Target Product Profiles

Lassa Fever

Vaccines

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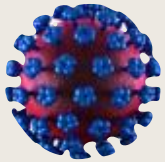
Global level

Critical path for research and potential use
Criteria for candidate products prioritization
Dashboard progress (Taskforce)



Lassa

Roadmap Jan 2018

Non product **research** plan

TPP
Vax 2017
Dx – April2018
Tx – April2018

Dashboard of candidate products vs TPPs
R&D Observatory

CORE
Protocols Designs
Vx- June 2018
Tx – April 2018
Dx – FIND May 2017

No. of doses for Phase 2b/3 trials
Site selection
Modelling
Method.s discussion

Deployment (outside trials) 2018

EUAL or SAGE or R&D Blueprint recommendations
Gloobal coordination plan
Access to candidate products

Country level

NRAs + ERCs - AVAREF joint reviews of protocols - established

Support to countries for liability and compensation - available

Tools for review/design of trials at country level - available

Tools for data sharing and sample sharing- MTA - available

Surveillance, laboratory, case management, …

NRA or NITAG recommendations
Trained teams, logistics
National coordination plan
Community engagement
Access to candidate products

During outbreaks

Mapping of stakeholders

WHO expert Groups

Recommendations priority research during event

WHE/IMS

Country Operational Emergency Plan

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Purpose of the TPP

Lassa virus, target product profile development followed prioritization of Lassa fever as part of the WHO R&D Blueprint for Action to Prevent Epidemics

The target audience includes vaccine scientists, product developers, manufacturers and funding agencies.

All the requirements contained in WHO guidelines for WHO policy recommendations and prequalification will also apply.

The criteria below lay out some of the considerations that will be relevant in WHO's case-by-case assessments of Lassa virus vaccines in the future.

None of the characteristics in the tables below dominates over any other.

Therefore, should a vaccine's profile be sufficiently superior to the critical characteristics under one or more categories, this may outweigh failure to meet another specific critical characteristic.

Vaccines which fail to meet multiple critical characteristics are unlikely to achieve favourable outcomes from WHO's processes.

In the development of a Lassa virus vaccine TPP, two scenarios were considered:

1. Non-emergency setting (preventive use):

- The vaccine is intended for **protection of populations living in areas where Lassa virus is endemic*.**
- HCW at particularly high risk of LF due to their profession (i.e., HCW in endemic areas, laboratory personnel, deployed international HCWs) would also benefit from a preventive use vaccine.

2. Emergency setting (reactive/outbreak use):

- The vaccine is intended for protection of **at-risk persons in the area of an ongoing outbreak** for the prevention of LF as well as to interrupt chains of virus transmission and to terminate outbreaks.
- A reactive use vaccine will be very useful if a large outbreak occurs, potentially in a new/unexpected setting, with extensive human-to-human transmission.

* While better epidemiological data is being generated, one possible strategy is vaccination where LF is hyper endemic and where clusters of cases are reported annually.

The highest priority between the two profiles is for preventive use and this TPP is focused on that scenario.

- The rationale is based on the current epidemiology of LF and towards addressing the burden of LF in endemic countries.

- It is possible that some vaccine products may address both scenarios, such as a vaccine predominantly targeting preventive use with features allowing use for outbreak control (i.e., some protection after the first dose with more durable protection after the second dose). Such a product would be ideal and have a practical advantage including simplification of stockpiling.

The vaccine strategy envisioned in this TPP relies on better and standardized diagnostic tests for LASV as well as enhanced surveillance capacity in endemic countries.

There was a need for a more accurate estimate of the incidence, seroprevalence and geographic distribution of LFV.

The true incidence of LF was unknown.

- The estimated incidence of 100,000 to 300,000 and 5,000 deaths per year (extrapolated from a prospective study in Sierra Leone in the 1980's) was considered out-dated.

Likewise, mapping the distribution of LF would need further work.

- Previous estimates were limited by varying degrees of confidence in diagnostic tests that have been used (i.e., degree of specificity for LASV identification) and may be biased due to limited availability of testing capacity.

Vaccine efficacy studies evaluating prevention of LF disease will require a reliable diagnostic test for LASV.

Non-emergency settings: Preventive use

Vaccine characteristic	Preferred	Critical or minimal
Indication for use	For active immunization of **persons considered potentially at-risk**, based on specific risk factors, to protect against LF disease. Risk groups will include certain communities in endemic areas, health care workers (HCWs)* .	
Target population	All age groups Suitable for administration to pregnant women5	Healthy adults and children, excluding pregnant and lactating women

Non-emergency settings: Preventive use

Vaccine characteristic	Preferred	Critical or minimal
Safety/ Reactogenicity	Safety and reactogenicity at least comparable to WHO-recommended routine vaccines, providing a highly favourable risk-benefit profile, ideally with only mild, transient adverse events related to vaccination and no serious AEs related to vaccination, including in individuals with compromised immune function No neurological complications associated with LF, including sensorineural deafness and neuropsychiatric side effects	Safety and reactogenicity whereby vaccine benefit clearly outweighs safety risks Safety profile demonstrated primarily mild, transient health effects and rare serious AEs related to vaccination

Non-emergency settings: Preventive use

Vaccine characteristic	Preferred	Critical or minimal
Measure efficacy	At least **90%** efficacy in preventing infection or disease	At least **70%** efficacy in preventing infection or disease If demonstration of clinical efficacy is not feasible, pre-clinical immunogenicity and efficacy in a standardized and relevant animal model together with clinical immunogenicity may be considered If regulatory authorization is provided without clinical efficacy data, effectiveness data are to be generated during use in a future outbreak to the extent possible

Non-emergency settings: Preventive use

Vaccine characteristic	Preferred	Critical or minimal
Dose regimen	**Single-dose** regimen preferred without requirement for a booster	**No more than 3 primary doses**, and with preference for short interval between doses Homologous schedules preferred over heterologous prime boost Booster doses: No more frequent than every 3 years
Durability of protection	Confers long-lasting protection of **5 years or more** following the primary series and can be maintained by booster doses Duration of protection may be inferred from immune kinetics, as well as documentation of breakthrough cases	Confers protection of **at least 3 years** after primary series and can be maintained by booster doses Duration of protection may be inferred from immune kinetics, as well as documentation of breakthrough cases

Non-emergency settings: Preventive use

Vaccine characteristic	Preferred	Critical or minimal
Route of Administration	Injectable (IM, ID or SC) using standard volumes for injection as specified in programmatic suitability for WHO PQ or needle-free delivery Oral or non-parenteral route desirable	Injectable (IM, ID or SC) using standard volumes for injection as specified in programmatic suitability for WHO PQ
Route of Administration	Injectable (IM, ID or SC) using standard volumes for injection as specified in programmatic suitability for WHO PQ or needle-free delivery Oral or non-parenteral route desirable	Injectable (IM, ID or SC) using standard volumes for injection as specified in programmatic suitability for WHO PQ
Coverage	Coverage against Lassa virus lineages I to IV	

Non-emergency settings: Preventive use

Vaccine characteristic	Preferred	Critical or minimal
Product Stability and Storage	Shelf life of **at least 5 years at 2-8ºC** Additional data on thermostability at higher temperatures The need for a preservative is determined and any issues are addressed Vaccine Vial Monitor (VVM): Proof of feasibility and intent to apply a VVM to the primary container Vaccines that are not damaged by freezing temperatures (<0oC) are preferred Vaccines that can be delivered via the Controlled Temperature Chain are preferred	Shelf life of at least 12 months at -20ºC and 6 months at 2-8ºC The need for a preservative is determined and any issues are addressed Vaccine Vial Monitor (VVM): Proof of feasibility and intent to apply a VVM to the primary container

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Non-emergency settings: Preventive use

Vaccine characteristic	Preferred	Critical or minimal
Co-administration with other vaccines	The vaccines can be co-administered with other vaccines licensed for the same age and population groups without clinically significant impact on immunogenicity or safety of the Lassa virus vaccine or the co-administered vaccines	The vaccine will be given as a stand-alone product not co- administered with other vaccines

Non-emergency settings: Preventive use

Vaccine characteristic	Preferred	Critical or minimal
Presentation	Vaccine is provided as a liquid product in mono-dose or multi-dose presentations with a maximal dosage volume of 0.5 mL Multi-dose presentations should be formulated, managed and discarded in compliance with WHO'smulti-dose vial policy.	Vaccine is provided as a liquid or lyophilized product in mono- dose or multi-dose presentations with a maximal dose volume of 1.0 mL Multi-dose presentations should be formulated, managed and discarded in compliance with WHO's multi-dose vial policy Lyophilized vaccine will need to be accompanied by paired separate vials of the appropriate diluent

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World Health Organization

Thank you

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The power of coordinating global research

The Constitution of the World Health Organization (WHO) defines that one of WHO's key roles is to promote, conduct and coordinate research in the field of health.

> **By embedding research at the heart of the pandemic response we can achieve two goals: to help end the acute phase of the current pandemic and protect us from the epidemics and pandemics of the future.**
>
> **Tedros Adhanom**
> Director-General,
> World Health Organization (WHO)

World Health Organization

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