**PROTOCOL REVIEW COMPANION**

**Protocol Description and Background**

1. Does the protocol provide the purpose, relevance, and scientific justification for the current study?

2. What are the specific data the researchers plan to collect, and have they explained how these data and the participants selected will help to answer the research question(s)?

3. Does the protocol provide enough background information or details from past trials to support this study?

4. Based on the answers above, are the researchers in true equipoise about conducting the study?

5. Are there enough resources available for the completion of the trial?

6. What is the study design (e.g., quantitative, qualitative, mixed methods, quasi-experimental, randomized controlled)?

7. What are the primary and secondary endpoints or objectives of the trial and do these adequately represent the potential clinical benefit (e.g., efficacy and safety) of the prevention, diagnostic, or treatment intervention under study? Will data be collected according to a timeframe that best supports determination of whether these endpoints or objectives have been reached? Are there any endpoints or objectives of interest to affected communities that are not captured in the study design (e.g., acceptability, tolerability, feasibility, improvements to quality of life)?

8. Will the study have a control group (a group of people who will not be receiving the intervention being studied, for a basis of comparison)? Have the principal investigators explained the procedures and purpose of using a control group?

9. If the control group is made up of participants with a disease or condition, will they be receiving, at minimum, the standard of care they would be receiving from their health providers if they were not part of the study?

10. What is the comparator treatment or regimen against which the investigational treatment(s) or regimen(s) will be compared? For TB prevention or vaccines studies, is there a standard of prevention against which the investigational preventive therapy or vaccine will be compared? For TB diagnostics studies, what is the reference standard that will be used to evaluate test performance? Are these the best choices to demonstrate performance, considering the participant populations and use case?

**Locations Where Research Will Be Performed**

1. Do study sites include countries or regions where the disease is prevalent or has a high health, economic, or societal impact? (Note: many regulatory authorities require that drugs, drug regimens, vaccines, and diagnostics be tested in their countries before approval.)

2. Will the investigational products (drugs, diagnostics, vaccines, etc.) be made available in these countries after the trial ends? How will access to the investigational products be made available and continue after the trial (e.g., pre-approval access, post-trial access, operational research)?

**Requirements of Study Participants**

1. How many participants will be enrolled in the study and do the investigators provide an explanation of how they determined the number of participants? (Note: this is important to ensure that the results are not misinterpreted, that the studies are large enough to generate statistically valid results, and that the results will be generalizable to the larger patient population outside the trial.)

2. What activities are the participants expected to engage in by participating (e.g., surveys, focus groups, interviews, diagnostic procedures, blood draws, medication adherence requirements)?

3. What is the duration of the activity, the number of times the activity will occur, and the total time period of active participation per participant (e.g., days, weeks, months, years)?

4. How long will researchers follow participants and is the follow-up period well justified? Is this information clearly described in the consent forms and supporting materials?

5. Where will data collection take place (e.g., waiting room, exam room, research office, other location)?

6. Will participants be compensated for their participation through financial or other forms of support? (Note: common forms of payment include reimbursement for transportation to and from the research site, compensation for time off from work, or a small incentive awarded for participation or completion of all study visits.)

7. If participants will be receiving compensation after their participation in the trial ends, how will research staff link their names/contact information confidentially to their compensation?

8. Will the study collect any private or sensitive information from participants? How will this information be protected and where will it be stored? Is this information discussed and explained in consent forms?

9. Does the study use interpreters, and if so, what are the procedures for recruiting interpreters and ensuring their cultural competence (awareness of and ability to understand and appropriately respond to cultural differences when providing care to patients with diverse values, beliefs, behaviors, and needs)? Will study materials be translated into local languages?

**Description of Research Risks and Benefits**

1. What are the risks, if any (physical, psychological, social, legal, or other), to the participants and their families or other close contacts?

2. What is the likelihood of these risks occurring, and/or how serious are they?

3. How have the investigators worked to minimize these risks, and are these risks made clear in informed consent materials?

4. Is there a compensation plan for unanticipated severe risks or adverse events resulting from the intervention under study (e.g., clinical trials insurance)?

5. Are the study approaches adequate to maximize safety and minimize potential adverse events?

6. How will potential drug-drug interactions (especially for people living with HIV on antiretroviral therapy, people taking hormone-based therapies, and people taking opioid substitution therapies) be prevented, monitored, or mitigated if they occur?

7. In diagnostic, TB preventive treatment, and vaccine studies where a proportion of participants are expected to develop active disease during the study, how will the investigators ensure participants receive the best quality of care?

8. Are the study procedures and follow-up schedule designed to maximize the health and well-being of the participants during the study and after study completion, especially in studies where participants may develop active disease or be at risk of relapse?

9. Where the study intervention may result in health risks for pregnant people or fetuses, does the study provide adequate options for contraception and birth control and promote gender parity in preventing health risks related to pregnancy?

10. Does the study protocol articulate processes for ensuring that a distressed participant gets the help they need? If a participant experiences negative physical or psychological effects, are there referral procedures in place to ensure that the participant is linked to appropriate psychological and/or physical treatment or assistance?

11. What are the potential benefits to the participants of this study (e.g., access to nutritional support, drugs, diagnostics, evaluations, screening, counseling, medical referrals, training, additional screening, and monitoring at no cost to the participants)?

**Eligibility Criteria**

1. Does the study include vulnerable populations?

2. Does the study exclude any classes of participants (e.g., by gender, class, race, age)?

3. Does the study use inclusive language that recognizes transgender and non-binary people?

4. Does the study leave out important groups of people affected by the disease (e.g., adolescents and children, women, pregnant or lactating people, people living with HIV, people living with HIV on antiretroviral therapy, people with other comorbidities such as diabetes, incarcerated populations, sex workers, people who use drugs, people who use alcohol)?

5. If the study purposely excludes any class of participants or important groups of people affected by the disease, do the investigators present an adequate justification for this exclusion?

6. Are any classes of participants excluded from early-stage (phases I and II / analytical validation) versus late-stage (phase III / clinical performance verification and demonstration) trials? If certain populations are excluded, are there plans to include them in later stages of research?

7. Are the populations that are either included in or excluded from the trial represented in community advisory structures, like a CAB? (Note: particularly for those who are excluded, this can help them advocate for inclusion either in the current trial or in future trials of the same drug or other intervention.)

**Description of Recruitment and Procedures**

1. Does the study describe the methods used to recruit participants?

2. How and from where will participants be recruited (e.g., flyers, public announcements, word of mouth, digital recruitment campaigns, clinic-based recruitment, patient advocacy network engagement)?

3. Are there existing, site-specific community engagement structures in place? If not, are there plans to create them? How will these community engagement mechanisms be structured (e.g., site CABs, a consortium-level CAB with site representation, a combination of the two)?

4. Will budget be allocated to support community engagement structures and activities?

5. How will investigators protect the identity and personal information of participants (e.g., codes, pseudonyms, masking of information) during and after clinical trials, including for any biological specimens collected for storage in biorepositories for future evaluation of diagnostics?

**Procedures for Obtaining Free and Informed Consent**

1. What is the procedure for obtaining a participant’s free and informed consent to enter the trial?

2. Is the consent process in a language that likely participants can understand? Are there supporting materials to ensure that people understand the consent process for participation in the trial and, where applicable, for the collection of biological specimens to be stored in biorepositories?

3. Does the consent process give people enough time to read, understand, and ask questions about the trial and to make a choice free of coercion and undue influence?

4. Does the consent process include the names and contact information of the researchers and/or community members in a position to address potential questions about the trial?

5. Are the risks posed to participants by the trial clearly and comprehensively described in the informed consent materials, including potential adverse events resulting from the investigative products under study?

6. Are method of administration, dosing intervals, pill burden, and any adherence requirements clearly explained along with any systems for adherence support during the trial?

7. Does the consent process describe what is offered to people who choose not to participate or who withdraw from the study?

8. Are alternative treatments, procedures, or other interventions described clearly to all participants? (Note: it is important for study participants to be made aware of all their options for receiving care, including those available outside of the trial setting, before consenting to participate.)

9. If the trial intervention offers no direct benefits to participants, has the study protocol stated this in the informed consent form?

10. What communication technologies or platforms will be used to contact the participants and, if applicable, to perform virtual visits?

**Results Dissemination**

1. Does the protocol include a post-trial communication plan that will be informed by community representatives?

2. Does the protocol include draft materials for sharing study results with participants and their communities or outline other means to do so (e.g., a findings letter addressed to individual participants or site-specific dissemination plans)?

3. Are there plans for community groups to review and provide input on results dissemination materials?

4. Before recruitment begins, will the trial be registered in a publicly accessible location, such as clinicaltrials.gov or the World Health Organization’s International Clinical Trials Registry Platform (<https://www.who.int/clinical-trials-registry-platform>)?

5. Does the protocol include any plans for sub-studies or evaluations that will address pragmatic concerns about implementing the intervention in a real-world setting (e.g., qualitative studies of patient experiences, cost comparisons between the intervention and the control, evaluations of adherence strategies, etc.)?

**Financial Conflicts of Interest**

1. Do the investigators have any financial conflicts of interest with any of the research or product sponsor(s)? Does the study have any corporate funding sources?

2. Is the protocol transparent about funding sources? Is the research being conducted in partnership with a privately or publicly funded entity? Where public funding is being leveraged, are there any access conditions or other safeguards in place to promote access to investigational products post-trial? (Note: pricing of new drugs, diagnostics, or vaccines should always be fair and accessible to ensure that all people benefit from scientific progress and its applications, and access conditions or other safeguards should always be in place wherever public funds have been used to help advance the development of these technologies.)

**Ethics Reviews**

1. Will the trial be reviewed by one or more institutional review boards (IRBs), independent ethics committees, or any other applicable regulatory entity? (Note: this should be a basic requirement for all research involving human participants.)

2. If the trial is multinational or multisited, will national or local level IRBs or ethics committees also review the protocol?

**Additional Resources**

Many of the concepts in this document are elaborated in guides that have been developed to help activists and community representatives understand the fundamentals of clinical research. For more information, we recommend consulting:

**Research Fundamentals for Activists**, developed by Consortium to Respond Effectively to the AIDS and TB Epidemic (CREATE) and Treatment Action Group. Available from: <https://www.treatmentactiongroup.org/wp-content/uploads/2013/05/RFA-FINAL.pdf>

**Clinical Trials: A Community Guide to HIV Research**, developed by HIV i-Base. Available from: <https://i-base.info/wp-content/uploads/2015/12/MANUAL-trials-mar09-EN-FINAL-NO-graphic.pdf>

**Good Participatory Practice (GPP) Guidelines**, developed by AIDS Vaccine Advocacy Coalition (AVAC). Available from: <https://www.avac.org/good-participatory-practice>

**Basic Scientific Literacy Training Module**, developed by HIV/AIDS Network Coordination (HANC). Available from: <https://www.hanc.info/resources/training/bsl-training.html>

**How to Critically (and Quickly) Read a Protocol**, developed by HANC. Available from: [https://www.hanc.info/content/dam/hanc/documents/community/How%20to%20Read%20Protocol(short)%20HANC%20-FINAL%208-19-21\_English.pdf](https://www.hanc.info/content/dam/hanc/documents/community/How%20to%20Read%20Protocol%28short%29%20HANC%20-FINAL%208-19-21_English.pdf)

**Recommendations for Community Engagement in HIV/AIDS Research: A Guide for Communities and Researchers**, developed by HANC, Community Partners, and the United States National Institutes of Health (NIH) Division of AIDS (DAIDS). Available from: <https://www.hanc.info/content/dam/hanc/documents/community/Recommendations-for-Community-Engagement-v3.0-Nov2020-English.pdf>

**The Representative Studies Rubric: A Tool to Enhance the Representativeness of Study Populations in Clinical Research**, developed by HANC. Available from: <https://www.hanc.info/content/dam/hanc/resources/RSR-HANC-Website.pdf>

**Bill of Rights and Responsibilities for HIV Research**, developed by HANC. Available from: <https://www.hanc.info/content/dam/hanc/documents/community/Bill-of-Rights-and-Responsibilities-FINAL-10-1-19.docx>

**Glossary of Terms: Community Engagement in TB Research & Development**, developed by Moldova National Association of Tuberculosis Patients (SMIT). Available from: <https://drive.google.com/file/d/1qMsz-ZhQNWcov4ZkY9OVlbEOaxYl8ZaD/view>

**Words Matter: Suggested Language and Usage for Tuberculosis Communications**, developed by Stop TB Partnership. Available from: <https://www.stoptb.org/news/tb-language-guide-20-launched-stop-tb-partnership-board-meeting>