LASSA FEVER DIAGNOSTICS
Performance evaluation and access

Devy Emperador, Senior Scientist
Pandemic Threats Programme
26 October 2022
Diagnostics can reveal the **true public health burden of Lassa fever** and help find the **right treatment and vaccine strategies**.

**Current diagnostics challenges:**

- No single reference test (or gold standard)
- Difficult to differentiate Lassa fever from other conditions
- LASV strain variability
- Limited number of facilities

https://www.who.int/publications/m/item/lassa-fever-research-and-development-(r-d)-roadmap
FILLING THE GAPS

LASA FEVER R&D ROADMAP: KEY PRIORITY AREAS

**Research**
- Performance evaluation of promising new assays
- Appropriate evaluation standards
- Field evaluation of new diagnostic tests

**Product development**
- Diagnostic target product profiles
- Diagnostic use cases (screening/confirmatory)
- Biobanks of reference samples
- Point-of-care tests
- Multiplex diagnostics
- Gold standard test

**Policy and commercialization**
- Diagnostic algorithms and case definitions
- Guidance on testing for viral persistence
- Guidance on testing deployment in endemic-disease and outbreak situations

Supported by FIND

Others

Sequencing of virus strains

https://www.who.int/publications/m/item/lassa-fever-research-and-development-(r-d)-roadmap
# Diagnostic Use Cases for Lassa Fever

<table>
<thead>
<tr>
<th>Intended use case</th>
<th>Level 0</th>
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<th>Level 2</th>
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<td>• District hospitals</td>
<td>• Referral hospitals</td>
<td>• National reference labs</td>
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<td>• Field settings</td>
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**Case detection and management**

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<tbody>
<tr>
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<td>• POC MDx*</td>
<td>• MDx*†</td>
<td>• MDx*†</td>
<td>• MDx*† sequencing</td>
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<tr>
<td>• POC IA*</td>
<td>• POC MDx*</td>
<td>• POC MDx*</td>
<td>• POC MDx*</td>
<td>• POC MDx*† sequencing</td>
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<td>• IA*</td>
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**Outbreak response**

<table>
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<th>Level 3</th>
<th>Level 4</th>
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<td>• RDT*</td>
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<tr>
<td>• RDT*</td>
<td>• IA*†</td>
<td>• IA*†</td>
<td>• IA*†</td>
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</tbody>
</table>

*Requires pan-LASV detection. †Requires pan-VHF differentiation.

IA: immunoassay (e.g. ELISA); LASV: Lassa virus; MDx: molecular diagnostics (e.g. reverse transcriptase PCR); POC: point-of-care or near-patient; RDT: rapid diagnostic test (e.g. lateral flow immunoassay); VHF: Viral haemorrhagic fever

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6407552/
Few commercially available tests on the market (N=17)

Among immunoassays:
- **Antibody tests**: anti-LASV IgM/IgG against NP, pre-fusion GP
- **Antigen tests**: target NP

Several tests can detect multiple LASV lineages

Few tests (n=2) with regulatory approval

Update study, extending the landscape provided in the previously mentioned article: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6407552/
EVALUATION OF LASSA FEVER IgG/IgM ASSAYS

- Lab evaluation of 5 IgG and 4 IgM serology assays compared to US CDC LASV IgG/IgM ELISA
- Evaluations conducted with partners in LASV endemic countries (IgG study: Nigeria and Sierra Leone; IgM study: Liberia, Nigeria and Sierra Leone)
- Status: IgG study completed; IgM study close to completion

EVALUATION OF LASSA RDT

- Lab evaluation of ReLASV Pan-Lassa antigen test at one site in Nigeria
- Status: ongoing (results analysis expected by the end of 2022)
RESULTS

PROMISING IgG PERFORMANCE COMPARED TO REFERENCE TEST

### Positive Results in Terms of Sensitivity
- Sensitivity/PPA >90% in 4/5 assays
- **Ideal: ≥90%**

### Mixed Results in Terms of Specificity
- Specificity/NPA <95%
- **Ideal: ≥95%**
FIND ACTIVITIES
SUPPORTING QUALITY ASSESSMENT AND RESEARCH

PCR reference material (NIBSC)

- **Reference panel** for Lassa virus RNA (lineage II, III, V, VII)
- **WHO international standard** for Lassa virus RNA (lineage IV)

Lassa biobank in Nigeria

- Sample collection for suspected LASV cases in Owo, Nigeria (200 people)
- **Status**: enrollment completed. Follow-ups to be completed by November 2022. Opening soon for sample requests.
REMAINING CHALLENGES FOR LASSA FEVER DIAGNOSTICS

- WHO-endorsed target product profile for LASV diagnostics
- Further evaluation studies on PCR tests detecting multiple LASV lineages
- Continued development of point-of-care tests
- Understand kinetics of LASV antigen and immune profile in humans
- Capacity strengthening of national and regional labs to conduct PCR and serology testing
- Clarify regulatory requirements at national and global level to ensure access to quality tests
- Promote local manufacturing of quality tests (molecular/antibody)
- Test procurement mechanisms at national and global levels
MANY THANKS

Devy Emperador, Senior Scientist
Pandemic Threats Programme
26 October 2022
<table>
<thead>
<tr>
<th>Assay Type</th>
<th>Developer</th>
<th>Assay/System</th>
<th>Regulatory status</th>
<th>Product Links</th>
<th>Assay Cost</th>
<th>Sample Type</th>
<th>Assay Target</th>
<th>LOD</th>
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<tbody>
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<td>PANDAA qDx LASV</td>
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<td>Primerdesign™ Ltd Lassa virus Josiah GP gene genesig® Standard Kit</td>
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<tr>
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<td>LASV specific RNA</td>
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<tr>
<td>MDx kit</td>
<td>Luminex/GenArraytion Inc. (US)</td>
<td>xMAP® MultIFLEX® Febrile RUO Agent Panel 3</td>
<td>RUO</td>
<td><a href="https://www.luminexcorp.com/research/applied-markets/xmap-multiflex-bioassays/">Link</a></td>
<td>-</td>
<td></td>
<td>5 agents: Chikungunya, JapEnceph. Lassa, Lepto, Malaria (4)</td>
<td>&lt;10 copies per rxn</td>
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</table>

**Molecular Tests**

**Lassa Fever Diagnostic Landscape - Detailed**
### IMMUNOASSAYS

#### LASA FEVER DIAGNOSTIC LANDSCAPE - DETAILED

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<th>Sample Type</th>
<th>Assay Target</th>
<th>LOD</th>
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<tbody>
<tr>
<td>ELISA</td>
<td>Diagnostics Development Laboratory, Bernhard Nocht Institute for Tropical Medicine (DE)</td>
<td>BLACKBOX® LASV IgG/IgM ELISA Kit</td>
<td>RUO</td>
<td><a href="https://www.european-virus-archive.com/evag-portal/product-categories/detection-kit-ruo">https://www.european-virus-archive.com/evag-portal/product-categories/detection-kit-ruo</a></td>
<td>serum</td>
<td>Detection of human IgG/IgM to LASV protein</td>
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<tr>
<td>ELISA</td>
<td>Zalgen Labs (US)</td>
<td>ReLASV® Pan-Lassa NP IgG/IgM ELISA Test Kit</td>
<td>RUO</td>
<td><a href="http://www.zalgen.com/hemorrhagic-fever-tests">http://www.zalgen.com/hemorrhagic-fever-tests</a></td>
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<tr>
<td>ELISA</td>
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<td>ReLASV® Pan-Lassa GP IgG/IgM ELISA Test Kit</td>
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<td>Serum, EDTA plasma, or citrated plasma</td>
<td>Detection of human IgG/IgM to LASV glycoprotein (GP) antigen for lineage II, III and IV</td>
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<td>Serum, EDTA plasma, or citrated plasma</td>
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<td>ELISA</td>
<td>Zalgen Labs (US)</td>
<td>ReLASV® Pan-Lassa NP/pre-fusion GP IgG/IgM ELISA Test Kit</td>
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<td><a href="http://www.zalgen.com/hemorrhagic-fever-tests">http://www.zalgen.com/hemorrhagic-fever-tests</a></td>
<td>$1600, 2x 96-well plate</td>
<td>Serum, EDTA plasma, or citrated plasma</td>
<td>Detection of human IgG/IgM to LASV glycoprotein (GP) and nucleoprotein antigen for lineage II, III and IV</td>
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<td>Serum, EDTA plasma, or citrated plasma</td>
<td>Detection of LASV lineage II, III and IV nucleoprotein (NP) antigen</td>
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<tr>
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<td>Zalgen Labs (US)</td>
<td>ReLASV® Antigen Rapid Test</td>
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<td>FS or VP whole blood, serum</td>
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<td>RDT</td>
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<td>FS or VP whole blood, plasma</td>
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