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Key success factors in clinical trial operation of the smallpox vaccine LC16m8 against mpox in Colombia

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Abstract: In 2023, the Japan Institute for Health Security (JIHS) and the Universidad Nacional de Colombia (UNAL) conducted a successful clinical trial of the LC16m8 mpox vaccine in Colombia. The joint Japan-Colombia research team categorized the trial's challenges and success factors into several key operational aspects for analysis. Key success factors were an established database of Colombian human immunodeficiency virus (HIV) patient and pre-exposure prophylaxis (PrEP) population registries, and strong experience with large-scale clinical trials of HIV and COVID-19. In addition, a strong network of infectious disease specialists in Colombia enabled close communication between the study site directors and the research team. This allowed for rapid staffing and training, which was consistent with the study schedule. The outcome of this research identifies key success factors for the immediate implementation of large-scale clinical trials and will contribute to preparedness for future pandemics.

***Keywords*:** pandemic, preparedness, HIV, PrEP

Introduction

Intermittent outbreaks of infectious diseases highlight the need for rapid responses. Following the COVID-19 pandemic, the World Health Organization (WHO) declared mpox (formerly known as monkeypox) a public health emergency of international concern (PHEIC) in July 2022 (*1*), with another declaration in August 2024 (*2*), signaling the risk of recurring pandemics. Furthermore, international organizations have promoted "100 Days Missions" to accelerate vaccine and therapeutic development (*3*). In the U.S., Operation Warp Speed was activated and vaccine development took place at a remarkable pace, but numerous challenges still remain to be overcome to achieve the 100 Days Mission (*4-6*).

Under these circumstances, in 2023, the Japan Institute for Health Security (JIHS) in Japan and the Universidad Nacional de Colombia (UNAL) in Colombia conducted a clinical trial in Colombia to evaluate the LC16m8 mpox vaccine against mpox. Despite challenges such as vaccine expiration, budget constraints, and regulatory hurdles, the Colombian research team successfully completed the trial. That is, we were able to initiate the study under all the restrictions, enrolled more than 500 cases in less than 2 months, and conducted the observations as planned. In the preparation of the study, we could save considerable time in several processes as we described in the following sections.

Given the likelihood of future pandemics requiring rapid, large-scale international clinical trials, this correspondence focuses on operational lessons from our study and identifies key success factors to inform future preparedness. Detailed vaccine background and trial design are beyond our scope and will be presented in other protocol and results publications.

The challenges of the clinical trial

The research team from both countries categorized the challenges of the clinical trials into the following categories: *i*) regulatory aspects (Institutional Review Board (IRB)/regulatory authority), *ii*) administrative aspects (contracts), *iii*) technical aspects (electronic data capture (EDC)/electronic patient-reported outcomes (ePRO)), *iv*) training, *v*) subject recruitment, and *vi*) personnel (Table 1).

i) Regulatory aspects (IRB/regulatory authority)

Long time for approval by the regulatory authority

Conducting a clinical trial in Colombia requires ethics committee approval and regulatory authority permission, but the strict review process often leads to delays. Recognizing the mpox vaccine's public health importance, the Colombian Ministry of Health (MOH) prioritized the trial under a Japan-Colombia cooperation agreement. The MOH and research team emphasized the study's significance through multiple meetings with regulatory agencies, successfully reducing the regulatory review time. Usually, it takes 6 months to 1 year or more, but through the team's efforts with direct negotiations, we were able to shorten the time to 2 months.

Additional GMP documentation required for extended vaccine expiration

Since the expiration date of the vaccine had been extended from 4 to 10 years, documentation was requested by the Colombian regulatory authorities regarding stability testing of the vaccine against light, temperature, and humidity. Most required documents showing the vaccine stability were already available, but a Good Manufacturing Practice (GMP) certificate was also required. The MOH, Labor and Welfare (MHLW), and vaccine manufacturing companies, the Japanese research team, successfully cooperated to obtain it.

ii) Administrative aspects (contracts)

Short time to make alliances with research sites

Colombia has a strong network of infectious disease specialists, enabling close communication between study site directors and the research team. This facilitated rapid recruitment and training of personnel, ensuring the study timeline. The clinical research centers involved have extensive experience with HIV and pre-exposure prophylaxis (PrEP) populations, and their directors are highly experienced in clinical research. Two centers had also conducted major public health studies on COVID-19, allowing for swift collaboration. Additionally, all principal investigators are members of the Colombian Association of Infectious Diseases (ACIN), which plays a key role in academic events and clinical guidelines for infectious diseases. Normally, in an area where we had no experience or relationships at all, it would have taken us a year or more to gain the understanding of the institution, build relationships, and sign a contract. Thanks to our experience and relationships in the research field, we were able to shorten that period to 2 months.

iii) Technical aspects (EDC/ePRO)

Short period of time to develop the data management system

The Colombian research team selected research electronic data capture (REDCap), a secure and user-friendly electronic data capture (EDC) system, for clinical data management, ensuring privacy and confidentiality standards. For electronic patient-reported outcomes (ePRO), the team developed a cross-platform mobile application using Flutter, integrated with REDCap *via* an application programming interface (API). The app also supports photo uploads for enhanced data entry. Normally, it would take at least 6 months to a year to develop an app that can be used with Apple and Android and allows photo storage and an API to work with REDCap, but with the help of our talented engineers and team, we were able to complete this in just 3 months. These integrated systems were developed efficiently, prioritizing usability and privacy.

In-depth training for medical staff at facilities with no EDC experience

A training program was introduced for vaccination-specialist nurses unfamiliar with EDC systems, focusing on accurate data entry. It included regular evaluations, real-time support from a physician, frequent simulations, and instructional videos. The application development team and EDC focal point also provided support during participant visits.

iv) Training

New vaccination method

As multiple puncture vaccinations with bifurcated needles are not common in Colombia, the Japanese research team collaborated to provide the training videos (*https://youtu.be/0Y1F9-E7zks?if=76MZFcr7TzKWSI5o*) and had the vaccinators replicate the procedures demonstrated in the video.

Accelerated training period

We implemented several strategies to rapidly train staff and equip them with the necessary knowledge. Those materials were developed for the investigators, research center coordinators and tech professionals, such as protocol training video (*https://1drv.ms/v/s!AolrGsZiZ0cdhKs1LgMm2SFIrNXwNA?e=5cxbAU*), case report form (CRF) training video (*https://drive.google.com/drive/folders/1n2dN7t1C64ZoCZBDZER1VIaGNJbR3Wx-?usp=sharing*), adverse events video (*https://1drv.ms/v/s!AolrGsZiZ0cdhKs0GmVYc4Ulv8hiUg?e=Ffhdwf*), and also provided the staff with pocket guidelines (*https://1drv.ms/b/s!AolrGsZiZ0cdhK0XSr93wCvK9m34Cg?e=dFgSfg, https://1drv.ms/b/s!AolrGsZiZ0cdhK0YCflQhXc3q4-GYQ?e=AxN0bc*).

Staff lacking experience with diverse populations

The Colombian team observed that some staff members had limited experience working with diverse populations. To address this, they developed diversity guidelines (*https://onedrive.live.com/?authkey=%21ACbLxVnWPgHnU1w&id=1D476762C61A6B89%2171321&cid=1D476762C61A6B89&parId=root&parQt=sharedby*

Table 1. Summary of the key success factors

Category	Challenge	Solution
i) Regulatory aspects (IRB/regulatory authority)	• Long times for approval by the regulatory authority	Conducting a clinical trial in Colombia requires ethics and regulatory approvals, but through direct negotiations and the prioritization of the mpox vaccine under a Japan-Colombia cooperation agreement, the review process was shortened from 6 months to 2 months.
	• Additional GMP documentation required for extended vaccine expiration	The Colombian regulatory authorities requested stability testing documentation for the vaccine, and with successful cooperation between the MOH, MHLW, vaccine manufacturers, and the Japanese research team, a GMP certificate was obtained.
ii) Administrative aspects (Contracts)	• Short time to make alliances w ith research sites	Colombia's strong network of infectious disease specialists and experienced clinical research centers enabled rapid collaboration, recruitment, and contracting — reducing a process that normally takes over a year to just 2 months.
iii) Technical aspects (EDC/ePRO)	• Short period of time to develop the data management system	The Colombian research team efficiently developed an integrated clinical data system using REDCap and a custom cross-platform mobile app with photo upload and API functionality, completing in 3 months what typically takes 6–12 months, while ensuring usability and privacy.
	• In-depth training for medical staff at facilities with no EDC experience	A comprehensive training program was implemented for vaccination-specialist nurses unfamiliar with EDC systems, combining evaluations, simulations, real-time support, and instructional materials to ensure accurate data entry and smooth participant visits.
iv) Training	• New vaccination method	Due to the rarity of multiple puncture vaccination with a bifurcated needle in Colombia, the Japanese research team provided training videos and had vaccinators practice the demonstrated procedures.
	• Accelerated training period	To rapidly train staff, we developed and provided targeted educational materials — including training videos on the protocol, case report forms, and adverse events, as well as pocket guidelines—for investigators, coordinators, and technical professionals.
	• Staff lacking experience with diverse populations	To address limited experience with diverse populations, the Colombian team developed diversity guidelines with visual aids, conducted workshops to enhance understanding of gender diversity, and provided a participant invitation script, ensuring respectful and inclusive trial engagement.
v) Subject recruitment	• Selection of Medical Centers for HIV Patient Recruitment	The participating medical centers were selected for their specialized HIV and PrEP programs and used Colombia's existing HIV patient database to optimize recruitment.
	• Managing Holiday-Related Challenges in a Clinical Trial	A major challenge in the clinical trial was participants traveling to warm regions with swimming pools, which contradicted the vaccination instructions to keep the arm dry for 14 days; the team addressed this by emphasizing vaccination benefits, offering alternatives, and rescheduling vaccinations as needed.
	• Stigma surrounding mpox	To reduce mpox-related stigma, particularly toward LGBTIQA+ individuals, we implemented confidentiality protocols, held focus groups with community leaders supported by PAHO/WHO, and strategically located vaccination centers in private settings to ensure a safe, inclusive, and nonjudgmental environment for all participants.
	• Strengthening Community Partnerships: Collaboration with REDSOMOS	A cooperation agreement with REDSOMOS, a community-based organization promoting sexual and gender diversity, was established to enhance outreach to the LGBTIQA+ community, ensuring confidentiality and strengthening trust and inclusivity within the project.
vi) Personnel	• Maintaining staff motivation during schedule delays	To maintain staff motivation during the study's delay, the team used the extra time for skill enhancement, process refinement, and participant education, while participating centers provided financial support by temporarily covering salaries until reimbursements were processed.

&o=OneUp) featuring a mascot illustration explaining the distinctions between sex, gender, gender identity, sexual orientation, *etc*. Through dedicated guidance and workshops, staff gained a deeper understanding of gender diversity, enabling the trial to proceed smoothly with fair and respectful engagement of all participants. Furthermore, the Colombian team provided the team with a script to use when inviting people to participate.

v) Subject recruitment

Selection of Medical Centers for HIV Patient Recruitment
The participating medical centers were selected based on the target population. All three centers, which are *Clínica Universitaria Colombia*, *Infectoclinicos*, and *Hospital Universitario San Ignacio*, have specialized programs for HIV patient care and PrEP. These sites leveraged Colombia's existing HIV patient database to optimize recruitment.

Managing Holiday-Related Challenges in a Clinical Trial
One of the biggest challenges in the clinical trial was the common practice of traveling to warm regions with swimming pools and the sea, as wetting the vaccinated arm was contraindicated for the first 14 days. Being in a tropical country without distinct seasons, such trips are frequent, especially during holidays, because Bogotá is located 2,600 meters above sea level. To address this, the team emphasized the benefits of vaccination, provided alternatives like keeping the vaccinated arm dry while swimming, and highlighted the increased infection risk during holidays (Figure 1). When necessary, vaccinations were rescheduled to accommodate participants' travel plans.

Stigma surrounding mpox
To address the stigma surrounding mpox, particularly the misconception that the infection exclusively affects lesbian, gay, bisexual, transgender, intersex, queer, asexual and other sexually or gender diverse (LGBTIQA+) individuals, we took measures to minimize the risk of stigmatization. It should be noted that a focus group was previously carried out with the leaders of the LGBTIQA+ population with the support of Pan American Health Organization (PAHO)/WHO

Figure 1. Invitation infographics for candidates for the clinical trial.

to understand their feelings and perceptions regarding the possibility of vaccination against mpox. Vaccination centers were strategically placed in private locations to ensure participants could access the study without fear of judgment or discrimination. Additionally, strict confidentiality protocols were implemented to protect the privacy of all participants throughout the process. These measures were essential in fostering a safe and inclusive environment for the study.

Strengthening Community Partnerships: Collaboration with REDSOMOS

A cooperation agreement was established with REDSOMOS, a community-based organization promoting sexual and gender diversity, sexual health, and community empowerment since 2007 (*https://www.redsomos.org/*). Given that the study centers already had experience managing participants with HIV and had prior conversations with REDSOMOS, the partnership was strengthened to ensure effective outreach to the LGTBIQA+ community. Furthermore, a legal agreement was established to guarantee the confidentiality of all sensitive data, preventing any risk of information leaks. This collaboration improved the project's visibility and reinforced trust and inclusivity within the targeted population.

vi) Personnel

Maintaining staff motivation during schedule delays

To maintain staff motivation during the study's delay, we reframed it as an opportunity for further preparation. The extra time was used to enhance team skills, refine the vaccination process, practice inclusive language, and improve participant education on mpox infection. This proactive approach kept staff engaged and better prepared for the study's launch.

Conclusion and suggestions

In 2023, JIHS and UNAL conducted a successful clinical trial of LC16m8 mpox vaccine against mpox in Colombia. Key success factors identified from this trial include having an established HIV patient/PrEP registry and extensive prior experience with large-scale clinical trials (*e.g.*, in HIV or COVID-19). Additionally, Colombia's strong network of infectious disease specialists enabled close communication between sites and researchers, allowing for rapid staff recruitment and training in line with the study schedule. Importantly, establishing such disease-specific participant databases and cultivating trial experience ahead of time are critical steps for any country to prepare for future pandemics.

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