- To establish and maintain a central and accessible repository of isolates of strains from across the whole *Arenaviridae* family.
- To conduct studies to investigate and compare the mechanisms of viral entry across emerging arenaviruses, including studies to better understand the relevance of alternative receptor binding and endosomal receptors.
- To map replication and transcription kinetics, promoter architecture and polymerase regulation across representative arenaviruses.
- To characterise assembly sites, budding mechanisms and intracellular trafficking in primary human cells.
- To conduct studies to compare viral proteins (NP, Z, etc) across New and Old World arenaviruses for immune evasion functions.
- To better understand how arenaviruses suppress innate immune signalling.
- To conduct studies to better understand how neutralising antibodies develop and to define rates of neutralising antibody presence in survivors of arenavirus disease, including the role of glycosylation in this process.
- To establish efficient and immunologically robust animal models of disease for key mammarenavirus species and assess generalisable cross species principles between models.
- To create a validated panel of humanised house models and non-human primate protocols that accurately replicate the pathogenic and immunological characteristics of major mammarenavirus infections.

Diagnostics

Primary challenges

- There are currently no reliable or available rapid point of care diagnostics for any of the arenaviruses that are either specific to New or Old World arenaviruses or pan-arenavirus.
- Sample handling for mammarenaviruses without inactivation requires high containment levels (BSL3/4) which is resource intensive and complex.
- There are inconsistencies in diagnostic agreement among some of the available PCR diagnostic platforms. This issue would need to be addressed to provide accurate case reporting.
- Enzyme-linked immunosorbent assays (ELISA) can detect antibodies against the virus, but they are not always reliable during the acute phase of infection or when antibody response is not induced at a detectable level. There are issues with cross-reactivity across arenaviruses.
- Assays utilising virus culture, such as neutralising antibody assays and infectivity studies may provide additional information but are costly, resource intensive, complex to carry out and require high containment facilities.
- For all arenaviruses, there are no unified standards for diagnosis, which leads to misclassification and inconsistency in comparison of the epidemiological data.
- The impact of available and emerging diagnostic tools is limited if they are not effectively integrated into clinical decision-making and surveillance pathways at the point of care.

Key Needs/Research Priorities

- To improve sample stability, for example by improving sample inactivation, to underpin the development of a standardised RT-PCR diagnostic tool.
- To integrate genomic data into diagnostic assay design; arenaviruses evolve rapidly, resulting in new species emerging. Diagnostics can be informed by and benefit from real-time genomic data.
- Improvements in sample inactivation and stability at point of collection. This reduces the number of assay failures due to poor sample quality. Inactivation at point of collection also reduces the need for BSL-3 facilities for sample processing prior to PCR.
- To build infrastructure to enable sustainable access to affordable commercial nucleic acid diagnostics.
- To develop rapid pan arenavirus diagnostic tests (for both human and reservoir case detection) that are validated, sensitive, specific and affordable that can be deployed in the field at the point of care. RDT and POCT evaluations must include enough samples spanning low to high viral loads so that the true performance limits of each test, for both detecting and excluding infection, are accurately understood.

- To develop target product profiles for arenaviruses with clearly defined scopes, performance metrics, operational characteristics, and pricing to enable test developers and manufacturers to work within a unified development framework.
- RT-qPCR assays demonstrating an acceptable validation (for example: Clinical and Laboratory Standards Institute (CLSI)) with published data (for example: Minimum Information for Publication of Quantitative Real-Time PCR Experiments (MIQE) standards) must be developed for several viruses listed in the Supporting Information in order to provide a basis for Laboratory Developed Test (LDT): a compilation of such data should be made available as a digest for easy access.
- To use the European Virus Archive repository (as an example) as source of material for exchange between academics and industry for diagnostic development and validation (https://www.european-virus-archive.com/), as well as the WHO International Standards where appropriate to assess, compare and standardise new PCR-based kits.
- To develop proficiency panels of inactivated virus (for full process evaluations) or synthetic ribonucleic acid (RNA) constructs (for assay evaluations) for standardised quality assurance across affected countries.
- To develop specific and sensitive rapid diagnostic tests serological assays to help differentiate between different arenaviruses, to enable rapid first response screening. Tests should detect a given arenavirus at exclusion of other related arenaviruses.
- To improve biosafety features of RDT/POCT assays where BSL3 facilities are lacking.
- To conduct large-scale studies evaluating C-reactive protein (CRP) and other biomarkers to confirm their utility in disease severity assessment and triage.
- To develop protocols to incorporate biomarker testing into standard diagnostic algorithms to optimize patient management and resource allocation.
- To develop specific and sensitive ELISAs to help differentiate between different arenaviruses.
- To consider protocols to incorporate information storage and dissemination of POCT data into surveillance programmes via suitable software and/or cloud solutions.
- To promote development and deployment of validated rapid point-of-care tests suitable for outbreak settings.
- To establish and disseminate harmonized, evidence-based diagnostic and triage guidelines locally and regionally to reduce misclassification and improve early detection and improve level of care needed dependent on severity of infection.
- To ensure that diagnostic tools are embedded within clinical algorithms and surveillance pathways to guide appropriate test selection, interpretation, and reporting
- To ensure PCR-based assays are available for use on open platforms as well as cartridge-based proprietary PCR systems, and to ensure labs can benefit from the equity of access and affordability associated with open system assays.
- To improve regional mechanism(s) for regulatory approval in multiple countries, which would facilitate more rapid in vitro diagnostic approval, particularly in countries where the Lassa fever annual testing volumes are low.

385 ● To provide access to cold-chain-free diagnostic reagents including temperate stable
386 positive controls and inactivated viruses.

Therapeutics

Primary challenges

- Treatment options remain limited, with existing drugs such as ribavirin offering only partial effectiveness and ongoing efforts focussed on developing more targeted antiviral strategies and immune-based approaches.
- There are differing studies investigating ribavirin as a therapeutic for treating arenavirus infection, with some suggesting that it is an effective treatment, and some suggesting that it may be harmful in mild cases of Lassa virus infection.
- The use of ribavirin as a standard of care for treatment makes conducting any kind of randomised trial of ribavirin very difficult.
- One of the key challenges in performing clinical trials for therapeutics is the lack of standardised diagnostic tests.
- Currently there is limited evidence on whether early treatment or prophylactic use of antivirals or antibodies could prevent disease following high-risk exposure in cases such as household contacts or healthcare worker exposure.
- Clinical efficacy trials for arenavirus therapeutics require sufficiently sensitive surveillance systems to enable timely detection and enrolment of adequate numbers of cases.
- Ethical and logistical challenges associated with conducting randomised controlled trials during outbreaks or in high-fatality settings restrict evidence generation for non-Lassa arenaviruses.
- Logistical barriers include limited trial sites with appropriate research capacity, inconsistent patient follow-up and challenges in enrolling patients early in disease when treatments are most effective.

Key Needs/Research Priorities

- To conduct studies into the effectiveness of ribavirin and favipiravir as a therapeutic option for treatment of a range of arenaviruses. These studies would include rigorous pharmacokinetic and pharmacodynamic studies.
- To develop adaptive platform trials or *mammarenaviruses*, allowing for multiple therapeutic candidates.
- To establish composite primary endpoints that measure all-cause mortality alongside major complications.
- To examine adjunctive/supportive therapies and interventions that can mitigate disease complications and complement antiviral or antibody-based therapies rather than replacing them.
- To evaluate pan-arenavirus antiviral options, for example RNA-dependent RNA polymerase inhibitors that target highly conserved mechanisms between species.

- To evaluate monoclonal antibody (mAb) cocktails engineered for therapeutic breadth to ensure efficacy across variants.
- To establish standardised BSL2 assays for first line drug screening and develop reverse-genetic based surrogate systems. In addition to this, engineering attenuated strains for BSL2/3 work.
- To assess different drug combinations e.g. antibody with antiviral, for optimal treatment.
- To investigate the role of immune-based therapies beyond monoclonal antibodies, including immune plasma (convalescent plasma), particularly for New World arenaviruses.
- To develop and have ready clinical trial protocols, including pre-established ethical frameworks, that can be rapidly implemented during outbreaks or in settings with low numbers of arenavirus cases.

Vaccines

Primary challenges

- When viable candidates emerge, proactive planning for the path to licensure in the affected countries is needed. This includes how the country and/or region's future participation in the production/distribution of the countermeasure can be assured to ensure sustainable access.
- Due to the extensive genetic diversity between Old and New World arenaviruses, it is difficult to develop cross-protective or generalisable vaccines.
- There is a lack of standardised neutralisation assays, including alternative systems to the live virus, such as pseudotyped virus with differences in pseudotype backbones, target cell lines and readouts.
- Developing countermeasures is hampered by the need for BSL4 containment, and by a lack of animal models that fully reproduce human disease.
- Endemic areas often have limited health infrastructure, making mass vaccination logistically challenging. In addition to this, outbreaks are often sporadic, further complicating decisions about who to vaccinate in these settings.
- Incomplete understanding of which immune responses protect from severe arenavirus disease. Without clear immune correlates, it is difficult to evaluate vaccine candidates or predict vaccine effectiveness in real-world settings.
- Phase 3 randomised controlled trials (RTC) for Lassa fever require a large sample size (up to 30K participants) to achieve full licensure of a vaccine might not be feasible.
- Similarly, Emergency Use Listing (EUL) or availability of Investigational reserve for rare outbreaks of new world arena viruses are challenging due limited understanding of epidemiology of the viruses and lack of diagnostics.
- There is a lack of rapid response platform data to allow for arenavirus outbreak response.
- There are challenges when designing vaccines that target LASV GP due to the dense glycan shield or uncleaved GP.

Key Needs/Research Priorities

- To develop robust small animal models to better reproduce human disease outcomes across arenaviruses.
- To conduct studies to investigate the correlates of protection for a broad range of arenaviruses. It would be desirable to establish and validate simpler assays that could assess cellular and antibody responses to vaccination, without requiring advanced infrastructure and resources, that could then be used in late-stage vaccine studies. Ideally, where possible the assays should be based on whole blood, to give a representation of the immune system's natural state as accurately as possible.
- To integrate genomic surveillance into vaccine development; sequencing of viral isolates from human and reservoir hosts to identify diversity, update vaccine antigens depending on circulating strains and monitoring for potential immune escape.

- To ensure appropriate laboratory infrastructure, established standardised protocols and trained personnel for peripheral blood mononuclear cell (PBMC) collection and storage are available at the clinical trial sites.
- To investigate the development of vaccines suitable for endemic regions, taking into consideration single-dose or short-schedule vaccines, heat-stable formulations to reduce reliance on the cold chain, affordable and scalable vaccine platforms.
- To make critical reagents, including antigens for ELISA and PBMCs more accessible, taking into consideration the challenges with cold chain storage and the associated high costs. This also includes the processing of PBMC samples. Currently there isn't a commercial source of LASV GP.
- To generate comprehensive T cell epitope landscapes and track escape mutations across Old and New World arenaviruses. Additionally, to monitor and model antigenic drift in endemic regions.
- To conduct studies to identify conserved glycoprotein epitopes for designing cross-protective vaccines.
- To gather evidence of arenavirus exemplar vaccine in animal models and human clinical trials.
- To evaluate novel vaccine technologies, including messenger RNA (mRNA)-based platforms as suitable candidates for arenaviruses.
- To establish vaccine stability profiles for key candidates to mitigate challenges in vaccine delivery to remote or resource constrained settings.
- To develop model efficacy trial design methodologies including ring vaccination and step-wedge with pre-prepared ready-to-use protocols in the event of outbreaks.

Regulatory and Clinical Development

Primary challenges

- Currently, many clinical trial sites lack essential infrastructure, trained staff and research governance in order to run trials. For this reason, there should be investment in platform-oriented research capacity rather than pathogen-specific.
- There are currently gaps in diagnostics, clinical monitoring and data systems for mapping arenaviruses in endemic regions. This limits the establishment of clinical trials before they can start. Research should be focussed on enabling clinical trials.

Key Needs/Research Priorities

- To validate and refine the primary endpoint of clinical trials for pan arenaviruses, potentially using Lassa as an example, and to standardise outcomes across clinical trial sites.
- To develop and validate supportive care and therapeutic guidelines for use in resource-limited settings, and to identify which supportive care interventions most influence outcomes.
- To conduct prospective cohort studies to characterise disease progression, improve understanding of early symptoms and prognostic markers.
- To validate the feasibility of multi-arm, multi-stage platform trials in low-incidence, geographically dispersed diseases.
- To generate suitable outbreak plans and protocols should be developed and socialized with potentially affected regions to allow for evidence generation during small or large outbreaks.
- To develop clinical trial protocols for use in outbreaks should be designed and pre-approved or reviewed by regional regulatory authorities to allow for rapid implementation during increased transmission (Lassa fever) or outbreaks.

Social and Behavioural Science and Community Engagement

Primary challenges

- Currently, there is a lack of funds to support rapid outbreak investigation and response deployment, and limited trust in health systems and authorities, and stigma surrounding arenavirus infection compounds the issue.
- Centralized testing causes delays in diagnosis. Specimen transport systems to diagnostic centres can be weak, especially in remote areas.
- Fear and misinformation may cause non-compliance, escape from isolation, or refusal of contact tracing. Insufficient community health volunteers in many rural regions. Limited training or support for community-based reporting.

Key Needs/Research Priorities

- To improve frontline diagnostic laboratory capacity especially in rural, remote and/or under resourced health facilities.
- To reduce funding and resource constraints: surveillance systems often rely on donor funding. Stock-outs of supplies (e.g., gloves, disinfectant) can undermine outbreak control.
- To provide access to rapid point of care diagnostics, for early detection of cases.
- To increase laboratory capacity; strengthen laboratory infrastructure and improve access to high-quality diagnostic facilities in endemic regions.
- To improve risk communication and community engagement and surveillance**:** To improve community outreach and education to improve poor health seeking behaviour. The poor health seeking behaviour of some persons in Lassa fever endemic communities contributes to the late presentation, delayed diagnosis and high mortality from the disease.
- To investigate community-level perceptions of arenavirus disease and healthcare access limitations that delay or prevent case detection.

Supporting Evidence

Arenaviridae – Old World Mammarenaviruses

Lassa Virus (LASV)		
General Information	Reservoir	Multimammate rat (*Mastomys natalensis*).
	Transmission	Primary transmission is through contact with excreta from infected reservoir, however some direct contact with excreta from an infected human can occur and vertical transmission is suspected.
	Distribution	West Africa.
	Disease	Lassa fever
Status of Diagnostics	Surveillance Programmes	**Integrate Consortium**; an international consortium (15 institutions across 10 countries) with a 5-year initiative that focuses on surveillance, diagnostics, outbreak response and capacity building in endemic regions. This consortium is funded by the European and Developing Countries Clinical Trials Partnership 3 (EDCTP3) European Union programme. **Integrated Disease Surveillance and Response (IDSR)**; a strategy developed by the WHO to provide technical guidance and outbreak alert and coordination during epidemics. Through this programme, the WHO works with local Health Ministries to strengthen early warning systems. **Nigeria Centre for Disease Control and Prevention (NCDC)**; this is the primary agency coordinating Lassa fever response in Nigeria. They publish weekly situation reports, track confirmed cases and coordinate laboratory testing. **Africa Center of Excellence for Genomics of Infectious Diseases (ACEGID)**; this programme conducts genomic surveillance of Lassa virus strains in order to support early detection of outbreaks and tracking viral evolution.

		Enable Lassa Research Programme (Coalition for Epidemic Preparedness Innovations (CEPI) Initiative); the aim of Enable 1.0 was to conduct a large-scale epidemiological study of Lassa virus infections across West Africa to deepen understanding of the virus and better support medical countermeasure development. Enable 1.5 recruitment of 5000 participants has been completed at all sites, with participant follow-up ongoing until Q1 2026.
	RDT/POCT	None commercially available.
	Lab Diagnostics	**Altona RealStar RT-PCR**; CE/IVD certified (until Dec 2027) for detecting Lassa virus RNA. **Aldatu Biosciences:** PANDAA Lassa Virus for pan-lineage detection of Lassa virus. RayBiotech Lassa Virus Nucleocapsid (N) Human IgG ELISA Kit; research use only (RUO). Panadea LASV (NP) IgG ELISA Kit; RUO. Panadea LASV (NP) IgM ELISA Kit; RUO.
Status of Vaccines	Licensed Vaccine	None, multiple vaccines in development.
	Assays – Cellular	**Integral Molecular Rady Reporter Virus Kit – Lassa**; Lassa GP pseudovirus with a fluorescence readout. **Virongy Lassa Pseudoviral Neutralization Assay Kit**; Lassa GP Alpha pseudovirus with a luminescence readout. **IVANO Bioscience/RetroVirox Custom Pseudovirus Production**; custom pseudovirus with either a fluorescence or luminescence readout.
	Assays – Humoral	**IBT Bioservices**; IgG and IgM ELISA kits for RUO. **Creative Diagnostics**; RUO ELISA kits. **Alpha Diagnostic International**; IgG and IgM ELISA kits for RUO.

	Clinical Trials	**rVSV-LASV-GPC (IAVI)**; Phase II is ongoing in Ghana, Liberia and Nigeria with a Phase IIb efficacy trial scheduled for 2026. **LASSARAB (NIH/University of Jefferson)**; enrolment for the Phase I begun in early 2025 following on from promising preclinical (NHP) studies. **INO-4500 (Inovio)**; Phase I immunogenicity and safety trial conducted in the US completed and data published in 2025. Measles-Lassa (THEMIS BIOSCIENCE); Phase I safety and immunogenicity trial conducted in Belgium, completed and data published in 2023. MOPEVAC Lassa (Institut Pasteur); Phase I safety and immunogenicity trial in progress in France (enrolment will begin in April 2026).
Status of Therapeutics	Antivirals	**Ribavirin**; currently used off label but there are concerns over efficacy and safety. **Favipiravir**; undergoing efficacy and safety trials. **Taribavirin**; Ribavirin prodrug, developed to reduce the toxicity seen in Ribavirin treatment, trials are planned. **Umifenovir**; currently licensed for some respiratory viruses in Russia and China and not for Lassa but is on the WHO list of repurposing candidates for Arenavirus treatment.
	Monoclonal Antibodies	**Arevirumab-3 (mAb cocktail)**; specifically developed for Lassa treatment, Phase I trials are planned pending Food and Drug Administration (FDA) approval.
	Other	**Losmapimod**; pre-clinical studies showed strong inhibition of Lassa virus entry into cells, currently listed as a therapeutic option by the WHO.
Lymphocytic Choriomeningitis Virus (LCMV)		
General Information	Reservoir	House mouse (*Mus musculus*).
	Transmission	Via contact with infected excreta from the reservoir. Vertical transmission has also been documented.

	Distribution	Worldwide (~5% of the world has been exposed as its natural host has a worldwide distribution).
	Disease	Lymphocytic choriomeningitis.
Status of Diagnostics	Surveillance Programmes	There are no specific LCMV surveillance programmes, however agencies such as UKSHA's mSCAPE metagenomic surveillance programme aim to detect emerging pathogens such as LCMV through genomic screening, and Boston University's biosafety and occupational health programmes monitor LCMV exposure in lab staff working with rodents.
	RDT/POCT	There are no LCMV-specific RDTs or POCTs.
	Lab Diagnostics	**Emelca Bio RealCycler LCMV PCR Kit;** CE/IVD certified for *in vitro* use in Europe and is suitable for clinical use. Aldatu Biosciences; under development. BioStone AsurDx LCMV RT-PCR Kit; clinical LCMV diagnostic kit. **Creative Biolabs LCMV RT-PCR Kit;** designed for LCMV diagnostic research, not clinical use. **MyBioSource Human LCMV IgG ELISA Kit;** RUO to detect IgG in human samples.
Status of Vaccines	Licensed Vaccine	None.
	Assays – Cellular	**Sigma-Aldrich/MilliporeSigma Anti-LCMV Nucleoprotein Antibody;** used in immunofluorescence (IF), immunohistochemistry (IHC) and flow cytometry (FC) for detection of LCMV-infected cells and viral nucleoprotein expression. Based on clone VL-4. **Bio X Cell InVivoMAb Anti-LCMV Nucleoprotein;** used for both *in vivo* and *in vitro* functional assays. Based on rodent clone VL-4.
	Assays – Humoral	Creative Diagnostics Mouse LCMV IgG ELISA Kit; RUO. Thomas Scientific Mouse LCMV ELISA Kit; RUO. Assay Genie Mouse LCMV ELISA Kit; RUO.

	Clinical Trials	There have been no LCMV-specific clinical trials for medical countermeasures.
Status of Therapeutics	Antivirals	There are no licenced antiviral treatments for LCMV, treatment focusses on supportive care. **Ribavirin** and **Favipiravir** have been suggested but are not approved for use against LCMV infection.
	Monoclonal Antibodies	There are no licenced mAbs for LCMV treatment, however there are several undergoing investigation as potential treatment options.
Lujo Virus (LUJV)		
General Information	Reservoir	Unknown.
	Transmission	Most likely through contact with infected excreta from a likely reservoir, with some documented cases of human-human transmission.
	Distribution	Zambia.
	Disease	Lujo Haemorrhagic Fever.
Status of Diagnostics	Surveillance Programmes	There are no dedicated surveillance programmes for Lujo virus, but agencies such as Centers for Disease Control (CDC) and UKHSA include Lujo virus on their wider emerging pathogen monitoring programmes.
	RDT/POCT	There are no Lujo-specific RDTs or POCTs.
	Lab Diagnostics	There are no Lujo-specific lab diagnostics, however some institutions with BSL4 facilities are able to diagnose Lujo using RUO RT-PCR.
Status of Vaccines	Licensed Vaccine	None.
	Assays – Cellular	There are no commercially available cellular assay kits for Lujo virus.
	Assays – Humoral	There are no commercially available humoral assay kits for Lujo virus.
	Clinical Trials	There have been no Lujo virus-specific clinical trials for medical countermeasures.

Status of Therapeutics	Antivirals	There are no licenced antiviral treatments for Lujo virus.
	Monoclonal Antibodies	There are no licenced mAb treatments for Lujo virus.

Arenaviridae – New World Mammarenaviruses

Chapare Virus (CHAPV)		
General Information	Reservoir	Pygmy rice rats (Oligoryzomyz microtis).
	Transmission	Via contact with infected excreta from the reservoir, with some documented cases of human-human transmission in healthcare settings.
	Distribution	Bolivia.
	Disease	Chapare Haemorrhagic Fever.
Status of Diagnostics	Surveillance Programmes	**The International Health Regulations Focal Point for the Plurinational State of Bolivia** monitors patients presenting with symptoms that align with Chapare virus infection and reports these cases to the WHO.
	RDT/POCT	There are no Chapare-specific RDTs or POCTs.
	Lab Diagnostics	There are no Chapare-specific lab diagnostics, however some institutions with BSL3/4 facilities are able to diagnose Chapare using RUO RT-PCR and serological assays.
Status of Vaccines	Licensed Vaccine	None.
	Assays – Cellular	There are no commercially available cellular assay kits for Chapare virus.
	Assays – Humoral	There are no commercially available humoral assay kits for Chapare virus.
	Clinical Trials	There have been no Chapare virus-specific clinical trials for medical countermeasures.
Status of Therapeutics	Antivirals	There are no licenced antiviral treatments for Chapare virus.
	Monoclonal Antibodies	There are no licenced mAb treatments for Chapare virus.

Guanarito Virus (GTOV)		
General Information	Reservoir	Short-tailed cane mouse (*Zygodontomys brevicauda*).
	Transmission	Via contact with infected excreta from the reservoir.
	Distribution	Venezuela.
	Disease	Venezuelan Haemorrhagic Fever.
Status of Diagnostics	Surveillance Programmes	**The Venezuelan Ministry of Health** monitors viral haemorrhagic fever cases across healthcare systems, including Guanarito virus infection.
	RDT/POCT	There are no Guanarito-specific RDTs or POCTs.
	Lab Diagnostics	There are no Guanarito-specific lab diagnostics, however some institutions with BSL3/4 facilities are able to diagnose Guanarito using RUO RT-PCR and serological assays.
Status of Vaccines	Licensed Vaccine	None.
	Assays – Cellular	There are no commercially available cellular assay kits for Guanarito virus.
	Assays – Humoral	There are no commercially available humoral assay kits for Guanarito virus.
	Clinical Trials	There have been no Guanarito virus-specific clinical trials for medical countermeasures.
Status of Therapeutics	Antivirals	There are no licenced antiviral treatments for Guanarito virus.
	Monoclonal Antibodies	There are no licenced mAb treatments for Guanarito virus.

Junín Virus (JUNV)		
General Information	Reservoir	Drylands Vesper Mouse “ratón maicero” (*Calomys musculinus*).
	Transmission	Via contact with infected excreta from the reservoir. Person-to-person transmission is rare but can occur through contact with blood or bodily fluids. Agricultural workers are at higher risk, especially during the harvest season.
	Distribution	Argentina.
	Disease	Argentinian Haemorrhagic Fever (AHF).
Status of Diagnostics	Surveillance Programmes	**The Argentine Ministry of Health** monitor AHF cases through healthcare setting surveillance. The **WHO** and **Pan American Health Organisation** (PAHO) provide technical support and reporting during outbreaks. **National Argentine Haemorrhagic Fever Control Programme**; coordinated by the National Institute for Human Viral Diseases (INEVH–ANLIS), under the Ministry of Health, which leads national surveillance for Argentine haemorrhagic fever, serves as the national reference centre for clinical and laboratory diagnosis, provides technical leadership for case investigation, outbreak response and clinical management, coordinates the national network of immune plasma banks for treatment, and is the institution responsible for the production of the Candid#1 vaccine. INEVH–ANLIS serves as a PAHO/WHO Collaborating Centre on Viral Haemorrhagic Fevers and Arboviruses.
	RDT/POCT	There are no Junín -specific RDTs or POCTs.
	Lab Diagnostics	There are no Junín -specific lab diagnostics, however some institutions with BSL3/4 facilities are able to diagnose Junín using RUO RT-PCR and serological assays. In Argentina, molecular diagnosis by RT-PCR / RT-PCR Real Time is routinely performed at INEVH–ANLIS and at selected provincial laboratories in endemic areas, operating within the national surveillance framework. Serological diagnosis (ELISA and neutralization tests), as well as virus isolation, are performed exclusively at INEVH–ANLIS.

Status of Vaccines	Licensed Vaccine	**Candid-1 Live Attenuated Vaccine** was licenced in 2006 by the Argentine Ministry of Health for use in humans in Argentina. Although vaccine efficacy exceeds 95%, its use is currently indicated for individuals aged 15 years and older, and it is contraindicated in pregnant women and immunocompromised persons. Concomitant administration with other vaccines has not been formally evaluated; a clinical trial is planned and in preparation to assess the safety and immunogenicity of simultaneous administration, and a subsequent clinical study is planned to evaluate safety and efficacy in individuals under 15 years of age. However, additional vaccine candidates are needed to address populations for whom Candid#1 is contraindicated, particularly immunocompromised individuals and pregnant women. CEPI and the University of Oxford are currently developing a ChAdOx-based vaccine for use against Junín.
	Assays – Cellular	There are no commercially available cellular assay kits for Junín virus.
	Assays – Humoral	There are no commercially available humoral assay kits for Junín virus.
	Clinical Trials	There have been no Junín virus-specific clinical trials for medical countermeasures, with the exception of those leading to the licensure of the Candid-1 vaccine. Clinical trials have been conducted for AHF, including trials supporting the development/licensure of the Candid#1 vaccine and a placebo-controlled trial of immune plasma therapy. Ribavirin was also evaluated in a limited number of patients, primarily in late-stage disease. A clinical trial on concomitant administration of Candid#1 with other vaccines is planned and under preparation; however, no other contemporary clinical trials evaluating additional Junín virus–specific medical countermeasures have been conducted to date.
Status of Therapeutics	Antivirals	There are no licenced antiviral treatments for Junín virus.
	Monoclonal Antibodies	There are no licenced mAb treatments for Junín virus.

	Other	Administration of immune plasma (>3500TU/kg) from convalescent patients in AHF cases within 8 days of symptoms onset reduces the mortality rate to 1%. Although highly effective, immune plasma is a limited resource, and the reduction in AHF incidence following the introduction of Candid#1 has decreased the pool of eligible convalescent donors, highlighting the need for additional therapeutic options.
Machupo Virus (MACV)		
General Information	Reservoir	Vesper mouse (Calomys callosus).
	Transmission	Via contact with infected excreta from the reservoir. Agricultural workers are at higher risk.
	Distribution	Bolivia.
	Disease	Bolivian Haemorrhagic Fever.
Status of Diagnostics	Surveillance Programmes	There is no widespread surveillance programme for Machupo virus, but some local surveillance does take place in Bolivia. The WHO have provided technical support during outbreaks.
	RDT/POCT	There are no Machupo -specific RDTs or POCTs.
	Lab Diagnostics	There are no Machupo -specific lab diagnostics, however some institutions with BSL3/4 facilities are able to diagnose Machupo using RUO RT-PCR and serological assays.
Status of Vaccines	Licensed Vaccine	None.
	Assays – Cellular	There are no commercially available cellular assay kits for Machupo virus.
	Assays – Humoral	There are no commercially available humoral assay kits for Machupo virus.
	Clinical Trials	There have been no Machupo virus-specific clinical trials for medical countermeasures.
	Antivirals	There are no licenced antiviral treatments for Machupo virus.

Status of Therapeutics	Monoclonal Antibodies	There are no licenced mAb treatments for Machupo virus.
Sabia Virus (SABV)		
General Information	Reservoir	Unknown.
	Transmission	Most likely through contact with infected excreta from a likely reservoir.
	Distribution	São Paulo/Brazil.
	Disease	Brazilian Haemorrhagic Fever.
Status of Diagnostics	Surveillance Programmes	There is no widespread surveillance programme for Sabiá virus.
	RDT/POCT	There are no Sabiá-specific RDTs or POCTs.
	Lab Diagnostics	There are no Sabiá -specific lab diagnostics, however some institutions with BSL3/4 facilities are able to diagnose Sabiá using RUO RT-PCR and serological assays.
Status of Vaccines	Licensed Vaccine	None.
	Assays – Cellular	There are no commercially available cellular assay kits for Sabiá virus.
	Assays – Humoral	There are no commercially available humoral assay kits for Sabiá virus.
	Clinical Trials	There have been no Sabiá virus-specific clinical trials for medical countermeasures.
Status of Therapeutics	Antivirals	There are no licenced antiviral treatments for Sabiá virus.
	Monoclonal Antibodies	There are no licenced mAb treatments for Sabiá virus.

Acknowledgements

To be completed on final version

Annex I

Agenda for the Arena CORC call held on 31st July 2025.

UK BST	Topic	Speakers
14:00 – 14:10	Welcome	Ana Maria Henao-Restrepo, WHO
14:10 – 14:20	CORC Objectives	Yper Hall, UKHSA
14:20 – 14:30	CCHF Roadmap	Amanda Semper, UKHSA
Session 1: Epidemiology and Transmission Chair: Catherine Houlihan, UKHSA		
14:30 – 14:40	Arenaviruses in Brazil: Reservoirs and Eco-Epidemiological Insights	Jorlan Fernandes, Fiocruz – Oswaldo Cruz Foundation, Brazil
14:40 – 14:50	Epidemiology and Transmission of Lassa Fever	Sylvanus Okogbenin, Irrua Specialist Teaching Hospital
14:50 – 15:00	Epidemiology and Transmission of South American Hemorrhagic Fevers Caused by Arenaviruses	Anabel Sinchi, Instituto Nacional de Enfermedades Virales Humanas (INEVH)
15:00 – 15:15	Panel/Q&A	Panellists
15:15 – 15:25	Break	
Session 2: Virology and Pathogenesis Chair: Tommy Rampling, UKHSA		
15:25 – 15:35	AI-assisted immunogen design	Jimmy Gollihar, Houston Methodist Research Institute
15:35 – 15:45	Insight into the scope of New World Arenavirus receptor usage	Giulia Gallo, Pirbright UK
15:45 – 15:55	Arenavirus–Host Interactions: From Restriction Mechanisms to Structural Insight	Toshana Foster, University of Nottingham
15:55 – 16:10	Panel/Q&A	Panellists
Session 3: Diagnostics and Serology Chair: Danny Asogun, Irrua Specialist Teaching Hospital, and Ambrose Alli University, Ekpoma, Nigeria		

UK BST	Topic	Speakers
16:10 – 16:20	Validation and implementation of a commercial real-time PCR assay for diagnostics of Lassa fever in West Africa	Stephan Günther, Bernhard-Nocht-Institute for Tropical Medicine
16:20 – 16:30	Rapid Diagnostic Tests (RDTs) in the Diagnosis of Lassa Fever in West Africa	Danny Asogun, Department of Community medicine & Public Health, Irrua Specialist Teaching Hospital, and Ambrose Alli University, Ekpoma, Nigeria.
16:30 – 16:40	Arenaviridae and Bunyaviricetes diagnostics at UKHSA	Dan Bailey, UKHSA
16:40 – 16:55	Panel/Q&A	Panellists
16:55 – 17:05	Break	
Session 4: Pre-clinical Models, Vaccine & Therapeutic Development Chair: Stuart Dowall, UKHSA		
17:05 – 17:15	MOPEVAC, a live-attenuated vaccine against Lassa virus: from preclinical development to first-in-human phase 1 trial	Sylvain BAIZE, Institut Pasteur – Centre International de Recherche en Infectiologie, Lyon, France
17:15 – 17:25	Lassa and South American HFs: differences in pathogenesis justify different preventive and therapeutic strategies	Igor Lukashevich, University of Louisville
17:25 – 17:35	Structural blueprints for better Arenavirus vaccines	Kathryn Hastie, La Jolla Institute for Immunology
17:35 – 17:45	Panel/Q&A	Panellists
Closing		
17:45 – 18:00	Conclusions, Wrap up and Next Steps	Yper Hall, UKHSA Catherine Houlihan, UKHSA
18:00	Close of meeting	