SABIN
VACCINE INSTITUTE

Clinical Partnership Framework

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Sabin's Mission and Role in Powering Research & Development

The Sabin Vaccine Institute's (Sabin) mission is to make vaccines more accessible, enable innovation, and expand immunization across the globe. We accomplish this mission through our Research & Development (R&D) and Global Immunization programs, which center on vaccine preventable diseases that disproportionally affect people in low and middle-income countries (LMICs).

Sabin's R&D program focuses on advancing vaccines for diseases that are often overlooked by traditional vaccine developers with a goal of licensure to ensure all people - everywhere - have access to safe and effective vaccines. Central to this focus is engaging in clinical research to generate data to support licensure and World Health Organization (WHO) prequalification. As a public health organization with strong ties across the globe and access to a broad range of expertise and resources, Sabin is uniquely positioned to drive this clinical research to support vaccine development and licensure.

R&D Partnership Philosophy

Sabin engages in clinical research through partnerships. In some of these, Sabin may act as the clinical trial sponsor and/or investigational vaccine developer. Sabin partners with organizations that support our mission and provide complementary and synergistic expertise in vaccine development and licensure. It is essential that these organizations demonstrate a commitment to global health needs and transparency, including commitments to data sharing, working to meet regulatory requirements, and funding projects with a focus on supporting LMICs. Sabin's goal is to enter partnerships that provide broader, timely access to data to improve decision-making in global vaccine development and licensing/pre-qualification strategies and ultimately drive better outcomes for the populations we seek to serve.

The core values of our partnership philosophy are:

1. Equity and respect for the unique strengths that each partner organization brings to the table.
2. Commitment to a shared vision of equitable access, including support for licensure of vaccines.
3. Trust, inclusiveness and transparency through sharing data/information, maintaining clear lines of communication, and discussing challenging issues.

To articulate our clinical research partnership philosophy, we created this **Sabin Clinical Partnership Framework**, which is designed to provide transparency and guidance as we work together to advance vaccine candidates through the clinical development and regulatory processes with the goals of licensure and WHO prequalification.

Clinical Partnership Framework

The sections below provide an overview of Sabin's expectations for clinical trial partnerships, outlining baseline assumptions, defining roles, and setting ground rules for clinical trial efforts. While these sections are intended to give insight into our preferences, Sabin recognizes that this structure may not be feasible in all situations and may need to be tailored to the unique circumstances of each trial.

Definitions & Assumptions

For purposes of this Framework, we use the WHO definition of a clinical trial: "Any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes."

In this Framework:

- "Sponsor" refers to the clinical trial sponsor and any agents the Sponsor engages to execute the clinical trial (e.g., a contract research organization, consultants, etc).
- "Developer" refers to the investigational vaccine developer and any agents the Developer engages to manufacture, test and store the investigational vaccine prior to delivery to the Sponsor. More than one Developer may participate in a trial partnership but is referred to in the singular throughout this document.
- "Partners" include the Sponsor and the Developer(s).

Sabin expects the Partners to adhere to the following principles:

- Clinical trial protocols must be designed, implemented, and reported in accordance with the ICH (International Council for Harmonization) Harmonized Tripartite Guidelines for Good Clinical Practice, with applicable local regulations including European Directive 2001/20/EC and US Code of Federal Regulations Title 21, and with the ethical principles laid down in the Declaration of Helsinki (European Council 2001, US Code of Federal Regulations, ICH 1997)
- Scientific data management and stewardship are guided by the FAIR Guiding Principles (Findability, Accessibility, Interoperability, and Reuse of digital assets.)

Furthermore, Sabin expects the Partners to:

- Establish and implement clear, timely processes for safety data communication and reporting. The Developer's full access to all safety data generated from clinical trials must be guaranteed to ensure compliance with their responsibility as manufacturer.
- Provide transparent communications regarding regulatory processes prior to, during, and after the trial.
- Share regulatory feedback, including Institutional Review Board (IRB or equivalent) comments, openly and in a timely manner.
- Make Standard Operating Procedures (SOPs) available for review, upon request.
- Align on key clinical and data components including clinical design and testing (i.e., collection of clinical samples and assays to measure immune responses to the vaccine) prior to protocol submission.

- Align on data analysis plan, ideally prior to the protocol submission but if not, then within 30 days.
- Review and agree to any external communication regarding the trial and its results prior to distribution or public comment.
- Meet their individual regulatory obligations to support trial approval, trial conduct, licensure, and WHO prequalification as applicable.
- Provide relevant information to the other parties upon request to support regulatory activities.
- Take all actions in a timely manner as defined by the Clinical Trial Steering Committee.
- Maintain and share with the Partners evidence of adequate insurance coverage appropriate to the risks of the specific trial and in compliance with any statutory requirements in the location where the trial is conducted.

Sabin understands that each Partner may withdraw from the trial if one of the other Partners is unable to adhere to this Framework prior to dosing of the first clinical trial participant.

Trial Protocol Development & Amendments

Sabin expects the Sponsor to be responsible for:

- Drafting the protocol and subsequent amendments.
- Providing the draft protocol to the Developer for review and incorporating Developer's requested edits.
- After the Developer comments are incorporated, providing the updated draft protocol to the Clinical Trial Advisory Committee for review and incorporating the Committee's requested edits as appropriate.
- Incorporating feedback from the IRB (or equivalent) and regulators and updating the protocol accordingly.
- Sharing final copies of the protocol and all substantive amendments with the Developer prior to submission.

Sabin expects the Developer to be responsible for:

- Providing comments and feedback on the protocol (draft and final) and amendments (draft and final) in a timely manner.

The Sponsor and Developer agree to the protocol and amendments prior to any submission to IRBs (or equivalent), national or regional (i.e., European Medicines Agency, African Medicines Agency) regulatory authorities, international organizations (i.e., the World Health Organization) and potential and current funders.

Trial Registration & Approval

Sabin expects the Sponsor to be responsible for:

- Completing all applicable trial registrations following all required conventions for creating the trial documentation.

- Updating all regulatory registrations and/or filings in accordance with the specific regulatory authorities and, if registered with the U.S. Food and Drug Administration (FDA), completing and filing the Annual Report.
- Obtaining all required regulatory approvals for the conduct of the trial, including approval from relevant IRBs.

Sabin expects the Developer to be responsible for:

- Providing all necessary information, reviews, and approvals to support trial registration and approvals in a timely manner.

Investigational Product & Trial Material Handling

Sabin expects the Developer to be responsible for:

- Providing the Sponsor with manufacturing information to complete the pharmacy manual.
- Completing the investigational vaccine manufacturing dossier (IMPD).
- Labeling the investigational vaccine and developing the package insert.
- Obtaining export/import permits as required.
- Shipping the investigational vaccine to the clinical trial sites.

Sabin expects the Sponsor to be responsible for providing the Developer with full visibility, including documentation as requested, through the course of the clinical trial, including, but not limited to:

- Investigational vaccine information and documentation, including but not limited to use, location, storage temperature & monitoring, freezer preventative maintenance records, reconciliation records, and backup power system.
- Temperature monitoring records throughout the chain of custody, including for any movement of the investigational vaccine; access to shipment approval forms and supporting documentation.
- SOPs/manuals/forms for Investigational Product prep, use and handling.
- Open communication lines with clinical site operational staff, clinical study quality assurance staff, and partnership stakeholders.

Clinical Data Management (CDM)

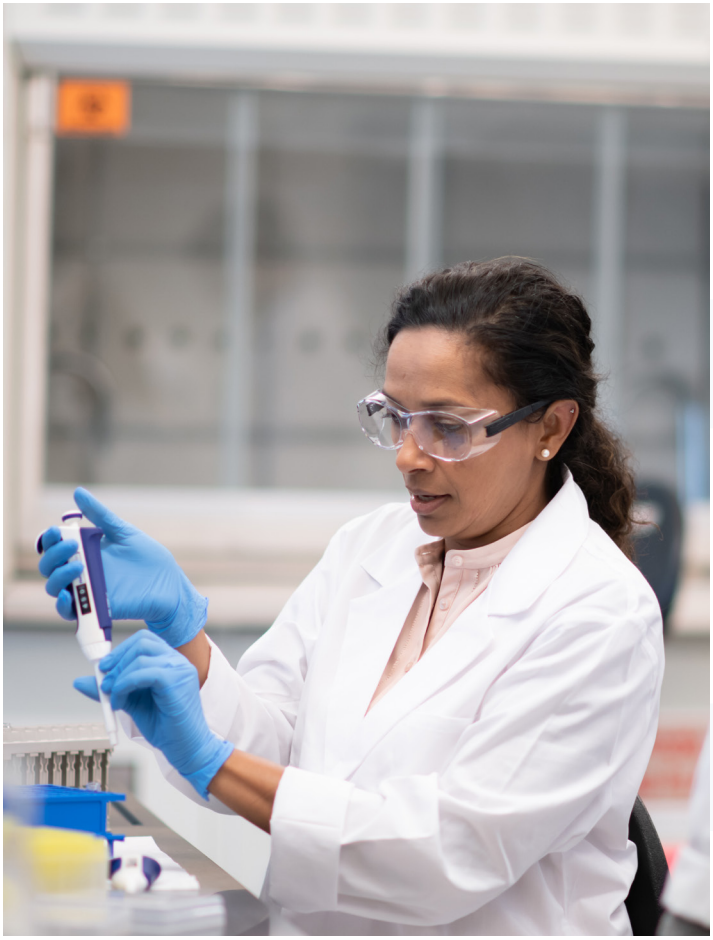
Sabin expects the Sponsor to follow current CDM practices in accordance with Good Clinical Practices (GCP) to ensure collection of high-quality, accurate, complete, and consistent statistically sound data. This includes but is not limited to Case Report Form design and annotation, database design, data entry and validation, discrepancy management, medical coding, data extraction, and database locking.

Data Management, Sharing & Access Rights

Sabin expects the Sponsor, in consultation with the Developer, to create a data management plan based on the FAIR Guiding Principles that is updated during the trial as needed. This plan includes the following elements:

- Establishment of a Data Access Committee that will be responsible for reviewing and assessing data access requests.
- Prior to the start of the trial, the Partners will agree to fixed timelines for access to study outcomes, including but not limited to final study reports, raw datasets, trial database, regulatory actions, and regulatory communications of any nature.

Sabin expects the Sponsor to provide the Developer with license-free data access rights.



Publications

Any Partner intending to publish data collected from the trial or any other trial information is responsible for notifying the other Partners and extending the best effort to obtain their approval prior to submitting for publication.

Regulatory Support After Trial Closes

Sabin expects the Partners to provide continued support for the regulatory filings of the Sponsor and/or the Developer to advance the vaccine towards licensure after trial closeout. Such support may include responding to regulatory inquiries and/or providing documentation including, but not limited to original data and clinical records as requested by the Sponsor, the Developer or a regulatory authority.

Governance Structure

To provide strategic guidance and oversight of the trial, Sabin expects the Sponsor to establish and administer a Clinical Trial Advisory Committee (Advisory Committee) and a Clinical Trial Executive Committee (Executive Committee).

Sabin expects the members of both the Advisory Committee and the Executive Committee to work in a timely manner to reduce impacts to the trial schedule and recognize that specific public health circumstances may require increased urgency with no delay in convening and decision-making.

The role of the Advisory Committee is to provide expert advice to improve trial outcomes and mitigate risks. The Advisory Committee includes technical representatives of the Partners, funders and recognized experts in respective fields as agreed by the Partners. The Advisory Committee provides advice and can raise concerns related to safety, study integrity, and regulatory matters to the Executive Committee.

The role of the Executive Committee is to discuss issues related to the execution of the trial and to work towards consensus. The Executive Committee includes one executive-level representative from each Partner. The Executive Committee is responsible for considering the advice from the Advisory Committee and discussing issues raised by the Advisory Committee with the goal of reaching consensus on the path forward. Members of the Executive Committee may also raise concerns for discussion outside of those referred by the Advisory Committee. If the Executive Committee is unable to reach consensus, the Sponsor makes the final decision.

Responsibilities of the Clinical Trial Advisory Committee to Include:

1. Develop and approve the Committee charter which remains operative until the end of the trial and includes agreed upon timelines for receipt and review of all documents and data required for successful completion of the trial.
2. Convene on a regular basis and document discussions and decisions made. The Advisory Committee also convenes on an emergency basis as requested by the Partners.
3. Following approval by the Partners, the Committee reviews the protocol, substantial amendments, sample assay plan, data management plan, and statistical analysis plan and provides feedback in a timely manner.
4. Establish and implement safety data communication procedures.
5. Review and discuss all study results, including interim analysis results if any; and review and provide timely feedback on any external communication regarding the results prior to distribution or public comment.
6. Review and discuss all Clinical Study Reports and provide feedback in a timely manner.
7. Review and agree upon all manuscripts prior to submission for publication.

Responsibilities of the Clinical Trial Executive Committee to Include:

1. Consider advice from the Advisory Committee and work to reach consensus on incorporating Advisory Committee advice, if warranted.
2. Consider issues raised by the Advisory Committee and work to reach consensus on resolution.
3. Prior to protocol submission, agree on a schedule for regular trial update meetings.

Responsibilities of the Sponsor to Include:

1. Establish and administer the Advisory Committee and Executive Committee, including coordinating membership and managing meetings.
2. Host regularly scheduled trial update meetings with the Executive Committee to provide clear updates on trial progress.
3. Act as the ultimate authority if the Executive Committee consensus cannot be reached on an issue.