



Report:

Enable Lassa Research Programme

Mid-term Workshop

22-24 October 2022, Abuja, Nigeria

Meeting report prepared by:

Ana Goios
Anshu Varma
Carol Kagia
Mark Otiende
Patrick Suykerbuyk

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Executive summary

Lassa fever is one of the nine emerging infectious diseases according to the World Health Organization. Found predominantly in West Africa, Lassa fever may cause tens of thousands of deaths. However, there is a significant knowledge gap about the Lassa fever disease burden which urgently needs to be filled in order to prepare for clinical trials for Lassa fever vaccine development. To address this knowledge gap, in 2019 CEPI launched the largest Lassa fever epidemiological study to date, the *Enable* Lassa Research Programme. *Enable* is a prospective multi-site cohort study to estimate incidence of infection and disease due to Lassa fever virus, following 23,000 participants across five West African countries.

To discuss the interim results of the *Enable* study and share experiences and lessons learned, a mid-term Workshop of the *Enable* Lassa Research Programme was conducted. The workshop was co-organized by CEPI together with Programme Headquarters partners and hosted by the National Centre for Disease Control in Nigeria.

The workshop was a hybrid meeting to allow the participation of as many partners and stakeholders as possible. Over three days from 22-24 October 2022, in Abuja, Nigeria, and online, the following attended the workshop:

- Programme headquarters partners (P95 in Belgium, Margan Clinical Research Organization in Ghana, Bernhard Nocht Institute of Tropical Medicine in Germany, Epicentre in France)
- Implementing partners from Nigeria, Benin, Guinea, Sierra Leone, Liberia (principal investigators, project managers, laboratory, data and field staff)

The format of the workshop was a combination of plenary sessions and breakout sessions. Plenary sessions allowed knowledge sharing and wider strategic discussions, while breakout sessions allowed delving into details and problem solving on key technical issues.

Day 1 covered three sessions. First, overall study progress was presented by Benin, Guinea, Liberia, Sierra Leone, and Nigeria teams. Then, a discussion on key study achievements, challenges, and lessons learned was guided by five focus areas: case definition and surveillance, study operations, study participant retention, community engagement, and capacity strengthening. Finally, results from interim analyses were shared by addressing context, recruitment, participant characteristics, baseline seroprevalence, disease cohort, infection cohort, and confirmed cases in a pooled analysis.

Day 2 included three parallel breakout sessions. The 'laboratory management' session covered practical discussions related to the logistics and technical details of sample transportation, storage, and laboratory analysis. The 'data management' session covered issues with database locking and archiving and sampling methods. The 'project management' session included discussions on how to improve logistics, data sharing, community engagement, team organization, risk management, and reporting.

Day 3 covered two discussions. 'Clinical trial readiness' touched upon sites, equipment, staff, quality control systems, investigational product, sample management, research deviations, and consent processes. 'Impact' partly touched upon informing future clinical trial designs regarding incidence rates, case characteristics, and the role of baseline positivity on immune response, and partly how experiences could improve country level Lassa fever and pandemic surveillance systems and how the *Enable* consortium could advocate for improved pandemic preparedness and response in West Africa.

CEPI closed the mid-term Workshop of the *Enable* Lassa Research Programme by acknowledging challenges faced with the study design, the community engagement, and the COVID-19 pandemic. Co-hosts, attendees, and support staff were thanked for their enthusiasm and commitment. This meeting report is expected to facilitate the next call for action to ensure continued progress towards informing strategic decisions on the significant public health issue of Lassa fever in West Africa.

Acronyms and abbreviations

AFI	Acute febrile illness
BNITM	Bernhard Nocht Institute of Tropical Medicine
CEPI	Coalition for Epidemic Preparedness Innovations
CFR	Case-fatality rate
CLO	Community Liaison Officer
ID	Identification
Ig	Immunoglobulin
ISTH	Irrua Specialist Teaching Hospital
LASV	Lassa virus
LF	Lassa fever
NCDC	Nigeria Centre for Disease Control
MMARCRO	Margan Clinical Research Organization
MTA	Material transfer agreement
NAFDAC	National Agency for Food and Drug Administration and Control
PHQ	Programme Headquarters
PI	Principal investigator
PSC	Programme Steering Committee
RACI	Matrix of responsibilities (Responsible, Accountable, Consulted, Informed)
RUN	Redeemer's University Nigeria
R&D	Research and development
SOPs	Standard operating procedures
SNHL	Sensorineural hearing loss
SWOT	Strengths, Weaknesses, Opportunities and Threats
UNC	University of North Carolina
WHO	World Health Organization

Day 1 - Saturday, 22nd October

Welcome and introductions

Gabrielle Breugelmans (CEPI, Director of Epidemiology):

CEPI was founded in 2017 in response to the Ebola outbreak in West Africa. From the beginning, Lassa fever (LF), one of the nine emerging infectious diseases in urgent need of research and development (R&D) activities on the WHO R&D Blueprint, was set as one of the core pathogens of CEPI. Considering the LF vaccine development, gaps in the knowledge about the true LF epidemiology and burden of disease needed to be filled to prepare for clinical trials.

In 2018, the Epidemiology Department at CEPI was created and a first Workshop was organized in 2019 in Ghana to discuss the best methodological approach to assess the incidence and prevalence of LASV infection and LF disease in West Africa. Just ahead of the emergence of the COVID-19 pandemic in 2020, the *Enable* programme launched in December 2019, with Nigeria very rapidly enrolling and other countries shortly following thereafter. An impressive 23,000 participants have finally been enrolled, making the *Enable* study one of the largest such studies undertaken in West Africa. This was only possible thanks to the tireless efforts of all involved, including all implementing partners, team members and Programme Headquarters (PHQ) partners, to whom CEPI is grateful.

The *Enable* Programme is now one of CEPI's flagship programmes, and scientists and authorities in Africa, USA and Europe await its results to inform on strategic decisions. CEPI, PHQ and the NCDC host this mid-term workshop to discuss the interim results, but also to share experiences and lessons learned.

N'Faly Magassouba (Guinea PI & Head of Programme Steering Committee (PSC)):

This is the largest epidemiological study financed by any organization in West Africa. Prof. Magassouba thanked CEPI for allowing everyone to meet and acknowledged the presence of all in the meeting. Field workers have been facing many challenges and lived different experiences. This meeting is an opportunity for them to share what goes on in the field. Low-income countries face difficulties in retaining human resources, and this study and this meeting provide a basis to strengthen local expertise and capacity in research, epidemiology, and laboratory in these countries.

Roice Fulton (CEPI, *Enable* Project Manager):

Not all participants in the Workshop were able to attend in person. A link has been provided for those who need to join remotely. Roice also remembered those team members and participants who have passed away during the study, and all attendees observed a minute of silence in their memory.

Margaret Williams (MMARCRO):

Teams have interacted remotely for almost three years, and they were now encouraged to interact individually during the meeting. The milestone of enrolling 23,000 participants was celebrated. However, informed consent was a challenge, particularly when language was a barrier, and a translator was needed. An example exercise was presented to explain the challenges of translations in consent. This presentation was followed by an ice-breaking activity.

Session 1 – Country study progress

For each participating country, a representative presented slides summarizing the field activities, LF statistics, challenges and assets and a SWOT analysis. The details of these presentations are available in the respective slides, and this report summarizes only the main points and relevant discussions.

Benin (LAVIHFIB)

Juvenal Honvou ([Link to presentation](#))

Since 30 July 2021, 5,129 participants were enrolled in three sites in Benin, for both infection and disease cohort. Of the 4,487 valid baseline samples, 106 (2.36%) were IgG-positive. There have been 1,250 suspected cases but only one confirmed LF case.

Table 1. Benin SWOT analysis

Strengths <ul style="list-style-type: none">• Dedicated team• Strategic initiatives• Good team collaboration• Febrile cases care subvention• Home visits for FUs• Serology and PCR results digitization	Weaknesses <ul style="list-style-type: none">• Delayed PCR & Serology results• Unstable field worker staff• Sample shipping: long distance
Opportunities <ul style="list-style-type: none">• Strong support: authorities, community leaders, study partners• Overall good community compliance• Capacity enhancement perspectives	Threats <ul style="list-style-type: none">• Poor community past research experience• False rumours• Poor network coverage and internet connection• Participant migration / unavailability• Villages accessibility issues

Guinea (GUILASSEPI)

N’Faly Magassouba ([Link to presentation](#))

A total of 1,022 subjects were enrolled to the infection cohort. Of the 1,002 valid samples at baseline, 28.13% were IgG-positive, and 17.47% were undetermined. The proportion of participants followed-up were 79% at 6-months and 65.7% at 12-months. Four villages decided to discontinue participation: one at 6-months and at 12-months. The team has built trust among community stakeholders, which has allowed to improve community engagement. Two examples of this were presented: a severely anaemic child was referred by the team members to the hospital for follow-up and recovered completely before the next visit; in one of the villages, study participants did not get sick during an influenza outbreak. Both examples helped increase community confidence in the study team and boost subject recruitment.

Table 2. Guinea SWOT analysis

Strengths <ul style="list-style-type: none">• Organization of information and awareness sessions of the project in the local language of local elected officials• Community relays on health workers under the high authority of the Prefect.	Weaknesses <ul style="list-style-type: none">• Common and seasonal migration in dry season• Delay of blood results
Opportunities <ul style="list-style-type: none">• Build trust and understanding among community stakeholders, to boost subject recruitment and retention.• Support outbreak preparedness and response to emerging infectious diseases	Threats <ul style="list-style-type: none">• Rumours

Liberia (CEPI-EPI-Enable)

Jefferson Sibley ([Link to presentation](#))

Enrolment started in April 2021, but community pre-enrolment engagement activities had been ongoing long before to increase trust in the study team. A total of 5,005 participants from 3 communities were enrolled to both cohorts. Sampling for the infection cohort is ongoing, with one community still in the 12-month follow-up and another currently at the 18-month follow-up. There were 848 febrile events. Of these, 6 were confirmed as LF cases and two of them died. For comparison, outside the study, 35 confirmed LF cases (26 died, 9 survived) have been registered at the Phebe Hospital between May 1st, 2021, and October 10th, 2022.

Table 3. Liberia strengths/growth analysis

Areas of strength	Areas for growth
<ul style="list-style-type: none"> • Strong community awareness of the project and engagement and trust-building activities • Cohesive staff with clear scopes of work and reporting lines • Well-trained with refresher trainings for field and lab teams • Increased field supervision activities • Improved conditions of isolation unit leading to greater acceptance of admission • Smooth workflow in the laboratory with sample reception, processing, and result sharing • Clear communication within the team 	<ul style="list-style-type: none"> • Testing febrile samples in a timelier manner (Goal = 100% <48 hours) <ul style="list-style-type: none"> ◦ Created 2 shifts to increase lab staffing hours • With increased cost of fuel explore more sustainable power sources <ul style="list-style-type: none"> ◦ Explore solar power options • Enhance disease surveillance training for community health volunteers to better serve their communities <ul style="list-style-type: none"> ◦ Develop additional trainings in coordination with county health authorities • Opportunity to share data <ul style="list-style-type: none"> ◦ Plan events to disseminate study findings to participating communities ◦ Develop publication and presentation plan • Increasing capacity building of staff <ul style="list-style-type: none"> ◦ Implement a capacity building fund to provide up to \$500 for any staff member to enhance relevant skills

Sierra Leone (COLECT)

Robert Samuels, on behalf of Donald Grant ([Link to presentation](#))

A total of 5,003 participants were enrolled to both cohorts. In the disease cohort, 512 suspect cases were evaluated, of which 105 matched the case definition and no cases were confirmed. Of the 4,808 valid baseline samples, 2,752 have already been analysed. Community engagement has been a strength, while the upcoming presidential elections could cause disruptions in the project activities.

Table 4. Sierra Leone SWOT analysis

Strengths	Weaknesses
<ul style="list-style-type: none"> • Regular community engagement and improved communication strategy using community focal people • Committed and diversified outreach team • Capacity building and training support from staff at Tulane University • Laboratory certifications and expansions improving workflow and quality assurance 	<ul style="list-style-type: none"> • Poor road network, unpredictable vehicle maintenance and upkeep, increased inflation • Rainy seasons, holidays, cultural activities affecting migration of participants, increases potential loss-to-follow up • Lack of consistent and reliable power (although improving) to site
Opportunities	Threats
<ul style="list-style-type: none"> • Consistent, regular training and capacity building from all partners and collaborators • Sharing experiences with other countries to improve protocol implementation in Sierra Leone • Improving passive surveillance strategies 	<ul style="list-style-type: none"> • Poor mobile phone network in some communities • Potential issues with rumours and distrust of medical system (false information being shared) • Upcoming presidential elections could cause disruptions to project activities

Nigeria (NiLE)

Benedict Azuogu, on behalf of **Adebola Olayinka** ([Link to presentation](#))

In Nigeria, the NCDC coordinates the study and lab activities. A total of 5,035 participants were enrolled into the disease cohort in Edo state (ISTH) site. Among these, 2,575 suspect cases were evaluated, and 18 cases tested positive for LF. Across three sites (Edo, Ebonyi and Ondo), 2,976 participants were recruited into the infection cohort. Baseline data collection and three subsequent follow-ups have been completed at a high success rate (92% at 18-months), and the 24-month follow-up is planned for December. Serology for baseline and 6-months follow-up has been completed, and results were disseminated to the participants. Community engagement was crucial to assure the participants of the appropriate use of their samples.

Table 5. Nigeria key achievements and challenges

Study achievements	Key challenges
<ul style="list-style-type: none">• Community mapping• Stakeholder and continuous community engagement• Strengthening of site capacities Lab, project offices• Development of SOPs, protocols, and training manual for different aspects of the study with training of study teams• Ethical Approval from NHREC & Launch of the NiLE Study/Enable Lassa Program in Nigeria• Participants enrolment and baseline sample collection.• Successful 04 follow up cycles of infection cohort (Baseline, T6, T12, & T18).• Disease cohort active and passive follow-up ongoing.• Serology testing (Baseline & T6, while T12 is ongoing).• Four-month post discharge follow-up for hearing loss assessment ongoing• Serology result dissemination to study participants	<ul style="list-style-type: none">• COVID-19 pandemic delayed the onset of recruitment.• Study extension had budgetary implications.• Lock-down slowed down procurement processes.• Challenges with insecurity leading contributing to delay in participant recruitment and follow-up in some communities.• Delay onset of serology testing – kits availability, NAFDAC approval and other logistics.• Rumours on “use of blood samples” for other things among study participants fuelled by not receiving test results early with refusal to continue participation

Session 2 – Key study achievements, challenges and lessons learned

Facilitator: **Suzanne Penfold** (P95)

Representatives: **Jefferson Sibley** (Liberia), **Chioma Dan-Nwafor** (Nigeria), **Ekaete Tobin** (Nigeria), **Robert Samuels** (Sierra Leone), **Parsifal Logbo** (Benin), **N’Faly Magassouba** (Guinea)

Country representatives initiated the discussion by sharing their experiences. The discussion then opened to contributions from other teams. The discussion was supported but not limited by pre-defined questions ([Link to questions](#)).

Focus Area I: Case definition and surveillance

Focus area Ia: Case definition

Chioma Dan-Nwafor (Nigeria) stated that the case definition is too sensitive as it captures other diseases. Having fever for two days as mandatory is not very helpful because some cases did not have it or could not recall if they had fever. She suggested that fever should not be compulsory in the case definition.

Ekaete Tobin (Nigeria) reported that, although they had one case without fever, most cases were captured because they had fever for more than 2 days. Compared with e.g., cough, using fever and additional symptoms to identify suspect cases was helpful. PCR-test confirmation was also helpful.

Robert Samuels (Sierra Leone) highlighted that initially they struggled in identifying suspect cases due to community stigma in presenting themselves as sick. Most participants would have taken antibiotics before visiting the hospital. Healthcare workers helped identify cases and explain the need to ensure health care seeking.

Ekaete Tobin (Nigeria) and **Jefferson Sibley** (Liberia) agreed, and added that, in Africa, understanding fever as a symptom is challenging, because people in the communities will first assume they have malaria. Field workers can help by asking the study participants how they are feeling.

Parsifal Logbo (Benin) also agreed and added that some questions for suspect case evaluation were related to experiencing chills, perspiration and whether any medications like paracetamol were taken recently. **Ekaete Tobin** (Nigeria) shared that they asked the study participants to bring their medicine to the health facility to address the issue of self-medication and ensure that they received proper medical advice.

Alpha Mamoudou Diallo (Guinea) explained that every infection in our organism will cause a level of fever. When self-medication is done, fever will be reversed. Therefore, it is important to better understand the disease history by in-depth interviews. The current definition of cases is very sensitive, and malaria is difficult to differentiate from other diseases that cause fever (I.e., Lassa fever). Another participant from the audience (**Nnennaya Ajayi**, Nigeria) reiterated that there are many causes of fever in the communities/environment. She suggested that people should be suspected of Lassa fever if fever persists after an initial treatment for common fever causes (e.g., malaria).

Ephraim Ogbaini (Nigeria) suggested adopting an objective approach by using thermometers. Adults in Nigeria with fever will not assign heat, fatigue, or weakness to fever but to the tropical climate. Study participants should receive thermometers for daily temperature measures. **Martha Okonoufua** (Nigeria, online) agreed that providing thermometers and probing questions to ascertain fever is important. Fever is very difficult to define in Western African climate because it can be interpreted as caused by weather change. Fever, unless it is high grade, is not taken seriously.

Donald Grant (Sierra Leone, online) asked about the experience of traditional medicine use, healthcare seeking behaviour and reporting fever among the study participants. (This was not discussed further.)

Participants from the audience added that the definition of fever is key, but it needs to be translated into the community language. An example was provided of a village where to ask if a woman is menstruating, they should use the expression “see the moon.” Language builds trust.

Robert Samuels (Sierra Leone) noted that stigma plays a key role in preventing study participants from informing the community engagement team about their illnesses. Study participants are afraid of becoming isolated as for previous infections, and so they avoid sharing their illnesses. **Jefferson Sibley** (Liberia) added that healthcare personnel should be aware of the stigma to bridge the gap between the people with illness and community workers. The number of confirmed cases was significantly reduced during the COVID-19 pandemic – patients not reaching health facilities – because of the attitude of healthcare workers. The role of traditional healers should also not be underestimated. **Chioma Dan-Nwafor** and **Ekaete Tobin** (Nigeria) agreed and added that the problem with stigma is not on the fever, but only when LF is confirmed. **Martha Okonoufua** (Nigeria, online) shared that a recovered LF patient was fired from her job. Stigma can be dealt with through health education.

Focus area 1b: Active/passive surveillance

Ekaete Tobin (Nigeria) applauded passive surveillance as it closed the gaps left in active surveillance field visits. However, this focus area needs a bigger budget.

Chioma Dan-Nwafor (Nigeria) highlighted that active surveillance yielded better data/information than passive surveillance. **Parsifal Logbo** (Benin) added that active surveillance provided many options for direct observation.

For example, during a household visit, a field worker could notice a sick participant looking and could later target specific questions on fever to this participant.

Robert Samuels (Sierra Leone) highlighted that passive surveillance was challenging and called for the use of focal persons. **Jefferson Sibley** (Liberia) agreed that active surveillance was more informative (e.g., also other health “issues” were captured) than passive surveillance, but community health workers required training. **Ekaete Tobin** (Nigeria) stressed the importance of treating diseases as malaria, for instance, as this will improve health seeking behaviour of participants.

Martha Okonoufua (Nigeria, online) highlighted that the proximity of the data collectors to the participants and language friendliness was an advantage to the success of active and passive surveillance. Furthermore, passive surveillance reinforced rapport among the participants. **Kamji Jan** (Nigeria, NCDC) agreed that the role of passive surveillance should not be downplayed because it creates additional rapport.

Bola Jones (CEPI) asked: *How have the sites overcome some of these challenges, in terms of, (i) male overrepresentation, (ii) migration, and (iii) rumours?*

- (i) Male overrepresentation: **N’Faly Magassouba** (Guinea) explained the male overrepresentation in Guinea was due to two factors:
 - 1) During the time of the baseline data collection women and children were in the field due to agricultural activities,
 - 2) Men wanted to be exposed to the LF study and not the remaining family.
- (ii) Migration: Seasonal migration for mining (e.g., gold, diamond) is high in Guinea and in Kenema (Sierra-Leone), for example, economic activities such as mining were a notable reason for migration.
- (iii) Rumours (e.g., other 'use' of blood samples): On rumours, **Ekaete Tobin** (Nigeria) gave an example where organized meetings between the PI and other key investigators, and the people who circulated the rumours and other community members, helped demystify these rumours. **Parsifal Logbo** (Benin) shared that they identified the channels of how the rumours were spreading and used the same channels (e.g., radio programmes) to disseminate information dispelling such rumours.

Focus area 2: Study operations

Focus area 2a: Procurement

Jefferson Sibley (Liberia) stated that procurement is a big challenge in Liberia due to the lack of systems. UNC does the procurement for the site. It is important to place procurement orders in a timely manner. **N’Faly Magassouba** (Guinea) also experienced shipping problems.

In Nigeria, getting import permits and NAFDAC clearance were challenges. As a suggestion, in the future, NCDC or CEPI should intervene instead of sites going through these processes individually. It was further suggested to involve relevant national authorities early in study planning.

The following examples of bottlenecks in procurement were mentioned: bureaucracy, obtaining customs duty exemption for research intended material, regulatory authorities requiring putting up adverts (based on the procurement cost) for weeks or even months; and inflation – suppliers doubled prices – during COVID raised issues with the funder noticing increased prices. The latter resulted in important differences between budgeted versus actual costs.

ALTONA kits shipment & delivery was a challenge in most sites. There were frequent gaps in communication between CEPI, suppliers and sites. Shipments would often stay at the port for long periods without the sites being aware. Therefore, the shipment process needs to be streamlined. This topic was highlighted for extended discussion later.

Chioma Dan-Nwafor highlighted the need for memoranda of understanding with different regulatory authorities in the future.

Focus area 2b: Safety and security

Jefferson Sibley (Liberia) highlighted that security is still an issue. It affects field activities, since participants are hard to find during the day and unable to be followed-up later in the evening for security reasons. The alternative approach of a phone call visit is not as efficient as in-person visits.

Catherine Nimley (Liberia) added that the teams feared for their security during enrolment because they were carrying study equipment (especially tablets) into the field. Field teams had to move as a team and be trained on how to hide study tablets.

Parsifal Logbo (Benin) shared that weather challenges (e.g., flooding in Benin) affected access to the communities. Furthermore, government restrictions to movement across some regions have affected study activities. A terrorist attack in the north of the country was also a concern.

Robert Samuels (Sierra Leone) highlighted that field teams sometimes need to spend the night in the communities by camping in the area or staying in lodges.

Ekaete Tobin (Nigeria) shared the approach from their team. Field teams make their visits in the evenings in communities where they live in to avoid spending the night outside their homes. During surveillance visits, no tablets are carried into the field, only paper records. Data is entered later for security purposes. Female field team members are accompanied by male Community Liaison Officers (CLOs).

In Owo (Nigeria), enrolment had to stop for some time because a chief from the community was killed.

Martha Okonoufua (Nigeria, online) added that security can be enhanced by integrating the community leaders before entry into the community. They are the gate keepers of their community.

Focus area 2c: Project management

Jefferson Sibley (Liberia) shared that their process entails regular meetings with the team to review study progress. Morning field team meetings are held to discuss the planned achievements for the day. There is regular supervision of the field teams as well as weekly work planning. Research nurses oversee the transitions in data collectors and community health volunteers to take up some guided tasks.

Robert Samuels (Sierra Leone) reported that the data manager notes down queries, and those raised repeatedly for specific staff trigger training for that team member.

Parsifal Logbo (Benin) shared that the Benin team has weekly meetings and reviews timelines based on pre-set estimates. The team uses a RACI matrix to follow-up on study tasks.

The NCDC holds meetings with coordinators at the different sites.

Mohamed Harding (Sierra Leone) highlighted that they held close-out meetings with field staff at every 6-month follow-up to learn about the challenges, which are then addressed in subsequent visits. Oversight of the PI also helps.

Danny Asogun (Nigeria) added that the coordination with key investigators and refresher trainings were helpful and suggested having more frequent study monitoring meetings.

Focus area 3: Study participant retention

Parsifal Logbo (Benin) shared that providing support for primary (non-LF) healthcare and referring participants to hospital when needed helped boost retention. He asked CEPI to fund more of these initiatives (primary healthcare). In-person follow-ups were helpful as they strengthened rapport. Regular community engagement

and respect for the community culture and beliefs were important. He suggested to other sites to try to adapt and learn the language, and to participate in ceremonies of the communities.

Ekaete Tobin (Nigeria) agreed that field teams' involvement in other social events of the communities where they work in helps builds rapport. There will always be attrition due to people moving, which is out of the teams' control, so efforts should be directed to addressing/minimizing refusals.

Austine A. Osagbaekhoe (Nigeria) suggested that rapport can be enhanced by recruiting CLOs from the same communities where they will work. Their motivation will also be increased. When participants are in a distant area, there needs to be a way of providing transport assistance to allow them to return for follow-up. Providing primary (non-LF) healthcare also helps retain participants.

Benedict N. Azuogu (Nigeria) emphasized that participants should clearly understand that they can leave the study at any time but that the investigators still have the right to ask why (although participants can always refuse to give any reason). This will help the trust relationship between participants and investigators.

N'Faly Magassouba (Guinea) highlighted that the participants need to have an interest in the study. Social actions can help persuade the community to stay in the study. As examples, the Guinea team helped dig boreholes or pit latrines.

Kamji Jan (Nigeria, NCDC) highlighted that the CLOs were selected from the communities. Before each 6-month follow-up, participants are informed about the upcoming visits to encourage them to be available for sampling.

Focus area 4: Community engagement

Robert Samuels (Sierra Leone) highlighted the continuous engagement with community stakeholders (who are the gateway to the community) as helpful. The PI is the District Medical Officer and engages with these stakeholders regularly. Due to difficulties with passive surveillance, the team decided to have focal people to help interact with community members and participants.

Catherine Nimley (Liberia) referred that blood draws scared participants away. The team recruited community health volunteers who helped engage participants and decrease the impact of rumours. She encouraged in-person data collection as opposed to phone-based surveillance.

N'Faly Magassouba (Guinea) agreed and suggested adopting a stepwise approach to community engagement where communities are reached via community health workers who in turn engage with stakeholders (e.g., chiefs). Social actions can provide an incentive to the whole community, even those members who do not participate in the study.

Henshaw Mandi (CEPI) agreed that community engagement should go beyond the project and include continuous engagement. He further asked *how to establish what the community needs*. In Nigeria's experience, needs can be identified by approaching the communities and providing them a free space to speak. Project staff should have community social responsibility. However, engaging the community is time consuming and needs funding.

Parsifal Logbo (Benin) shared that they communicate in wide broadcasts about upcoming visits. This prepares the community and helps diminish rumours. For blood draws, they demonstrate the quantity of blood drawn using water and units of measurement that participants relate to (e.g., teaspoons).

Ekaete Tobin (Nigeria) stated that involving senior team members (e.g., PIs, professors) to engage with communities helped diminish rumours about blood draws. Treating suspect or confirmed cases with dignity and being frank with timelines strengthens the relationship with the community.

Donald Grant (Sierra Leone, online) shared that starting by engaging the highest level or administrative authorities (e.g., agricultural heads, chief medical officers etc.) has helped. Then they descended to administrative chains from the district and local level administrators. The outcome of this strategy was better than that of Ebola in 2014.

In Liberia, widening the platform for announcements (e.g., using churches) and continuous work with the community health volunteers was helpful.

Focus area 5: Capacity strengthening

N’Faly Magassouba (Guinea) appreciated the training done by BNITM and added that overall training can be better in the next phase of the LF project and include master’s and PhD programmes. Input from social scientists and anthropologists from the participating countries can be valuable. **Parsifal Logbo** (Benin) and **Robert Samuels** (Sierra Leone) also welcomed opportunities for master’s and PhD programmes. **Ekaete Tobin** (Nigeria) added that other diplomas for field staff can also be helpful.

Catherine Nimley (Liberia) agreed and added that, besides the data, *Enable* has increased clinical care capacity for Lassa treatment in Liberia.

Anges Yadouleton (Benin) added that capacity building across the study countries is missing (student-focused training and lab staff training).

Panellists acknowledged PHQ, MMARCRO and BNITM for their training efforts and development of SOPs.

Henshaw Mandi (CEPI) encouraged capacity building across sites and suggested that team members visit the different partner countries and learn from each other.

The Abakaliki team appreciates the CEPI Programme and highlighted that it has already impacted on capacity building and understanding the burden of LF. They further appreciated training and patience from MMARCRO.

Nigeria applauds CEPI’s contributions to the sites’ infrastructure. Other laboratory personnel, not involved in the *Enable* study, have also benefited from the trainings, and this cushioned against effects of staff attrition.

Patrick Suykerbuyk (P95) highlighted that future reports and papers may not capture the sacrifices made by many team members and applauded these 'invisible' team members.

CEPI is happy with the extent of capacity building. This is a continuous process which requires strong scientific advocacy. All partners are urged to be advocating voices to their respective governments.

Key messages

- Sites equipped with GCP terminology
- Infrastructure capacity improved
- Research capacity expanded (trained field workers)
- More training opportunities
- More research collaboration

Session 3 – Interim analysis

Anton Camacho (Epicentre, [Link to presentation](#))

Details concerning sampling, analysis and results are provided in the slides, and only the main points are summarised next.

Context

Study populations across sites/countries vary in size and endemicity for LF. Similarly, not all sites participated in both cohorts, and assumptions and procedures for sampling and differed across sites. This highlights that not all sites are comparable: results for some countries (e.g., Nigeria) are focused on specific communities, while for others (e.g., Sierra Leone) they are more general. This should be considered when interpreting the results. Furthermore, the study timeline also differs, as countries launched at different dates and enrolment lasted from two weeks (Nigeria) to around 6 months (Liberia). Thus, the interim analysis here presented reflects different timepoints for the different countries.

Recruitment and participant characteristics

Recruitment rate was high overall. Some risk factors at baseline (e.g., rodents at home or around the house) were frequent (>75% of households) across countries, while others were country specific (e.g., eat rodent meat). All countries had a small proportion (<10%) of households reporting a previous case of LF in the house. The age-sex pyramid is similar across countries with overall symmetric pyramids in terms of sex, and a high proportion of subjects in the 5–17-year-old group. Guinea was an outlier, presenting more than 75% men. This has been discussed previously and it can be justified by the presence of women in the fields during enrolment and an issue with acceptability. The participants' occupations were heterogeneous. Participant retention is high overall (>95%).

Seroprevalence at baseline

Seroprevalence at baseline was highest in Liberia (50.5%), however only 13% of the baseline samples in Liberia have been tested so far. In Nigeria, seroprevalence at baseline was heterogeneous across sites (11%–43.2%). Benin had the lowest seroprevalence at baseline (2.4%), followed by Sierra Leone (25.9%) and Guinea (34.2%). Seroprevalence at baseline increased with age in all sites, between 2- to 3-fold from children <5 to adults >18 years-old. A multivariate logistic regression of baseline data on all risk factors (excluding data from Liberia, which were incomplete) showed that Edo site (Nigeria) and increasing age were the main determinants of a higher seropositivity ($p < 0.001$), while having a house with ceiling and well fitted doors/windows were associated with a lower seropositivity ($p < 0.05$). Storing food in open air was associated with an increase in seropositivity ($p = 0.09$), but there was no significant association with other risk factors (including eating habits involving rodent meat).

Disease cohort

Biweekly active follow-up in the disease cohort was very high overall across countries (>95%). The case definition used in this study considers as acute febrile illness (AFI) all individuals that self-report fever for more than 48h and a history of contact with a confirmed case or specific signs/symptoms. The incidence rate of AFI cases (per 1,000 person-years) was highest for Nigeria (Edo) (255) and Benin (252), followed by Liberia (166), but it was low in Sierra Leone (18 per 1,000 person-years). The proportion of AFI that have a PCR result recorded into the database varied from 42% to 91%. The pattern of case assessment over time in SL was different from the other countries, with a very low proportion of cases meeting the definition. In total, 26 confirmed cases have been registered: 18 in Nigeria (distributed across all the year), 7 in Liberia, and 1 in Benin. The resulting incidence rate of LF cases (per 1,000 person-years) was 2.03 in Nigeria, 1.32 in Liberia and 0.20 in Benin, however, given the small sample size, confidence intervals are large. These values were within the expected. There was a trend for higher incidence in younger age-groups, but the sample size was low to draw conclusions or proceed to additional analyses.

Infection cohort

Follow-up serology results were only available for Nigeria (3 sites) and Benin, and essentially for 6-month follow-up. Seroprevalence is stable over time, both overall and when analysed by age. In total, 144 cases of IgG seroconversion (IgG negative to positive), and 122 cases of seroreversion (IgG positive to negative) were found. The resolution for seroconversion/seroreversion cases did not allow to reveal seasonal patterns in Nigeria, although for Benin a very low seasonal pattern could be distinguished, with most cases occurring throughout the winter. In some cases, IgG measurements decreased before seroconverting, which could result from an artifact and should be retested. For the first 6 months of the study, incidence rate of seroconversion, in cases per

1,000 person-years, was higher in Nigeria (117 in Edo, 111 in Ondo, and 39 in Ebonyi) than in Benin (22). Incidence of seroreversion, in cases per 1,000 person-years, was highest in Edo (133), followed by Ebonyi (55) and Ondo (49), and lowest in Benin (17). Seroconversion incidence rates appeared higher in younger age groups, while seroreversions showed an inverse trend, although confidence intervals are still too large to draw conclusions. The ratio of confirmed cases (symptomatic) to seroconversions (asymptomatic) in Edo site was 1:58, or 1:71 if considering only confirmed cases which were seronegative at baseline. Four confirmed cases were seropositive at baseline.

Confirmed cases (pooled analysis)

There were 26 confirmed cases overall, in 21 households. Of these, 15 (58%) were female, and one was a pregnant woman (recovered). Four deaths were registered, yielding a case-fatality rate (CFR) of 16% (one participant is still hospitalised). Four (out of 19 tested, 21%) were positive at baseline, and 7 (27%) were also part of the infection cohort. Most cases (21/25, 84%) were positive for malaria. For households with multiple cases, it was possible to accompany the evolution of cases within the house. In four households, the time since the index case ranged from 8 to 82 days. The most common symptoms (20/26, 77% of cases) at admission were headache and abdominal pain, followed by muscle or joint pain (15/26, 58% of cases) and vomiting (13/26, 50% of cases). Sensorineural hearing loss (SNHL) was tested at hospitalization and at 4-months follow-up. Of 21 participants recovered, 3/15 (20%) were SNHL-positive at hospitalization, and 11/16 (70%) were positive at 4-months. Of 14 cases tested at both timepoints, 11 (80%) developed SNHL, 2 (15%) remained SNHL and 1 (5%) recovered. However, there is potential bias in these data because hearing tests could not be performed for all cases.

Summary

- This interim analysis was preliminary, with data as of 20th October 2022. Data cleaning was still ongoing and serology data were only partially available. The study population in the *Enable* study is not representative of the West African population, but it includes specific populations with previous evidence of being hotspots of Lassa transmission, particularly in Nigeria and Liberia. There was heterogeneity between countries in sampling and participant characteristics.
- Follow-up coverage was high, with limited attrition overall (<5%). However, the proportion of participants in the infection cohort seen at the 6-month follow-up decreased over time.
- The baseline seroprevalence ranged from 2% in Benin to 43% in Nigeria (Edo site). In Liberia, seroprevalence was ~50% but only 13% of samples had been tested. Sites, age, and house structure are key determinants of baseline seroprevalence.
- The incidence of LF disease ranged from 0 in Sierra Leone to 0.2% (95% CI: 0.1%–0.3%) in Nigeria (Edo). The incidence of LASV infection was more than 50 times higher than the incidence of the disease in Nigeria. Seroreversion rate was similar to seroconversion rate.
- The incidence of acute febrile illness was stable in Nigeria, Liberia, and Benin, but lower and fluctuating in Sierra Leone.
- A total of 26 confirmed LF cases were detected as of 20th October 2022. One case was still hospitalized and 4 had died (CFR = 16%). Four cases were IgG seropositive at baseline, and 4 households reported multiple cases. More than 50% of confirmed cases reported headache, abdominal pain, muscle pain and vomiting at admission.
- Among recovered cases, 3/15 (20%) reported SNHL at admission, and 11/14 (80%) developed SNHL within 4-months.

Next steps and points for discussion

As next steps serological testing needs to be carried out for all samples. Further analyses can then be carried out on risk factors for LF and LASV infection, clinical severity, and course of disease. IgM ELISA will help refine the understanding of seroconversion. Full genome sequencing of the virus will help refine understanding of circulating clades.

The following points for discussion were suggested:

- Complementarity of *Enable* data and national surveillance: Can datasets be compared to better understand the epidemiological context and spatio-temporal dynamics?

- Interpretation of serological trajectories in individuals: To clarify IgG results it might be useful to retest all samples from a given participant on the same plate.
- Planning for Phase 3 vaccine trial.

Q&A

Considering the differences between the Enable data with national surveillance, did we select the right sites? Has the epidemic changed?

Two suggestions have been proposed to address these questions: retesting samples on the same plate and exploring data from each individual further.

Based on these preliminary data, what could be foreseen for a Phase 3 trial?

The size of the trial depends on different variables. Overall, trial size is inversely proportional to the incidence rate. However, it also depends on the trial design. For Nigerian communities, for example, based on the current incidence rate, we could estimate how many people to vaccinate in the trial. The question is whether the number of people to vaccinate exceeds the population size of these communities. This can be refined by using a more targeted design to achieve a smaller sample size. For example, if incidence is higher among seronegative individuals, these could be targeted in the trial design. However, we are seeing that some seropositive individuals could also become cases. Overall, estimates are a bit lower than would be expected for a trial design, but 2021 seems to have been a low Lassa year. Lassa is very dynamic, and it could change over the years.

Although numbers are still very low, do we foresee that seroprevalence may increase with age, so that from a certain age individuals would almost certainly be seropositive?

In two Nigerian communities, the epidemic has been present for a certain time, with seroprevalence reaching a certain threshold in the population. However, in Ebonyi, overall seroprevalence is the lowest, and it increases with age. This is subject to interpretation, and it may be related to the history of exposure of the population to the virus.

Could it be possible that individuals fluctuate between seropositive and seronegative over time depending on exposure?

The sites are very different. Perhaps the trial should target communities where seroprevalence is at an intermediate level: high enough to ensure LASV is circulating but not too high that all subjects are asymptomatic. This would help maximise the number of confirmed cases, but establishing this threshold is difficult.

Comments concerning the 4 confirmed cases who were positive at baseline:

- To encompass these cases as infection cases, a further analysis needs to classify cases of “infection” by titre increase (2-fold, 4-fold, ...) instead of seroconversion. Epicentre and BNITM have already discussed this and will consider quantitative data for a future analysis.
- The 4 cases who tested seropositive at baseline need to be investigated further, as they may have implications for the vaccine trial.
- Historically, there have been no cases of people showing LF twice, so there is reason to believe that antibodies are protective. This information may be useful for future interpretation of these data.
- For most communities, data were only available for two timepoints: baseline and 6-months. Time of seroconversion can be analysed once more timepoints are available.

Additional points suggested for future analysis:

- Analysis of clinical data (including age) from LF cases who died, retrieved from hospital records.
- Comparison of titre values in healthcare workers vs. other participants.
- Implications of asymptomatic data, considering the large difference between infection and disease incidences.
- Clinical data from SNHL cases and their viral lineage.
- Introduction of IgM data into the analyses.

Day 2 - Sunday, 23rd October

Breakout A: Laboratory management

Facilitators: **Nathalie Vielle** and **Ndapewa Ithete** (BNITM, [Link to presentation](#))

Country presentations

Each site gave a presentation summarising the statistics of samples analysed, a SWOT analysis, and achievements and lessons learnt from laboratory activities. The details of these presentations are available in the respective slides, and this report summarizes only the main points and relevant discussions.

Benin

Praise Adewumi ([Link to presentation](#))

Haemolysed samples were a concern, and the disruption of the cold chain was presented as the main cause. Another factor that may have contributed to sample haemolysis is the delayed shipment from satellite laboratories to the central laboratory in Cotonou. In addition, samples placed close to the icepacks could have lost integrity during sample transportation in cold boxes. To improve on these limitations, the duration between shipments has been reduced, from weekly to twice a week, and a training and simulation on sample packaging and transfer to the laboratories has been organised.

On the topic of sample transportation, the Nigeria team shared from their experience. In locations where study participants could only be reached in the evening, refrigerators were placed in the community to store samples overnight before being transported to the main laboratory.

As a main conclusion from this discussion, efforts should be put in place to narrow the time between sample collection and analysis.

Liberia

Emmanuel Kerkula ([Link to presentation](#))

One of the threats presented were the problems in water supply to the laboratory. Currently, the only source of water for the laboratory is the Phebe Hospital supply, and any shortage has a considerable impact. The laboratory is looking for feasible local alternatives. The presentation also highlighted limitations in the laboratory space, despite the expansions already carried out. Furthermore, budgetary limitations meant that the study site could not recruit more than 6 laboratory staff to process the samples from the 5000 recruited participants.

As lessons learnt for future projects, a thorough evaluation of logistics, personnel and facilities needed should be carried out before study initiation to increase the study's success.

Sierra Leone

Mohammed Saio Kamara ([Link to presentation](#))

One of the main difficulties in collecting samples from participants at 6- and 12-month follow-ups was related to the study participants' temporary relocation to other areas. Although there have been no confirmed LF cases yet, surveillance data showed that there have been Lassa cases in the region. To confirm that no positive cases were being missed, the team has tested the suspected case samples using IgM and Ag ELISA kits. After a case of a sample collected in the wrong blood tube, periodic refresher trainings of field staff are conducted to prevent this from being repeated. The Nigeria team asked about the management of invalid samples, since in their cases these participants were resampled. However, due to the Ebola experience in Sierra Leone, study participants are frequently afraid to give blood. Therefore, the teams were trained periodically to ensure sample integrity, which was essential to avoid resampling.

PCR kits were expired before they could be used. To prevent this from occurring in the future, the shelf-life and consumption rate per site should be considered when procuring reagents. Communication with CEPI in prior to order is important. Furthermore, freezer maintenance and correct use of the different fridge zones were suggested to prevent reagents from freezing.

Nigeria

Omobude Osas (NCDC)

Across all timepoints (baseline to 12-months) proportion of indeterminate samples was higher for Edo and Ondo ($\approx 5\%$ - 13%) than for Ebonyi ($\approx 0.8\%$ - 1.3%). This difference could not be explained yet, but it needs to be investigated.

Trained staff are leaving the team to pursue their studies, but they may return in the future. New staff will need to be trained. Site representatives have previously requested CEPI to provide training on RT-PCR and serology to FMCO and AEFUTHA sites to build capacity. For now, favourable feedback has not been provided, as the priority was set on launching the serology testing in all the countries. As the facilitator, BNITM has committed to bring this up at the meeting with the project's funders and coordinators.

Ojide Chiedozie K (Abakaliki, [Link to presentation](#))

Abakaliki is only involved in infection cohort. Although there were invalid samples, the team has tried to resample all those participants. To reduce attrition in the follow-ups the team has called participants and offered to cover their transportation costs to the appointments. However, the target sample size foreseen in the protocol already accounted for attrition.

Samples from 6-month and 12-month follow-ups were stored at -20°C but shipped and received at the recipient laboratory (NCDC) at -3°C . This may be due to a faulty functioning of the mobile freezers used for transportation. Before engaging as a service provider, courier companies should demonstrate ability to ship samples at the required temperature from the site to the laboratory by producing dummy shipment records.

Ephraim Ogbaini-Emovon (ISTH, [Link to presentation](#))

ISTH is engaged in both cohorts. Delayed payments of salaries are perceived as a threat as they affect staff motivation. The 16 samples of positive cases were sent to RUN for sequencing; however, it was unclear if all sites should already send their samples. Sequencing results have not been received yet.

Nelson Adedosu (Owo, [Link to presentation](#))

Owo is only involved in the infection cohort. Main challenges identified were irregularities with power supply, the shipment of aliquots to NCDC, where temperature is not maintained, and equipment maintenance. The provision of alternative solar power supply was positive.

Guinea

Hadja Aïssatou Bah ([Link to presentation](#))

The attrition rate was high at around 20% per visit (6- and 12-months). This might be attributed to the relocation of participants due to the dry season and mining activities in other regions of the country. The 2-month delay in launching the study might have had an impact as it pushed the activities to synchronize with the dry season. The site intends to increase community engagement to encourage participants to increase adherence during follow-up visits.

Zalgen update

Matthew Boisen (Zalgen Diagnostics remote presentation, [Link to presentation](#))

The presentation summarised the logistics of Zalgen kit manufacturing and shipment. A total of 970 plates have been shipped to the five participating countries, but there are still 110 plates at Zalgen inventory, and a new lot will be produced. Technical support included online and hands-on training, a training panel, and support discussions. There was a concern regarding OD variability, which can occur due to varying laboratory conditions. To address this, Zalgen tested extreme conditions (from $2-8^{\circ}\text{C}$ to 35°C) of operational range and showed that assay temperature affected OD range. The OD of calibrator and positive control increased with lab temperature. The calibration curve compensated for the OD variability and positive control recovered consistently across the temperature range. Zalgen recommended to warm-up the kits at room temperature (around $20-21^{\circ}\text{C}$) for an hour before use, and to store sample diluent solution and wash concentrate at room temperature.

Sites reported issues with the positive controls. In Sierra Leone, experience has shown that outcomes are only satisfactory when reagents are used at room temperature. The analysis would fail when using the Epicentre web app, but it would succeed when using Prism platform. Benin reported better results when properly centrifuging the positive control. For laboratories that reported issues with the OD values of positive controls, Zalgen requested to receive the details on these situations to analyse and provide support. Epicentre and BNITM requested the raw data from Zalgen's analysis to compare with the countries' results. Regarding control reconstitution, Zalgen informed that reconstituted positive controls can be stored at 4°C, but they recommend reconstituting a new set of controls every week. The ratio of positive controls per kit can be adjusted with Zalgen depending on the sites' use of these reagents. They further recommend using laboratory-grade water (deionised or ultra-pure) for control reconstitution.

Discussion

The discussion focused on practical and specific issues regarding the use of the Epicentre web app for serology analysis. Participants from the different laboratories/sites presented their queries, and these were addressed by Anton Camacho (Epicentre) and Nathalie Vielle and Ndapewa Ithete (BNITM). BNITM summarised recommendations regarding serology testing. The main points addressed were:

- CEPI is responsible for shipment of study labels, Zalgen kits, and Altona PCR kits.
- Before inactivated Lassa positive samples are shipped to the external laboratory (RUN) for sequencing, material transfer agreements (MTAs) should be in place.
- Samples with indeterminate results should be retested a second time, and the second result will be considered final. There is a table in the app to help identify the samples that need to be tested or re-tested. Serology retesting should be done systematically every week and not at study end.
- Indeterminate results should be communicated to participants in a structured way.
- BNITM will schedule online refresher training sessions on serology for all sites.

Session summary

The laboratory discussion session allowed the teams to share experiences and lessons learned. The main points discussed were:

- The importance of maintaining the integrity of samples collected from the field to the analytical laboratories and need for evidence of competency from courier companies responsible for sample shipments.
- The need for efforts to arrest high attrition rate in some countries, and shared experiences from other countries which are more successful in this point.
- The lesson learnt for future projects on the importance to thoroughly assess capacity of the facilities and staff before study start.
- The request for support to build laboratory capacity for satellite sites in Nigeria.

Breakout B: Data management

Facilitators: **Anton Camacho**, **Mark Ndifon** and **Robert Nsaibirni** (Epicentre)

Anton Camacho and **Mark Ndifon** gave an introductory presentation on the data management choices for the Enable study ([Link to presentation](#)).

Country presentations

Countries presented the main issues, achievements and lessons learned from data management. These were discussed and a list of action points was collated.

Discussion points

- Ensuring security of participant's identifying information in follow-up schedules
- Ensuring that field visits are carried out and data is collected: how to detect and avoid data falsification
- Slow tablets in field work
- Long distance between the sites and the laboratory

- Use of paper CRFs for infection cohort follow-up before entry into REDCap
- Migration of participants out of the study's catchment areas
- Proper CRF change management and queries
- Inability to scan barcodes and need for manual recording of sample IDs due to barcode size in the sample stickers

Achievements and lessons learned

- Need for continuous sensitization of field workers on the use of study documents that contain participants' identifiers.
- Old schedules returned should be destroyed (shredded or burned) before release of new schedules.
- Involving the communities before and during study activities helped to achieve planned events in Guinea.
- Batching samples helped optimise sample shipment: participants' samples were batched to achieve three hundred blood samples per shipment before transporting to Conakry from Faranah.
- Re-training of field workers and specifying the roles and responsibilities in the field helped and achieve task completion.
- In Benin, Liberia, and Edo (Nigeria), field workers live in the community where they are assigned, which helps trace participants.
- Barcode scanning not working has led to occasional duplicated entry of sample IDs.
- Field supervisors usually accompany field workers during home visits.
- NCDC usually phone-calls selected participants to confirm visit attempts in Nigeria.

Action points/Follow-up

- Participant names should be removed from the follow-up schedules to ensure data security.
- Field supervisors to confirm field workers visit homes in countries that have not operationalized it.
- Countries reporting less data on household structure should collect more data to improve the analysis of risk factors for LF.
- All site data managers should ensure that visit attempts are captured in REDCap.
- Field teams to use the schedules that are given to avoid situations filling data on participants who have died or withdrawn from the study.
- Epicentre will organize a remote training for all site DMs on good clinical data management practices.

Database lock

Discussion points

Robert Nsaibirni (Epicentre) shared the process for database lock and archiving, addressing the following points:

- Data completeness
- Query resolution
- Data reconciliation
- Database lock checklist
- Database archiving and subsequent access
- Destruction of paper and electronic documentation after archiving

Achievements and lessons learned

- Some sites have procured archiving cabinets and archiving units in readiness for database lock and archiving.

Action points/Follow-up

- Other sites should start preparing for database lock.
- Certificate of database lock will be provided to indicate if the database lock is partial or final.
- Only documents related to data quality and integrity will be archived after database lock.
- Sites should accelerate query resolution to ease database lock at the end of the study.

Next steps

Discussion points

- Data completeness and timelines
- Retesting of serology samples
- Delays in query resolution on sample IDs in both databases
- Improvements in privacy management
- Misspecification of suspected cases
- Better equipment management
- Improvements of study visit supervision
- Tablet distribution

Achievements and lessons learned

- Retraining of field workers on the suspect case definition improved detection of suspect cases and data recording.
- Sites should work with Epicentre before refreshing of study tablets to ensure participants records are not deleted from REDCap.
- Security of participant data was achieved by shredding schedules after follow-up visits.

Action points/Follow-up

- PCR results should be entered for all suspect cases. Sites should ensure that the ID number of suspect cases and PCR results are reconciled and up to date.
- In cases where manual entry is needed due to barcode scanning not working, IDs should be entered twice.
- Visit attempts should be recorded, and reasons for missed visit attempts should always be filled.
- Delays in the entry of forms 13a at the lab should be reduced.
- All laboratory results should be entered into the laboratory database.
- Mismatched samples vs participants should be resolved in both databases.
- Incorporate signing of non-disclosure agreement with field workers, including deletion of study data, forms, and logs from their personal laptops.
- To improve equipment management, tablet logs should be used for signing in and out.
- The tablet specification file should be continuously updated for all sites.
- Participants' identifiers should be removed from schedule visit documents.

Statistical analysis

Discussion points

- Differences in sampling methods across sites and reasons for choice at each site
- Implications of sampling methods to the level of generalisation of results
- Shared experiences from GPS sampling from Benin and Liberia
- Alternatives for household selection (selecting points instead of households).
- Suggestions to document (and publish) the GPS sampling processes in different site.

Session summary

The main take-away messages from the Data Management breakout sessions were:

- Refresher trainings for study teams before each scheduled infection cohort follow-up activity has improved data quality.
- Data management technical assistance from Epicentre helped local data managers resolve queries in a timely manner.
- MMARCRO has provided the needed support and training to enhance data quality.
- The use of REDCap ensured data audit trails.
- Community engagement helped achieve planned activities.
- Site teams overall know how to appropriately fill study documents.
- Sites are aware of some clinical data management best practices.

Breakout C: Project management

Facilitators: **Patrick Suykerbuyk**, **Carol Kagia** (P95) and **Roice Fulton** (CEPI) ([Link to presentation](#))

Review of day 1 discussions

The first discussion topics focused on key points arisen from Day 1, including: study operations, participant retention, community engagement and capacity building and sustainability. The main question addressed overall was: *What does the Enable programme need to prioritise as we enter the “peak” Lassa season?*

Study operations: logistics and supply chain

Roice Fulton (CEPI) highlighted two key points where the country teams can help CEPI deal with logistics. The first point is import-export. CEPI is not equipped to deal with import-export processes because it has not been needed for any other project. These processes have been substantially optimized throughout the course of the project, but any information that the countries can provide in advance can be helpful. The second point is forecasting. If countries can provide realistic forecasts of their needs, particularly of Altona and Zalgen kits, this can optimize production and shipment of these materials in the appropriate quantities and at the needed time. The countries should also always provide signed confirmation of product receipt to the supplier. The only items that CEPI will procure centrally are labels, Altona and Zalgen kits, any other supplies should be procured locally following CEPI's requirements.

Alpha Mamadou Diallo (Guinea) asked whether CEPI could provide a dedicated focal person for logistics aspects such as ordering and monitoring shipments. This would be particularly important during clinical trials. CEPI has also been reorganizing this as the project evolves, and **Sophie Warren** (CEPI) is now the project coordinator who supports all logistic aspects of the project. Logistics and approvals have changed throughout the three years of the project, and the way of dealing with these changes and ideas of how CEPI can support should be communicated by the country teams.

Danny Asogun (ISTH, Nigeria) reported issues in receiving Altona kits recently. **Margaret Williams** (MMARCRO) clarified that the country teams can contract local courier companies for door-to-door services. **Danny Asogun** added that the staff's commitment to their job was being hampered by payment delays. **Henshaw Mandi** (CEPI) clarified that CEPI's financial department was addressing this issue and added that he would contact Zalgen to ensure door-to-door delivery (as per contract) and resolve the sites' shipping issues. CEPI is always open to help resolve any logistic issues and other challenges.

Participant retention and data sharing

David Wohl (Liberia) suggested that sharing overall study data (study results, not only individual results) with the communities can help increase retention. **Henshaw Mandi** (CEPI) agreed that the data can first be shared with the authorities, and then gradually be translated so that the communities can understand. However, at this interim analysis stage the data cannot yet be shared because the results are not definitive and may still change. It may be possible to share some intermediate-stage information with the communities if targeted stakeholders can be involved. Data sharing issues and ownership will be further discussed in PSC meetings, but, according to CEPI *Enable* Programme funding agreements, data ownership is assigned to the primary awardees. **Suzanne Penfold** (P95) suggested sharing monthly newsletters with the communities through the study staff. P95 could support in preparing a general newsletter that could be adapted with country-specific information.

Benedict Azuogu (Abakaliki) shared that attending community events, paying condolence visits to participants who have lost a loved one, and gifting new moms, has helped with participant retention. Additionally, the site has carried out a medical outreach visit, screening the community for hypertension and providing medication. **Margaret Williams** (MMARCRO) stressed the importance of distinguishing compensation from coercion. All compensations need to be approved by the ethics committees, particularly in clinical trials. It is also important to be careful with the prospect of inducement, and to ensure the participants do not feel obliged to participate or continue in the study.

Parsifal Logbo (Benin) stressed the importance of an anthropological evaluation of the communities before study start, to consider cultural and religious characteristics of the community or their health needs in the study design. For example, the need for different translations of the documents or the need to avoid the Ramadan period could be considered from the protocol stage.

Overall, there was general agreement that meetings with local stakeholders (such as district health authorities) are crucial in translating the message from the study results into local languages so that it can be understood by local communities. The importance of correct communication and interpretation should not be underestimated. It was further suggested that disease survivor testimonies can help advocate for further research. Future discussions should focus on strategies for data sharing: when to share data, with whom first, per country or overall, before or after publication.

Community engagement

Ekaete Tobin (Nigeria) and **David Wohl** (Liberia) asked what the project can give back to the community at a short- mid- and long-term, besides awareness of the *Enable* programme and perspectives of vaccination. For example, Phebe Hospital expects to improve quality treatment as a consequence of participating in the study.

Patrick Suykerbuyk (P95) highlighted that besides the scientific benefits, the programme should result in an improved quality of the patient’s pathway by removing any barriers that LF cases may encounter (an example infographic slide was presented (Figure 1). From the outside perspective, resources from the *Enable* programme (trained human resources, funding, infrastructure) should outperform the routine surveillance system and case management.

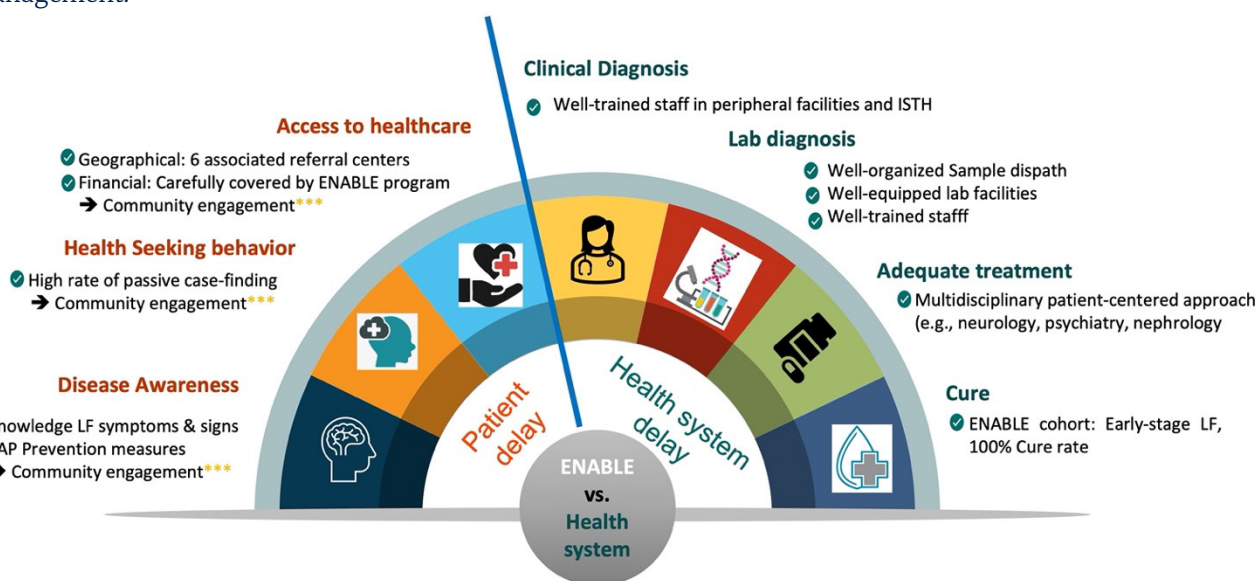


Figure 1. Patient pathway infographic example.

Alpha Mamadou Diallo (Guinea) highlighted the key points for effective community engagement. The main message is to plan and act together with the local communities, while working with trained staff. This can prevent missed visits due to other activities or rumours. Furthermore, the importance and difficulty of sharing data using the right wording for different audiences was stressed. As an example, health authorities may have a different perspective of the relevance of the total number of confirmed cases depending on how the information is presented.

Capacity building and sustainability

Ekaete Tobin (Nigeria) recommended using the resources available in each country. However, resources can be very limited in many sites.

Henshaw Mandi (CEPI) highlighted that sustainability is a shared responsibility. Infrastructural issues that may affect study activities, such as power supply shortages, should be reported at the feasibility assessment, and not at interim or final study stages.

Project management takeaways from Day I

Roice Fulton (CEPI) summarised the key points from the previous day's discussions that were relevant for Project Management:

- Challenges to study progress can be more generally considered *risks* to project integrity or continuity.
- Attendees identified diverse challenges (risks) regarding procurement, logistics, staffing, infrastructure, and capacity/competency.
- PIs have several obligations, which differ from study to study and country to country – in most cases, this results in delegation of duties to senior team staff.
- Delegation is done differently based on team composition, capabilities, and culture – but the need for appropriate and consistent delegation / empowerment to make decisions remains constant.

Place yourself in the PI's shoes

This session included a group discussion where participants were asked to do the exercise of imagining they were project Principal Investigators (PIs) and answer proposed questions. A summary of the contributions to each point is provided:

How is your team organized to identify and mitigate risks before they materialize?

- Teams are organised by technical capacities, each with a team lead.
- In Sierra Leone, teams meet with the PI regularly, at least once a month.
- In Nigeria (across 3 sites):
 - NCDC coordinated the development of a country risk management plan. The project manager at NCDC is responsible for this.
 - This risk management plan was developed based on the input of the site PIs (bottom-up).
 - During the project, risks are identified bottom-up: CLOs will inform the study or field coordinator, who will inform the site PI. Depending on the nature of the risk, the site PI and site management team will take necessary mitigation actions and/or inform NCDC management.
 - Identifying and mitigating risks are a "collective thing", and site PIs have a shared responsibility
- At AEFUTHA (Nigeria), communication is facilitated by monthly meetings, ad-hoc internal meetings and WhatsApp.
- At NCDC (Nigeria) there is regular communication with different departments at the site level. The NCDC team meets with site PIs monthly.
- The Benin team has weekly meetings with the PIs
- In Guinea, an emergency plan was developed by the community engagement team, epidemiologists, and data manager, inspired by the Ebola emergency plan. Community Health Workers will capture any concerns from participants and will inform both the district health authorities as well as the field coordinator. The latter will discuss with the investigation team (clinicians, data collectors, data manager(s), community engagement team) any immediate mitigation measures. The PI will be informed or actively engaged depending on the nature of the risk.

If a problem arises – operationally, scientifically, or otherwise – how is your team organized to triage and solve the problem?

- In Benin:
 - Problems are dealt by the responsible department.
 - Personal problems can be communicated directly to the PI.
 - Fieldwork-related issues are communicated via the field supervisor.
- Liberia has established a chain of command that is used to report any problems. A team from the University of North Carolina (UNC) is present on the ground every 3 months.
- In Nigeria:

- The ISTH has established channels through which problems are communicated.
- AEFUTHA's PI has an open-door policy. For field-related problems, CLOs hear the problems on the ground and are empowered to communicate to the PI.

Are the same people involved in both identifying/mitigating risks and solving problems? Why or why not?

- All sites reported the same people involved in identifying, mitigating, and solving problems.
- The main justification is that people familiar with each problem can solve it better: familiarity with the study helps solve problems at the study level, while familiarity with the community allows solving problems at the community level.
- Occasionally, technical discussions require the involvement of different people with more knowledge of the subject.

If you were to resubmit your Enable grant application today, having the knowledge of the challenges and risks that you confronted since study launch, would you organize your team differently to anticipate and address those risks? How?

- All teams would do things differently, including:
 - Create a risk management plan;
 - Establish quality control (QC)/quality assessment (QA) system;
 - Establish two-way traffic of communication;
 - Organise teams such that dedicated team members would have the responsibility to identify problems and solve them together with the team leads;

Think about how you will ensure oversight of the study at an appropriate level given many competing obligations (think about operational, scientific, and reputational risks).

- Operational:
 - Proper interviews for all staff
 - Proper inspection of staff qualifications
 - Proper recruitment of qualified staff based on the planned workload
 - Performance evaluations
 - Preference for clinicians & social scientists as part of the team
 - Clear definition and delegation of roles and responsibilities
 - Established payment schedule
 - Work with established courier companies
 - Established supervisory team
 - Decentralizing some logistics systems
- Scientific:
 - Conduct a pilot study to identify ahead all potential operational and scientific issues
 - Training and refresher trainings as appropriate
 - Training on compliance at start
 - Appropriate staff numbers for all project tasks, including study management and quality control
 - Qualified field staff should preferably be resident in the study area
- Reputational:
 - Develop a communication plan from the beginning
 - Plan and budget for social actions within the community to support community engagement activities

Project management

Patrick Suykerbuyk (P95) shared a presentation ([Link to presentation](#)) with tips about project management. First, he stressed the importance of understanding the difference of routine activities [read: business as usual] compared to a project. In short, *a project [read: the Enable programme] is a temporary organization that is created for the purpose of delivering one or more business products [read: the programme objectives] according to an agreed Business case [read: aim of this study (i.e., determine the feasibility of future Phase IIb or III clinical trials for assessing the efficacy of LF vaccine candidates)].*

Second, he emphasized the six aspects of project performance that should be managed by a project manager. In short, project management could be defined as the planning, delegating, monitoring and control of all aspects of the project, and the motivation of those involved, to achieve the project objectives within the expected performance targets for TIME, COST, QUALITY, SCOPE, BENEFITS, and RISK.

The key messages here are that:

- (i) project management is not the role of the PI;
- (ii) the PI's role is "to direct" the project, not to daily "manage" the project;
- (iii) the PI and/or the site project board should delegate sufficient responsibilities and authority (read: mandate) to the project manager to be able to fulfil its role; and
- (iv) project management should not be minimized to an administrative supporting role but plays a pivotal role in the successful implementation of the project;

Carol Kagia (P95) presented the revised CEPI Monthly Report form ([Link to form](#)). This form is aimed at facilitating the summarisation of data and any issues arising in each country. This new form will be presented in such a way that it is user-friendly, using (automated) pre-filled fields, logic branches, and less time-consuming. The report form will be open for feedback from the country teams before finalisation.

Session summary

In the Project Management session, participants discussed how to improve aspects related to logistics, data sharing, community engagement, team organization, risk management, reporting and future post-*Enable*. The main lessons learned were:

- There is a need for logisticians and agents specialized in customs clearance and clinical supply.
- Participant retention plans need to be developed from the protocol development stage.
- Community representatives should be involved and included ahead of study start.
- Mechanisms for sharing research data for public health should be put in place.
- Other items that need a sound preparation include: protocol, pilot study, roles and responsibilities, training/experience, QA, communication plan, strategic oversight

The following questions were lined up for further discussion:

- Logistics – What do countries need to self-facilitate logistics? Can they have door-to-door shipment?
- Participant retention – What is the role for traditional practitioners in research?
- Community engagement – How to engage the community without coercing?
- Results/data sharing – How to best share results in different forums? When should results be shared? At what level? Evaluate the need for accurate results interpretation regarding study continuity and future studies.
- Capacity building/training – Is there provision for higher education training within the *Enable* context? (To be evaluated in the context of the extension budget discussion)

Day 3 - Monday, 24th October

Clinical trial readiness

Facilitator: **Margaret Williams** (MMARCRO, [Link to presentation](#))

This session was a presentation from MMARCRO on clinical trial readiness.

The MMARCRO team covered various topics related to site preparedness towards clinical trial readiness. a variety of topics were covered as follows

Margaret Williams (MMARCRO)- site feasibility and selection which provided an overview of the requirements and importance of assessing a sites suitability for selection to conduct a clinical study

Phillip K. Ayivor (MMARCRO)- Equipment assessment which provided an overview of the different types of equipment, and documentation required for the various equipment needed to conduct a clinical study

Elisabeth L. Diallo (MMARCRO) - Staff assessment which provides details on how to recruit staff and ensure the required documentation for checking staff suitability for conducting a clinical study is in place.

Richard Osei Buabeng (MMARCRO)-Quality Management Systems, Study Data and SOPs which discussed the importance of setting up a quality management system to ensure quality in clinical research. He also discussed the different types of study documentation required for clinical study conduct.

Roseanne Onyia (MMARCRO)-CRF completion and data handling which provided details on the ALCOAC principles required for good documentation practice as well as the quality control system required for management of clinical research data

Uzoma Nwosu (MMARCRO)- Investigator site file management which provided an overview of the importance and contents of the Investigators site file as well as how to manage and organize the contents

Osman Kargbo (MMARCRO)- Investigational product (IP) and sample management which discussed the requirements for IP and sample handling including receipt, shipment, transport, storage, and processing.

Margaret Williams (MMARCRO)- Deviations which provided an overview of types of deviations in clinical research, their identification, management recording and reporting.

On completion of the clinical readiness presentations **Elisabeth L. Diallo** (MMARCRO) also provided an overview of the importance of the consenting process in clinical research, participant rights, language of consent and the documentation of consent.

The main recommendations for the sites are transcribed here:

- Know your site's capabilities
- Know your regulatory environment
- Know your needs
- Obtain your needs/plan for re-stocking
- Carefully select and know your team
- Train your team
- Put in place a risk management plan and a quality management system
- Prepare all study documents
- Know your protocol

Some of the key questions that were raised by the audience included:

- Is there enough data to show that people would easily go for oral investigative product rather than injectable vaccines?
- In case of a trial who pays for Adverse Events (AEs)?
- What is the feedback on the early phase trials?
- Are there any efforts towards contextualization of clinical trials in Africa? Resources? Challenges?
- How can we prepare the communities to participate in clinical trials?
- What are the vaccine candidates for Lassa?

Clinical trials and research partnerships: multiplying the impact of the Enable Lassa Research Programme

Facilitators: **Paul Oloo**, **Abebe Genetu Bayih**, and **Gabrielle Breugelmans** (CEPI, [Link to presentation](#))

The primary objectives of the *Enable* Lassa Research Programme are: “to assess the incidence rate of symptomatic confirmed LF separately for each Lassa-endemic study country” and “to estimate the incidence rate of LASV infection separately for each Lassa-endemic study country”, with the main aim of determining the feasibility of Phase 2b/3 clinical trials to assess efficacy of LF vaccine candidates. This study will inform the design of future clinical trials in terms of: incidence rates, characteristics of cases (age distribution; risk factors, endpoints regarding SNHL incidence), and role of baseline positivity on immune response.

Several LF vaccines are currently in development, of which six are funded by CEPI. Four of these vaccines are undergoing Phase 1 or 1/2 clinical trials. However, several challenges arise in planning for Phase 3 studies, which CEPI is working to address:

- Lack of accurate disease burden estimates to guide trial site selection (*Enable* study to inform)
- Inadequate clinical trial sites workforce and infrastructure capacity
 - *Enable* study already providing support
 - CEPI to provide training opportunities e.g., GCP training
- Inclusion of vulnerable populations in clinical trials (pregnant women, children immunocompromised)
 - Vulnerable populations need vaccine with low risk profile for adverse reactions
- Insufficient community awareness
 - CEPI to continue to work with sites to offer community sensitization on LF and vaccines
- Diverse LASV strains that could evolve over time
 - Different LASV lineages may vary in pathogenicity, virulence, disease manifestation
 - Need for further research on different lineages
 - CEPI centralized laboratory initiative to support regional laboratory capacities
- Lack of standardized & validated assays to distinguish acute illness, past infection, vaccine response
- Insufficient funding
 - CEPI to continue investing in Lassa vaccine Research and Development
- Occasional political instability

The Lassa R&D roadmap includes the following key milestones:

- *Enable* study – Lessons learned and what is needed to prepare for Ph3 clinical trials
- Workshop on Accelerating the licensure of Lassa vaccines- 25th and 26th October, Abuja
 - Epidemiology & surveillance systems
 - Host immune responses and efficacy prediction
 - Lassa vaccine TPP
 - Efficacy objectives, endpoints, study designs, statistical considerations
 - Ensuring equitable access to vaccines
- Collaboration and coordinated dialogue among stakeholders including clinical trial sites, National stakeholders, Africa CDC, WHO, vaccine developers, CEPI etc.

To multiply the impact of the *Enable* programme and support Lassa research, the following questions were discussed in the last session of the workshop:

- *How can you leverage the experience from the Enable programme to improve the LF and pandemic surveillance systems in your country?*
- *How can the Enable consortium become an advocate for improved pandemic preparedness and response in West Africa?*
- *How should CEPI support initiatives to maximize Enable’s impact to this end?*

The meeting ended with the following observations/acknowledgements by **Gabrielle Breugelmans** (CEPI):

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1. In many sites, this was the first study of such a magnitude. Therefore, it was important to identify good leaders (PIs), to set-up a good project management system, and to recruit qualified staff. Furthermore, roadmaps are available for clinical trials but not for observational prospective studies. Here, we did not have the luxury of randomisation, so we had to be more cautious to avoid biases.
 2. Community engagement is a continuous process. During this *Enable* programme, we were confronted with many challenges that needed solutions. We noted a tangible progress since the start, but we will need to continue till the end of the programme.
 3. I am very pleased with the observed engagement, enthusiasm, and commitment during the last 3 days. I would like to acknowledge the challenges due to the covid pandemic but there are still challenges ahead, though less important than previous ones.
 4. Many thanks to IT technical staff, kitchen staff, translators, and the organizing committee (NCDC, CEPI, PHQ).
 5. Next steps: looking forward to input from all in the meeting report and call for action.

Annex: Workshop presentations

Workshop presentations are linked throughout this report as separate files. Please contact epidemiology@cepi.net if you encounter difficulties accessing the linked presentations.