Challenges in establishing Vaccine trial capacity in Antananarivo: example from the MTBVAC Trial

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Background

While more than 95% of tuberculosis (TB) deaths occurred in low- and middle-income countries (LMICs), randomized controlled trials (RCT) conducted in these countries make up just 32% of all RCTs registered with the WHO. The need for also executing clinical trials in LMICs has led to the creation of the MTBVAC consortium and the initiation of TB vaccine trial preparedness in Madagascar and Senegal, two LMICs with high TB incidence, in addition to South Africa. Conducting trials in LMICs can be challenging due to barriers in local research infrastructure and governance issues. The aim of this study was to identify and mitigate these barriers during a comprehensive capacity building initiative set to prepare for the MTBVAC Vaccine Trial in Madagascar.

Methods

-Capacity Building in Madagascar consisted in human resources trainings and infrastructure upgrades for the biological analyzes and the clinical trial site location to acquire the ability to conduct the TB-RCT

-To validate the capacity-building effectiveness, criteria including lab competencies/proficiencies evaluations, GCP-GCLP certificates and site activation process were set.

-Barriers and challenges were recorded from participants questionnaires and from regular M&E and local stakeholders meetings

Capacity building

- Quality assurance, equipment maintenance
- Staff training and education
- Logistical and infrastructures
- Management of Essential Documents and Source Document (SOP, Log, Form, Document)
- Improving ethics and pharmacovigilance skills

Capacity Building activities and challenges

Period/Timeline	Activities	Challenges	Lessons learned
CB-1: Technology Transfer for Detection of whole blood T cell responses directed against vaccine antigens			
2018-2020	Trainings: Two Malagasy lab staff trained in South Africa (SATVI)	> Language barriers (English-French) > Frequent local staff turnover	Local Staff initiation to basic scientific english skills
	Technology Transfer: On-site training experiments	> Frequent power outages > Import/export permits delays > Procurement delays > Limited options for equipement maintenance	UPS and cooling systems installation Early identification of materials needed Early logistical planning and prospection for lab equipement maintenance
	Validation: Local operators at the site able to perform all the procedures from adult Healthy samples (n=20 volunteers)	> Local staff turnover	Developed comprehensive training programs for local staff Experiments simulations provide valuable insights
CB-2: Site Preparation through Childhood TB Infection Epidemiology Studies			
2019-2022	Perform a cross–sectional childhood TB prevalence survey of M. tuberculosis infection (n=500 infants)	> Lack of standardized SOPs between sites	Early and continuous communication with regulatory bodies Building trust with local authorities
	Database management and epidemiology analysis	> Limited bio-statistical skills capacities	Additional capacities to provide for bio-statistical analyses skills
Vaccine Trial Initiation: MTBVAC Phase 2a on Newborns			
2022 - To Present	Safety and Immunogenicity of MTBVAC administered in healthy HIV unexposed uninfected a newborns (n=60 newborns)	> Frequent power outages affecting vaccine storage on site > Short vaccines and reagents lifetime > Trial participants follow-up and access delayed by weather conditions	Stronger UPS system installation Earliest logistical planning as possible

Table 1 Activities, Challenges, and lessons learned in establishing the MTBVAC trial in Antananarivo, Madagascar

Conclusion

In conclusion, a comprehensive capacity-building program was designed and developed in Madagascar to develop infrastructure, provide resources, transfer knowledge, foster capabilities and creates networks of skilled researchers and ensure optimal conditions for conducting vaccine trial. Despite major challenges, Madagascar site was activated for a Phase2b of the MTBVAC vaccine trial in 2023. The need for greater diversity in clinical trials and a growing understanding that there is a large TB incidence in LMICs are driving interest in conducting trials in these traditionally overlooked locations.

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