Good participatory practice
guidelines for biomedical HIV prevention trials
second edition, 2010

Draft for Public Comment

UNAIDS
JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS
UNHCR UNICEF WFP UNDP UNFPA
UNODC ILO UNESCO WHO WORLD BANK

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Introduction

Purpose and intended audience of the good participatory practice guidelines

The good participatory practice (GPP) guidelines were created in 2007 to set global standards in stakeholder engagement for biomedical HIV prevention trials. The guidelines were reviewed in 2010 following extensive consultation. This revised version of the GPP guidelines is circulated in draft form for comments to be sent by 31 October 2010 to gpp@unaids.org or avac@avac.org. The GPP guidelines are intended to provide trial funders, sponsors, and implementers with systematic guidance on how to effectively engage with all stakeholders in the design and conduct of biomedical HIV prevention trials.

Stakeholders not directly involved in funding, sponsoring, or implementing the trials may also find the guidelines useful to better understand the goals and mechanisms of stakeholder engagement in biomedical HIV prevention trials and to evaluate engagement efforts by trial funders, sponsors, and implementers.

Trial funders, sponsors, and implementers include investigators, research staff, and all others involved in designing, financing and executing biomedical HIV prevention trials. They can include, governments, government-sponsored networks, nongovernmental organizations, academic institutions, foundations, public–private partnerships, and pharmaceutical or other companies.

Well-conducted biomedical HIV prevention trials are essential to discover additional technologies to reduce new HIV infections worldwide. Good participatory practice during the entire life-cycle of a biomedical HIV prevention trial can enhance both the quality and outcomes of research.[1] Improving the relationships that trial funders, sponsors, and implementers have with other stakeholders through effective engagement helps to reduce unnecessary conflict and ensure that research is meaningful.

Scope of the GPP guidelines

The GPP guidelines provide a framework for development of effective stakeholder engagement programmes. Consideration of specific trial and local contexts will dictate how the guidelines are best implemented.

These guidelines are not intended to provide comprehensive guidance on all aspects of the scientific and ethical conduct of clinical trials. Multiple guidance documents already exist that address overall trial conduct, such as good clinical practice,[2,3] good clinical laboratory practice,[4] the Declaration of Helsinki,[5] the Belmont Report,[6] guidelines of the Council for International Organizations of Medical Sciences (CIOMS),[7] the Nuffield Council guidance on ethics of research related to health care in developing countries[8,9] and the UNAIDS/WHO *Ethical considerations in biomedical HIV prevention trials*.[10]

Development of the GPP guidelines

The GPP guidelines were born out of a recommendation from the UNAIDS Creating Effective Partnerships in Research process in 2005,[11] which was a response to the controversies and debates of pre-exposure prophylaxis (PrEP) trials in Cambodia and Cameroon.[12,13,14] These consultations highlighted the complexities of conducting biomedical HIV prevention trials.

Development of the original 2007 guidelines involved exploration and analysis of different viewpoints and the creation of objective measures of community stakeholder engagement in the design and conduct of biomedical HIV prevention trials for trial funders, sponsors, and implementers. The drafting involved an international working group. Feedback on the draft set of guidelines was provided via interviews, e-mail requests, and listserv postings and from individuals and their organizations representing a diverse range of perspectives, geography, and expertise. People involved included advocates, trial site staff, researchers, clinical trial investigators, community liaison officers, community advisory board members, policymakers, industry representatives, research funders, and sponsors.

The GPP guidelines constitute a living document and are intended to be dynamic and responsive to community and research realities and needs.

Since publication in 2007, the guidelines have been applied in different settings and have been the subject of formal consultations. AVAC supported a process through which stakeholder groups in Africa, the Americas, Asia, and Europe critiqued and gave feedback on the guidelines. A participatory approach was used to design the consultations, which included focus group discussions, interviews, surveys, workshops, and consultative meetings. The global consultations validated the need for a guidance document on standards of stakeholder engagement and the importance of their adoption by trial sponsors and their implementation at trial sites around the world. Recommendations from the consultations concerning the guidelines were comprehensively compiled and analysed. These recommendations have been incorporated in the 2010 revision of the GPP guidelines.

Organization of the GPP guidelines

The GPP guidelines are divided into three main sections:

1. **Complexities of biomedical HIV prevention trials** describes the realities of the HIV epidemic, the underlying determinants of the epidemic, the context of conducting biomedical HIV prevention trials, and why a participatory approach is necessary to effectively conduct trials.
2. **Guiding principles of GPP in biomedical HIV prevention trials** outlines the set of principles that serve as the foundation of the relationship between trial funders, sponsors, implementers, and other stakeholders.
3. **Good participatory practice standards for biomedical HIV prevention trials** describes standards of good participatory practice for trial funders, sponsors, and implementers to follow when designing, preparing for, conducting, and concluding a biomedical HIV prevention trial. This section discusses stakeholder engagement activities to take place at each stage of the research life-cycle. Each topic in the standards section is divided into the following subsections:
   A. Definition.
   B. Relevance to good participatory practice
   C. Special considerations.
   D. Standards of good participatory practice.
   E. Additional guidance.

Figure 1. Timeline of GPP Genesis

Timeline of GPP and Ethical Considerations		
GPP Guidelines		*Ethical Considerations*
	2000	***February:*** UNAIDS Regional Consultations on ethical considerations in international HIV vaccine trials[a] ***May:*** *Ethical considerations in HIV preventive vaccine research guidance document* published by UNAIDS[b]
July: Cambodia government decides not to support PrEP trial[c]	2004	
February: Cameroon stops PrEP trial in progress[c] ***March:*** Nigerian PrEP trial is discontinued[c] ***May:*** Global PrEP consultation with trial sponsors, researchers and advocates[d] ***April & June:*** 'Creating Effective Partnerships' regional consultations[e] ***June:*** 'Creating Effective Partnerships' international consultation[e]	2005	
September: UNAIDS/AVAC working group drafts *GPP Guidelines for Biomedical HIV Prevention Trials*	2006	
May – June: Multiple global stakeholders review draft of *GPP Guidelines* ***July:*** Pre-publication draft of *GPP Guidelines* released ***November:*** UNAIDS/AVAC publish *GPP Guidelines*[f]	2007	***May:*** UNAIDS/WHO establish working group to revise *Ethical Considerations* ***July:*** Expert Committee Meeting to revise *Ethical Considerations* ***July:*** Pre-publication draft of *Ethical Considerations* released ***November:*** UNAIDS/WHO publish *Ethical Considerations in Biomedical HIV Prevention Trials*[g]
August 2008 – May 2009: Global GPP consultations sponsored by AVAC conducted with multiple stakeholder groups	2008	
May: Report-back meeting from global consultations	2009	
May 2009 – May 2010: Synthesis of recommendations from global consultations; revision of *GPP Guidelines* ***July:*** Draft version of revised *GPP Guidelines* released for comments Publication of *GPP Guidelines: 2nd Edition*	2010	

[a] Guenter D et al. (2000). Ethical considerations in international HIV vaccine trials: summary of a consultative process by the Joint United National Programme on HIV/AIDS (UNAIDS). *Journal of Medical Ethics,* 26:37-43.

[b] *Ethical considerations in HIV preventive vaccine research. UNAIDS guidance document* (2000). Geneva, UNAIDS, World Health Organization. (UNAIDS/04.07E).

[c] Singh J et al. (2005). The abandoned trial of Pre-exposure prophylaxis for HIV: what went wrong? *PLoS Medicine,* 2(9):e234.

[d] International AIDS Society (2005). *Building Collaboration to Advance HIV Prevention Research: Global consultation on tenofovir pre-exposure prophylaxis research.*

[e] UNAIDS (2006). Creating effective partnerships for HIV prevention trials: report of a UNAIDS consultation. Geneva 20-21 June 2005. *AIDS*, 20:W1-W11.

[f] *Good Participatory Practice Guidelines in biomedical HIV prevention trials* (2007). Geneva, UNAIDS, AVAC.

[g] *Ethical considerations in biomedical HIV prevention trials* (2007). UNAIDS/WHO guidance document. Geneva, UNAIDS, World Health Organization.

First published in 2007, the GPP guidelines were developed after a series of regional consultations in 2005 that focused on defining the key elements needed for creating effective partnerships for HIV prevention trials. These meetings were convened to address issues that were voiced when PrEP trials in Cambodia, Cameroon, and Nigeria were cancelled or closed.

The GPP guidelines were developed as a companion document to Ethical considerations in biomedical HIV prevention trials published in 2007 by UNAIDS and WHO. Ethical Considerations is a guidance document which contains explicit guidance on community participation, capacity building, monitoring informed consent, standard of prevention, and other key ethical issues in 19 guidance points with commentaries.

A living document

The GPP guidelines are a living document that is dynamic and will change over time. Recommendations for modifications and refinements based on experience and reflection should be sent by email to gpp@unaids.org or avac@avac.org. They will be gratefully received and considered in future updates of these guidelines.

1. Complexities of biomedical HIV prevention trials

1.1 Biomedical HIV prevention trials

There is an urgent need to develop additional public health interventions to address the HIV pandemic. Along with necessary individual, social, and structural changes, a broad range of biomedical HIV prevention and treatment options is required to meet the diverse needs of individuals and populations.

This guidance document focuses specifically on biomedical HIV prevention trials. Current biomedical HIV prevention options being developed and evaluated include vaccines, vaginal and rectal microbicides, different forms of pre-exposure prophylaxis (PrEP), and the use of antiretroviral treatment as prevention.

1.2 Underlying determinants of HIV

A wide range of factors create, enhance, and perpetuate the risk of HIV infection. These social and structural determinants can increase vulnerability to HIV at an individual or population level by undermining ability to avoid the risk of HIV exposure.

Underlying determinants of the HIV epidemic can be entrenched in the social, cultural, legal, institutional, or economic fabric of society. Examples of these determinants include gender and other power inequalities, gender-based violence, economic instability, including poverty and migration, human rights violations, homophobia, discriminatory practices, HIV-related stigma, social marginalization, and the criminalization of HIV.

In order to assess the effectiveness of new HIV prevention options, clinical trials must recruit large numbers of healthy, HIV-negative individuals as study participants. Research ethics stipulate that these new HIV prevention options be tested for safety and effectiveness in

populations who need these interventions and are likely to use them should they prove effective. Often, these locations are where the social and structural determinants of the epidemic are most pronounced. The design and conduct of biomedical HIV prevention trials must, therefore, recognize these social and structural factors and develop practices that address and mitigate them in order to avoid inadvertently replicating or reinforcing them.

1.3 Power dynamics within biomedical HIV prevention trials

Power inequalities always exist, in reality or in perception, between funders and funding recipients with respect to a range of issues, such as decision-making processes, priority setting, control of resources and equitable recognition of input. Biomedical HIV prevention trials are often funded by institutions in the global North and conducted with multiple partner institutions worldwide, including those in the global South. Disparities between these institutions and partners can reinforce or introduce power inequalities between and among trial implementers and the funders or sponsors of trials. Inequalities between trial implementers and their funders or sponsors can then translate to inequalities between trial implementers and all other stakeholders.

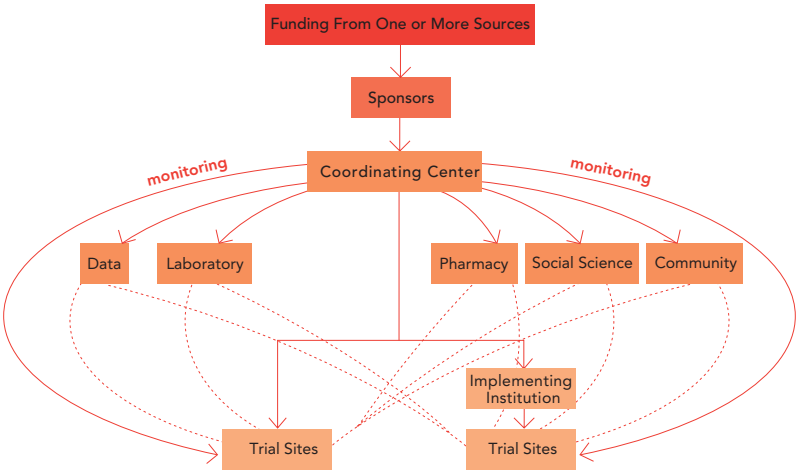
The fact that many biomedical HIV prevention trials are conducted in multiple settings and countries introduces another level of complexity. Variation in cultures, environments, infrastructure, research experience, health policies, and national laws can introduce inequalities between research teams and between site-level community stakeholders.

There can also be a host of power dynamics between research teams and community stakeholders. Power inequalities can include imbalances in literacy, education, and economic resources as well as the power imbalance inherent in patient–health-care provider relation-

ships. National, racial, ethnic, and linguistic differences between members of research teams and community stakeholders can also exacerbate or mask inequalities.

In order to achieve genuine community participation and partnership, it is essential to recognize these various power inequalities. The standards laid out in the GPP guidelines are intended to help research funders, sponsors, and implementers navigate the real and perceived inequalities that are inherent in conducting biomedical HIV prevention trials and facilitate constructive long-term stakeholder engagement.

Figure 2. Example of a Trial Network



Although every biomedical HIV prevention trial network is unique in various aspects, this figure shows the basic structure of a typical network. In general, sponsors receive funding from one or more sources and the funding is distributed through a network coordinating centre directly to trial sites or to implementing institutions such as universities that then fund trial sites. Trial networks may have several centres responsible for different aspects of the trials such as data management, laboratory, pharmacy, social science, and community engagement.

1.4 Stakeholders and community stakeholders

The starting point of good participatory practice is the identification of all stakeholders in the conduct of a biomedical HIV prevention trial. Stakeholders can be defined as individuals, groups, organizations, government bodies, or any other individuals or collection of individuals who can influence or are affected by the conduct or outcome of a biomedical HIV prevention trial. In this guidance document the term 'stakeholders' is all-encompassing to describe any individual or collection of individuals who have a stake in a biomedical HIV prevention trial.

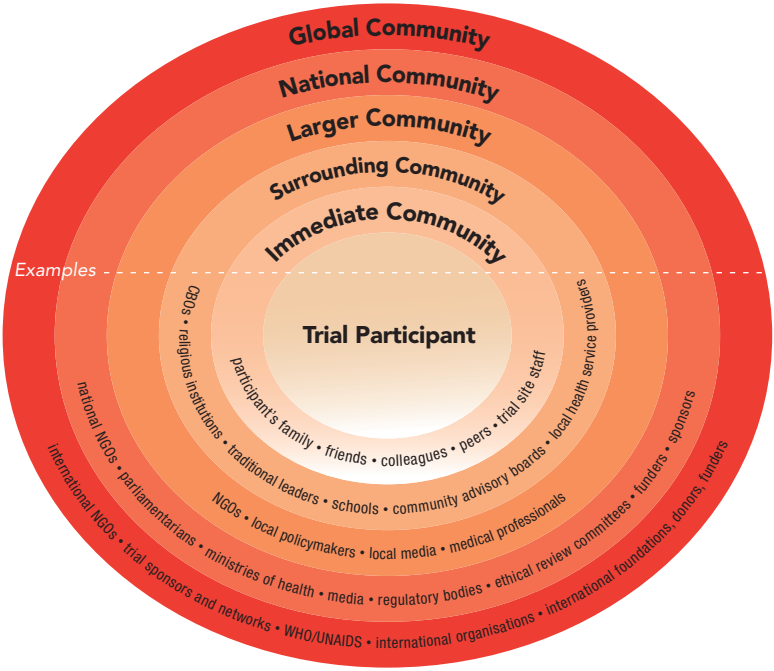
Examples of stakeholders are illustrated in Figure 3 and can include trial participants, families of trial participants, prospective trial participants, community members resident within, or surrounding, the research catchment area, people living with HIV or affected by HIV, prevention and treatment advocates and activists, nongovernmental organizations (NGOs), community-based organizations (CBOs), religious leaders, opinion leaders, media, government bodies, national and local health-care authorities, service providers, and trial funders, trial sponsors and trial implementers.

The definition of 'community' is more complicated, as different people understand the term differently at different times.[15] This term is often used to refer to a group of people who have a common set of interests, a common set of characteristics, or who live in a common area. It is also used to refer to the public at large or a physical location. In the GPP guidelines, the term 'community' refers to the people living in the trial catchment area.

In the GPP guidelines, the term 'community stakeholders' is preferred to the term 'community'. The term 'community stakeholders' refers to both individuals and groups that are ultimately representing the interests of people who would be recruited to or participate in a trial, and people living in the area where the trial is conducted. Examples

of 'community stakeholders' are the population to be recruited, trial participants, people living in the trial catchment area, people living with HIV in the area, people in the area affected by the HIV epidemic, local nongovernmental organizations, and community-based organizations. Trial funders, sponsors, implementers as well as government bodies or representatives of high-level authority structures are explicitly excluded from the term 'community stakeholders', but are clearly considered trial 'stakeholders'.

Figure 3. Layers of Biomedical HIV Prevention Trial Stakeholders



This figure shows the range of stakeholders who may influence and are affected by a biomedical HIV prevention trial – from those stakeholders most immediately close to trial participants, such as participants' family and trial site staff, to those at the community, regional, national, and international level, such as trial sponsors and international NGOs.

Meaningful stakeholder engagement requires identification and consideration of all relevant stakeholders. Of key importance in good participatory practice is sustained partnering and collaboration with community stakeholders. This requires ample time and can only be achieved with broad, inclusive, and multifaceted understanding of the context in which a biomedical HIV prevention trial is to be conducted.

1.5 Applying Good Participatory Practice

There are many inherent complexities in conducting biomedical HIV prevention trials. The GPP guidelines help to assist trial funders, sponsors, and implementers to avoid reinforcing the social determinants of HIV and mitigate power inequalities between stakeholders by developing better forms of stakeholder collaboration. By acknowledging and understanding these challenges, trial funders, sponsors, and implementers can more appropriately and effectively facilitate a mutually beneficial participatory approach to conducting biomedical HIV prevention trials. Developing meaningful stakeholder collaborations that begin at the trial planning phase and are sustained over the life-cycle of a trial takes time, resources, and commitment from trial funders, sponsors, and implementers, as well as all other stakeholders.

Collaborative relationships that trial funders, sponsors, and implementers have with all relevant stakeholders are guided by the principles of respect, mutual understanding, scientific and ethical integrity, transparency, accountability, and community autonomy. These principles serve as the foundation for stakeholder relationships and are defined in the second section of the GPP guidelines.

The third section of the guidelines lays out the standards of good participatory practice, which are underpinned by the guiding principles. Implementation of the good participatory practice standards can produce mutually beneficial collaborations. These standards are essential to biomedical HIV prevention trials that are relevant to community stakeholders, respectful of the local context, harness stakeholder expertise, and maximize trial outcomes, increasing the chances of finding effective new biomedical HIV prevention options.

2. Guiding principles of GPP in biomedical HIV prevention trials

The guiding principles of good participatory practice described below reflect a set of values that constitute the foundation for positive, collaborative, and mutually beneficial relationships that trial funders, sponsors, and implementers can foster with all other stakeholders. The GPP guidelines have been developed within the framework of these principles.

2.1 Respect

Respect among stakeholders is key to communicating effectively, fostering trust, and developing partnerships to achieve collective goals. Respect is demonstrated by all stakeholders communicating and acting in ways that value and honour each other's perspectives and realities.

Research requires fundamental respect for the human rights and confidentiality of trial participants. Local cultural and communal values are included in the human rights framework. Respect among stakeholders also serves to protect and empower legitimate social institutions and legitimate communal decision-making authorities.

2.2 Mutual understanding

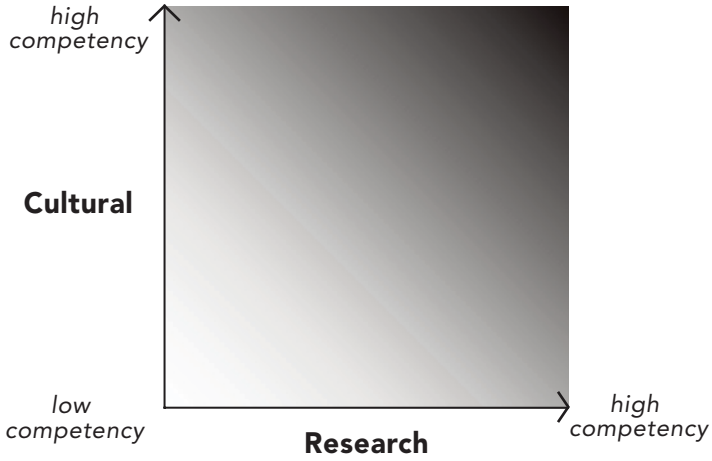
A common understanding is essential to effective partnerships among all stakeholders. It requires stakeholders to develop competency in both sociocultural issues and research processes. The initial competency level of different stakeholders will vary depending on their prior exposure to specific socio-cultural environments and to biomedical HIV prevention research.

Sociocultural competency includes understanding the norms, practices, and beliefs of relevant local cultures, local social circumstances, and diverse community stakeholder perspectives, priorities, and research needs. Building sociocultural competency frames the research dialogue within the local context, supports collaboration

across stakeholders with diverse priorities, and enhances the development of appropriate study procedures.

Research competency includes understanding the scientific process of defining research questions, developing appropriate study designs, and collecting and analysing data to ensure valid results. Building research competency frames the research dialogue within the requirements of the scientific process, enables and empowers all stakeholders to provide meaningful input into the research process, and enhances community-wide understanding of the concepts, purposes, practices, and limitations of biomedical HIV prevention trials.

Figure 4. Trial Competency Range



Sociocultural and research competency can be illustrated as a gradient along two axes, showing lesser to greater competency as one moves from left to right along the research competency axis, or from bottom to top on the sociocultural competency axis. Each individual stakeholder will start their involvement at a particular position on the graph, based on their competency around sociocultural and research issues. For example, a principal investigator new to a particular location may have high research competency, but low sociocultural competency at the start of designing a particular trial. A community stakeholder new to biomedical HIV prevention research may have high sociocultural competency, but low research competency when they begin their involvement with their first trial. All stakeholders share ongoing responsibility to review and strengthen both sociocultural and research competencies in order to improve mutual understanding.

2.3 Scientific and ethical integrity

Maintaining the highest standards of scientific and ethical integrity is fundamental to achieving the scientific goals of a biomedical HIV prevention trial, maximizing benefits for the trial community, and advancing global HIV prevention science.

Scientific integrity requires adherence to scientific processes in order to ensure trials meet the highest scientific standards and achieve valid results.

Ethical integrity requires consideration of broader societal and ethical issues, as well as adherence to universal ethical principles that include respect for persons, beneficence, and justice.[6]

2.4 Transparency

Open, honest, timely, and clear communication enables transparency and fosters collaborative, trusting, and constructive relationships. Transparency is relevant to the research process as well as to the roles of stakeholders.

Transparency about research includes ensuring that all stakeholders receive open, honest, and understandable information about the objectives and processes of a trial and that feedback from a broad range of stakeholders is acknowledged and addressed.

Transparency about the role of stakeholders includes ensuring that all stakeholders are clear on what their respective roles are, which constituents, if any, each stakeholder represents, and the extent to which stakeholder input will influence trial-related decisions. Adherence to the principle of transparency means that stakeholders communicate about circumstances that may affect previously agreed levels of consultation, involvement, collaboration, or decision-making.

2.5 Accountability

Accountability is fundamental to sustaining partnerships built on trust and mutual respect. It not only helps ensure the effective completion

of a single biomedical HIV prevention trial but also strengthens the foundation for future biomedical research.

Trial funders, sponsors, and implementers are accountable to all other stakeholders for conducting scientifically valid and ethical research, using participatory practices, and responding to input from relevant stakeholders as mutually agreed. They are also accountable for ensuring that funding is adequate to enable optimal engagement between research teams and all other stakeholders.

Community and other relevant stakeholders are accountable for ensuring that their input into the research process is fair and constructive, respects the scientific process, and is in the best self-identified interests of community stakeholders. Where stakeholders accept the responsibility to act as liaisons or representatives between research teams and specific sections of the community, they are accountable for representing the interests of their constituents, sharing information about planned or ongoing trials with their constituents, and expressing the needs and concerns of their constituents to research teams.

2.6 Community autonomy

Good participatory practice strives to maximize the opportunity for all stakeholders to understand local, national, and global benefits of a specific trial and to make informed decisions regarding the appropriateness of a trial being conducted in a specific area.

While a wide range of stakeholders participate in the design, approval, and implementation of a particular trial protocol, the interests of legitimate community stakeholders ultimately will determine whether a trial will be conducted in a particular area.

If objections about the trial exist from outside stakeholders, but fully informed community stakeholders are supportive of the trial, then the trial should proceed. If support for the trial exists from outside stakeholders, but fully informed community stakeholders do not support the trial, then the trial should not proceed in a particular area.

3. Standards of good participatory practice in biomedical HIV prevention trials

Introduction to good participatory practice standards

The design, planning, and implementation of biomedical HIV prevention trials are guided by a range of standards, such as good clinical practice, good clinical laboratory practice, and good manufacturing practice. This section describes the standards of GPP that provide a systemized framework that trial funders, sponsors, and implementers can use to develop meaningful and sustained collaborations with all relevant stakeholders in the planning and conduct of biomedical HIV prevention trials. The standards of GPP are intended to be adopted by trial sponsors, implemented at all trial sites globally, and monitored.

Appropriate and robust stakeholder engagement occurs at all stages of the research life-cycle, including during trial design, planning, implementation, and closure, and is not limited to the specific, discrete categories highlighted in this section. While this section describes stakeholder engagement processes in the general sequence in which they may occur, these processes are inherently non-linear.

The application of any one standard or set of standards will vary by location, the type of trial being conducted, and trial site experience with respect to previously established stakeholder engagement programmes. The GPP guidelines are intended to improve participatory practices; hence following these guidelines should result in an increase in the level of engagement.

Each topic in the standards section is divided into the following subsections:

A. Definition.
B. Relevance to good participatory practice.
C. Special considerations.
D. Standards of good participatory practice.
E. Additional guidance.

3.1 Formative research activities

3.1.A. Definition

Formative research activities enable research teams to gain an informed understanding of the local population, sociocultural norms and practices, local power dynamics, community perceptions, channels of communication and decision-making, and local history of research, as well as the needs and priorities of people living in the trial catchment area. Formative research activities usually constitute the initial phase of stakeholder outreach and engagement.

3.1.B. Relevance to good participatory practice

Collaborating with community stakeholders to devise questions, gather information, and analyse results related to formative research activities ensures that stakeholders' expertise and understanding of community perceptions, cultures, and traditions inform trial design and conduct. Collaborating with community stakeholders on formative research activities builds trust and is the foundation for a robust engagement programme.

3.1.C. Special considerations

1. Formative research activities can be conducted informally to gather information about the research areas and local communities, formally as a part of protocols requiring specific approval and funding, or can form part of a broader 'community-based participatory research' project.
2. Different sites will have different needs regarding formative research activities. New trial sites may require extensive formative research activities. Experienced trial sites may require more focused formative research activities when studying an experimental option that has not yet been introduced in the area, recruiting from a new location, recruiting a new study population, or gathering stakeholder feedback regarding previous trials.

3.1.D. Good participatory practice standards for formative research activities

1. Research teams identify key informants and relevant stakeholders that can assist in planning, implementing, and reviewing the process and results of formative research activities.
2. Research teams and relevant stakeholders develop a formative research plan that describes:
    a. Key information and questions that need to be gathered and answered in order to support effective planning and implementation of the trial.
    b. The most appropriate methods to collect the required information.
    c. Research team members and community stakeholders best suited to collect the required information.
    d. Approval or notification processes that are required for specific activities.
    e. Implementation plans, including timelines and required resources.
3. Research teams and relevant stakeholders discuss the findings and their implications for trial design, conduct, and development of a robust stakeholder engagement programme.
4. Research teams document formative research activities and findings, including participatory techniques used, information collected, areas where clarification or attention is needed, and how findings will inform the trial planning and implementation process.
5. Research teams create a budget that allocates sufficient funds and staff time to execute formative research activities.

3.2 Stakeholder advisory mechanisms

3.2.A. Definition

The term 'stakeholder advisory mechanisms' refers to strategies or approaches that facilitate meaningful dialogue among research teams and relevant stakeholders about planned or ongoing clinical trials. Stakeholder advisory mechanisms provide research

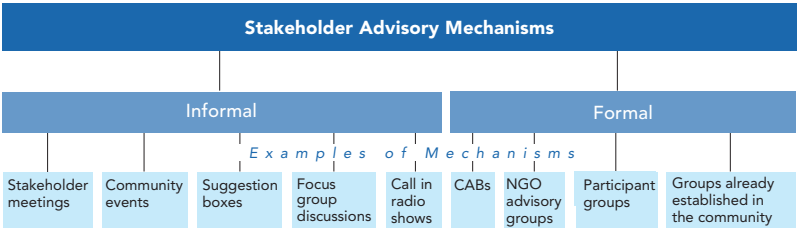
teams with information about relevant stakeholders' perspectives on the design, planning, and implementation of a specific clinical trial and facilitate open communication about research goals, processes, and results. These mechanisms also provide relevant stakeholders with the opportunity to engage with research teams during the life-cycle of the trial.

Stakeholder advisory mechanisms may be informal and formal. They can be built and sustained by the clinical trial site or may already exist in the area.

1. Informal stakeholder advisory mechanisms may be one-time events during which research teams seek relevant stakeholders' views on proposed or ongoing research. These may include stakeholder meetings, local events, focus group discussions, interviews, or consultations. They may involve community members, existing organizations, local employer associations, local government or traditional committees, or other advocacy, charitable, cultural, political, religious, or social groups.
2. Formal stakeholder advisory mechanisms typically involve established groups that develop an ongoing relationship with the research team at a particular trial site. Examples are trial participant groups (former or current participants), professional groups (local scientists, service providers, media, or experts on local sociocultural issues), nongovernmental organization advisory groups (with representatives from different nongovernmental organizations or community-based organizations) or community advisory boards (see definition below).
3. Community advisory boards (CABs), also referred to as community advisory groups (CAGs), are a common example of a formal stakeholder advisory mechanism. They are composed of community members or stakeholder representatives and meet regularly with research team representatives. Community advisory boards or groups inform community stakeholders about proposed and ongoing research. As an independent advisory voice, community advisory boards or groups provide feedback to research teams about community norms and beliefs, as well as community views and concerns

that arise in specific trials. The composition of these groups varies from site to site and may include members or representatives of the surrounding area, individuals in the population from which participants will be recruited, people living with or affected by HIV, current or former trial participants, religious or opinion leaders, and representatives of other sections of society as determined by the location of the trial and trial eligibility criteria.

Figure 5. Examples of Stakeholder Advisory Mechanisms



Stakeholder advisory mechanisms take many forms. This figure shows that they can be informal or formal and provides several examples of each type of stakeholder advisory mechanism. All of these mechanisms, as well as others, may be used to facilitate important dialogue between research teams and other stakeholders.

3.2.B. Relevance to good participatory practice

Establishment, maintenance, and engagement of stakeholder advisory mechanisms throughout the research process are key to establishing robust partnerships with community stakeholders and to ensuring continuous dialogue about biomedical HIV prevention research and specific trials.

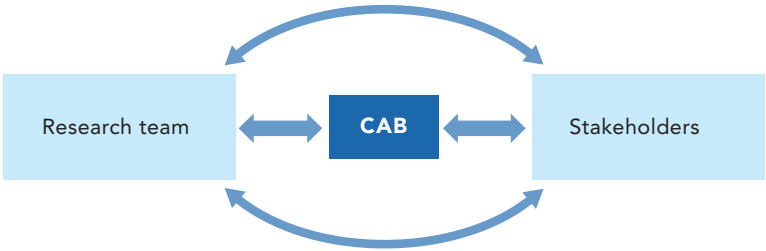
3.2.C. Special considerations

1. Research teams are responsible for establishing and maintaining stakeholder advisory mechanisms and for engaging already existing mechanisms. The first step is to identify and map all local stakeholders in order to determine which are relevant to trial implementation and key to sustained stakeholder engagement. Formative research activities help research

teams to determine which groups or individuals are key stakeholders and which ones are not considered valid voices of key stakeholders (see Section 3.1).

2. Community advisory boards or groups were first developed in the context of the HIV epidemics in the United States of America and Europe. Over the past two decades, they have become a standard element of HIV research worldwide. Nonetheless, the establishment of a community advisory board or group may not always translate as a best practice in all locations globally. In many settings, community advisory boards or groups are necessary but not sufficient for gaining adequate and appropriate community stakeholder input. Careful consideration needs to be given to the range and breadth of stakeholder advisory mechanisms that are required to best support effective participatory practices.
3. The need to identify and establish new stakeholder advisory mechanisms may vary from site to site, depending on whether a trial is being conducted in a research-naïve area, one with a well-established research facility, or one in which multiple stakeholder advisory mechanisms already exist.

Figure 6. The Role of Community Advisory Boards as a Bridge



One form of a stakeholder advisory mechanism is a community advisory board. Such boards can play an important role of translating information between research teams and stakeholders. While community advisory boards can be a key mechanism by which research teams inform stakeholders and receive their feedback, research teams can and should communicate via other mechanisms to reach a broader range of stakeholders.

3.2.D. Good participatory practice standards for stakeholder advisory mechanisms

1. Research teams designate trial site staff responsible for managing activities and relationships involving stakeholder advisory mechanisms.
2. Research teams and relevant stakeholders identify the full range of stakeholder advisory mechanisms needed for the trial to ensure the involvement of all relevant stakeholders, including representatives of populations that will be recruited into trials.
3. Research teams ensure that the development or identification of stakeholder advisory mechanisms is transparent.
4. Research teams and relevant stakeholders identify the training needs of members of advisory mechanisms and build their capacity to understand concepts, purposes, practices, and limitations of clinical trials that may be new to them so that they are able to provide meaningful input to the research process.
5. Research teams review on an ongoing basis the composition of existing mechanisms and the need for new advisory mechanisms to ensure that all relevant stakeholders continue to be represented during the course of a trial.
6. Research teams include in their stakeholder engagement plans (see Section 3.3) the identification, establishment, and maintenance of stakeholder advisory mechanisms.
7. Research teams maintain clear written records of all discussions and agreements with relevant stakeholders, including requests, concerns, recommendations, actions taken by the research team, and any unresolved issues that require further follow-up.
8. Research teams create a budget and allocate sufficient funds to support the ongoing capacity-building, maintenance, and activities of stakeholder advisory mechanisms.
9. For formal stakeholder advisory mechanisms, research teams and relevant stakeholders determine:

a. The purpose of each stakeholder advisory mechanism, which may result in establishing terms of reference or bylaws.
b. The scope of responsibilities of each stakeholder advisory mechanism, such as the responsibility to develop, review, discuss, and provide input on relevant trial documents and procedures.
c. The structure of each stakeholder advisory mechanism, which may result in establishing guidelines to elect a chairperson and define the duration of service for members.
d. The frequency of meetings and the frequency with which principal investigators or other key trial staff attend meetings, and the ways in which members can communicate with research teams between meetings.
e. Reimbursement policies, if appropriate.
f. Mechanisms by which individuals or groups can raise concerns with trial staff and with off-site trial sponsors in the event that a conflict or concern related to the site emerges.

3.2.E. Additional guidance

See the *Recommendations for community involvement in National Institute of Allergy and Infection Diseases HIV/AIDS clinical trials research* for additional guidance.[16]

3.3 Stakeholder engagement plan

3.3.A. Definition

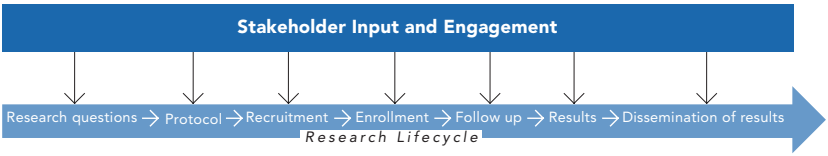
The stakeholder engagement plan describes strategies and mechanisms on how to build relationships and constructively engage with a broad range of local, national, and international stakeholders.

3.3.B. Relevance to good participatory practice

Meaningful engagement, along with effective stakeholder education and commu nication, is key to building capacity and, ultimately, empowering community stakeholders as decision-making agents. An effective stakeholder engagement plan also lays the foundation for a supportive environment for research

that extends beyond the lifespan of a specific biomedical HIV prevention trial.

Figure 7. Stakeholder Engagement in the Research Life-Cycle



Robust stakeholder engagement occurs at all stages of the research life-cycle including during trial design, recruitment, implementation, trial closure, disseminating results, negotiating next steps, and developing future research questions.

3.3.C. Special considerations

1. Stakeholder engagement, education, communication, and issues management (see Sections 3.3, 3.4, 3.5, and 3.6) are four distinct areas of planning to be addressed during the trial planning phase. Plans for these four topics can be created distinctly or collectively.
2. Being familiar with and appreciating the relationship dynamics among different stakeholders increases the research team's ability to effectively and constructively engage with a broad range of relevant stakeholders.

3.3.D. Good participatory practice standards for stakeholder engagement planning

1. Research teams identify all potential stakeholders within and surrounding the research area as well as regionally, nationally, and internationally.
2. Research teams and relevant stakeholders discuss and negotiate a stakeholder engagement plan to cover the life-cycle of the trial. The plan defines the following:
    a. The range of different stakeholders to be engaged, specifically ensuring inclusion of relevant nongovernmental organizations and community-based organizations.

b. The type of engagement that is appropriate for each stakeholder, such as being informed, consulted with, collaborated with, or empowered to make decisions.

c. The frequency and type of engagement methods to be used, such as public meetings, workshops, joint decision-making models, or delegated decision-making.

d. The criteria by which to review the success of the engagement plan.

3. Research teams and relevant stakeholders define how regularly the engagement plan will be reviewed to account for the identification or emergence of new potential stakeholders.
4. The principal investigator and community advisory board or group chairperson, where appropriate, jointly endorse the stakeholder engagement plan.
5. Research teams maintain clear written records of all discussions and agreements, as well as stakeholder engagement activities. This includes stakeholder recommendations, actions taken by the research team, and any unresolved issues that require further follow-up.
6. Research teams create a budget and allocate sufficient funds and staffing for the activities laid out in the plan.

3.4. Stakeholder education plan

3.4.A. Definition

The stakeholder education plan describes strategies and mechanisms for providing relevant education about a specific planned trial, as well as biomedical HIV prevention research in general, in order to enhance research literacy.

3.4.B. Relevance to good participatory practice

Effective stakeholder education, along with meaningful stakeholder engagement and communication, is key to building participatory capacity and, ultimately, empowering community stakeholders as decision-making agents. Additionally, building research literacy can lay the foundation for a supportive

environment for research that extends beyond the lifespan of a specific biomedical HIV prevention trial.

3.4.C. Special considerations

1. Stakeholder engagement, education, communication, and issues management (see Sections 3.3, 3.4, 3.5, and 3.6) are four distinct areas of planning to be addressed during the trial planning phase. Plans for these four topics can be created distinctly or collectively.
2. While it is important that all relevant stakeholders receive education to improve their knowledge of research processes, the focus of stakeholder education should be to enhance research literacy for community stakeholders.
3. The goals and outcomes of stakeholder education are distinct from recruitment activities. However, stakeholder education can positively affect trial recruitment activities. The development of a stakeholder education plan can help to clarify the overlaps and distinctions between stakeholder education and recruitment.

3.4.D. Good participatory practice standards for stakeholder education planning

1. Research teams, with input from relevant stakeholders, determine what education is needed in order to enhance stakeholder understanding of, and engagement with, a specific planned trial and biomedical HIV prevention research more generally.
2. Research teams and relevant stakeholders discuss and negotiate a stakeholder education plan to cover the life-cycle of the trial. The plan defines the following:
    a. The range of different stakeholders that could benefit from specific education around HIV, new HIV prevention options, and general research literacy.
    b. The level of knowledge required and desired by stakeholders to support effective engagement. This will be influenced by the type of engagement defined for each

stakeholder in the stakeholder engagement plan (see Section 3.3).

c. The methods and frequency of educational activities.

d. The stakeholders who could also deliver or support the delivery of the stakeholder education plan.

e. The criteria by which to review the success of the stakeholder education plan.

3. Research teams and relevant stakeholders define how regularly the stakeholder education plan will be reviewed.
4. Research teams document stakeholder education activities, including questions that arise, topics that cause confusion, and suggestions for future educational activities.
5. Research teams create a budget and allocate sufficient funds and staff for the activities laid out in the plan.

3.5 Communications plan

3.5.A. Definition

The communications plan describes policies and strategies that will increase broad awareness of the trial, facilitate dissemination and understanding of correct information about trial design, conduct, and results, and coordinate communication between the research team and relevant stakeholders.

3.5.B. Relevance to good participatory practice

Consultation with relevant stakeholders will help research teams to design communications strategies that are effective, locally acceptable, and help to create a supportive and conducive environment for trial initiation and implementation.

3.5.C. Special considerations

1. Stakeholder engagement, education, communication, and issues management (see Sections 3.3, 3.4, 3.5, and 3.6) are four distinct areas of planning to be addressed during the

trial planning phase. Plans for these four topics can be created distinctly or collectively.

2. The communication plan must consider the information needs of different stakeholders at the local, national, and international levels, as well as at various stages in the trial life-cycle.
3. The communication plan deals exclusively with external communication. However, effective internal communication, especially across multidisciplinary teams, is a prerequisite to effective external communication.

3.5.D. Good participatory practice standards for communications planning

1. Research teams and key stakeholders identify all potential audiences within and surrounding the research area as well as regionally, nationally, and internationally.
2. Research teams and relevant stakeholders discuss and negotiate a communications plan to support open channels of communication about the trial throughout its life-cycle. The plan describes the following:
    a. The information needs of the different stakeholders at various stages of the research life-cycle, from early phases of stakeholder engagement, to recruitment, enrolment, trial closure, and results dissemination.
    b. The key messages to be communicated about the trial, such as the purpose, risks, benefits, ongoing progress, closure, and results dissemination.
    c. The various communication methods that will be used for specific stakeholders, taking account of literacy levels and language needs.
    d. The local stakeholders that could also deliver or support the delivery of the communications plan, and specific training needs necessary to effectively deliver messages.
    e. The procedures and timelines for proactively disseminating information.

f. The procedures for actively addressing inquiries about the trial or HIV prevention research.

g. The criteria by which to review the success of the communications plan.

3. Research teams define how regularly the communication plan will be reviewed.
4. Research teams develop communication materials in understandable lay language and translate them as needed, seeking input from relevant stakeholders.
5. Research teams maintain clear written records of all discussions, agreements, and communication activities. This includes relevant stakeholder recommendations, actions taken by the research team, and any unresolved issues that require further follow-up.
6. Research teams create a budget and allocate sufficient funds and staff for all activities laid out in the communication plan.

3.5.E. Additional guidance

For additional guidance, see *Communications handbook for clinical trials: strategies, tips, and tools to manage controversy, convey your message, and disseminate results*.[17]

3.6. Issues management plan

3.6.A. Definition

The issues management plan describes how research teams intend to manage issues of concern or unexpected developments that may emerge before, during, or after the trial, including those that could limit the support for, or success of, the specific trial or future biomedical HIV prevention trials.

Examples of the types of issue that may emerge could include negative media coverage of the site, unsubstantiated rumours about the trial, unforeseen sociocultural taboos around certain trial procedures, developments in other HIV prevention trials, premature closure of a trial for reasons of harm, futility or proven efficacy in interim analyses, or particular issues related to recruitment challenges or protocol issues.

3.6.B. Relevance to good participatory practice

The risk that unexpected developments will negatively affect a trial can be mitigated if research teams work closely with key relevant stakeholders to identify and plan for such risks, and if relevant stakeholders provide advice, support and direction on how to resolve issues when they do arise. By developing an issues management plan prior to trial implementation, research teams are better equipped to deal with issues or risks as they arise and are more likely to avert a crisis situation.

3.6.C. Special considerations

Stakeholder engagement, education, communication, and issues management (see Sections 3.3, 3.4, 3.5, and 3.6) are four distinct areas of planning to be addressed during the trial planning phase. Plans for these four topics can be created distinctly or collectively.

3.6.D. Good participatory practice standards for issues management planning

1. Research teams identify and list all known potential issues that could emerge and undermine the success of the trial before, during or after trial completion.
2. Research teams and relevant stakeholders discuss and negotiate an issues management plan to cover the life-cycle of the trial. The plan defines the following:
    a. A site-level strategy to manage unexpected developments and emerging concerns.
    b. Key staff members who are responsible for addressing emerging issues.
    c. A chain of communication within the research team and with relevant stakeholders for emerging issues.
    d. Relevant stakeholders who can act as advisers and help implement steps of the issues management plan.
    e. Key messages created to address anticipated concerns.
    f. The process by which media reports and media requests will be addressed.

3. Research teams maintain clear written records of all issues that emerge, how they are responded to, and the outcome.
4. Research teams create a budget and allocate sufficient funds and staff to support the plan.

3.6.E. Additional guidance

For additional guidance see *Communications handbook for clinical trials: strategies, tips, and tools to manage controversy, convey your message, and disseminate results*.[17]

3.7. Site selection

3.7.A. Definition

Site selection is the process by which trial funders, sponsors, or networks evaluate sites for provision of funding for a trial protocol, inclusion in a multisite trial, or inclusion in a trial network.

3.7.B. Relevance to good participatory practice

As effective stakeholder engagement is essential for the successful implementation of biomedical HIV prevention trials, optimal trial sites are those with established participatory processes and strong community programmes, or, in the case of new sites, demonstration of commitment to establishing these.

3.7.C. Special considerations

Site assessment tools are used to review a site's anticipated ability to conduct a trial according to good participatory practice as well as good clinical practice. New sites may not have the full complement of stakeholder engagement and advisory mechanisms in place. For both established and new sites, stakeholder engagement programmes following GPP standards need to be in place or in development before the site is selected.

3.7.D. Good participatory practice standards for site selection

1. Trial funders, sponsors, or network representatives assess sites with respect to stakeholder engagement programmes, taking account of the following issues:
    a. Evidence or plans for development of meaningful relationships with all relevant stakeholders.
    b. Evidence of a previous stakeholder engagement programme.
    c. Findings from formative research activities, or a workplan for completing formative research activities.
    d. Previous development of multiple stakeholder advisory mechanisms or a workplan to develop them.
    e. Demonstrated awareness and consideration of human rights issues that may be raised by the trial, particularly as they relate to vulnerable, marginalized, or criminalized groups.
2. Trial funders, sponsors, or network representatives continue to monitor site progress towards developing appropriate plans, resolving issues identified, and following GPP standards during the site development phase of the trial.

3.8 Protocol development

3.8.A. Definition

Protocol development is the process of creating and modifying a trial protocol. The protocol describes the rationale, objectives, trial design, methodology, statistical considerations, ethical considerations, and organization of a trial.

3.8.B. Relevance to good participatory practice

A range of stakeholders can provide meaningful input into many aspects of trial protocol development. In particular, community stakeholders bring expertise that can assist research teams in ensuring that protocol designs and procedures are locally appro-

priate, are acceptable to the study population, and optimize successful implementation of the trial.

3.8.C. Special considerations

1. Opportunities for protocol review and input by local research teams and relevant stakeholders vary by trial. In some circumstances, particularly multicountry or multisite trials, protocol development may be largely centralized. Good participatory practice 'best practices' in protocol development incorporate mechanisms to facilitate stakeholder input early in the protocol development process.
2. Research teams can consider documenting community stakeholder input into protocol development and sharing these recommendations with protocol review bodies.

3.8.D. Good participatory practice standards for protocol development

1. Research teams maintain clear and transparent communication with relevant stakeholders, in particular advisory boards and groups, about the protocol development process.
2. Research teams provide relevant stakeholders with draft versions of the protocol and make technical information as accessible as possible by providing protocol summaries and translated materials, or by facilitating workshops, as necessary.
3. Research teams facilitate opportunities for relevant stakeholders to provide input into trial design issues such as recruitment strategies, informed consent materials and procedures, reimbursement policies, counselling approaches, follow-up procedures and community outreach plans.
4. Research teams inform relevant stakeholders of protocol reviews and approval processes and provide regular updates.
5. Trial sponsors or implementers make final protocols of publically-funded trials available and easily accessible to all stakeholders.

6. Research teams maintain clear written records of all discussions and agreements. This includes relevant stakeholders' recommendations, actions taken by the research team, and any unresolved issues.

3.9 Informed consent process

3.9.A. Definition

Informed consent is a process by which an individual is provided with enough information about a trial to make an independent decision whether or not to participate. In this process, research teams educate the prospective participant about the trial, including the potential risks and benefits, trial procedures, and what is expected of the participant. When an individual provides consent, it is documented on the informed consent form. Informed consent is an ongoing process in which participants may decide to drop out of the trial at any point, even after providing consent to enrol in the trial.

3.9.B. Relevance to good participatory practice

A wide range of stakeholders can help research teams to develop culturally acceptable and effective informed consent procedures and materials.

3.9.C. Special considerations

1. Community stakeholders can provide research teams with invaluable advice to improve the informed consent process and materials. However, the actual implementation of the informed consent process between an individual and the research staff is confidential. Only designated research staff have access to confidential information about the identity of trial participants.
2. Informed consent is a process and does not occur at only one specific point at the start of a trial. Repetition of trial information and ongoing assessment of participants' understanding of the trial and their voluntary participation is required during trial conduct.

3.9.D. Good participatory practice standards for the informed consent process

1. Research teams discuss the following topics with community stakeholders during development of the informed consent materials and procedures:
    a. Who needs to be consulted locally to enable research teams to invite individuals to join the study?
    b. What local cultural practices may affect individual decision-making ability and how can working within these structures be facilitated while ensuring protection of individual autonomy to provide informed consent.
    c. The general literacy level of the population to be recruited and how to assess the literacy level of prospective participants.
    d. Considerations and requirements for illiterate participants, including discussion of possibilities of who may serve appropriately as a witness to the informed consent process.
    e. The prevalence of different languages in the area, and which languages are required for consenting individuals.
    f. Local and legal forms of identity (name and age) verification and local practices around the use of names.
    g. The legal, community and sponsor definitions of a 'minor' and consideration of legal and community determinations of who can serve as a minor's guardian.
    h. Locally appropriate reimbursement and compensation.
    i. Appropriate strategies to ensure participant rights are protected, including voluntariness of participation, ensuring undue inducement is avoided, and mitigating the influence of social desirability in influencing individual agreement to enrol.
    j. Strategies to ensure comprehension of informed consent materials and critical trial-related terms and concepts, including the use of visual or audio formats, flipcharts, props, analogies, and other supportive materials and methods.

k. Techniques to assess comprehension and the frequency with which they are to be utilized.

l. Explanation of potential trial-related harms and how those harms will be addressed (see Section 3.13).

m. Strategies to ensure that community follow-up of participants after missed visits respects agreements between the participant and research team about how to contact the participant.

n. Consideration of the length of informed consent forms and the estimated time to complete the informed consent process.

o. Preferred ways for participants to contact research teams and stakeholders independent of the research team to ask questions or express concerns about trial participation.

p. Ways to pilot the informed consent materials.

2. Research teams maintain clear written records of all discussions and agreements. This includes community stakeholder recommendations, actions taken by the research team, and any unresolved issues that require further follow-up.

3. Trial sponsors and research teams ensure sufficient time and funds to allow informed consent materials to be properly developed, piloted, translated, and implemented, including assessment of participants' ongoing consent.

3.9.E. Additional guidance

1. Informed consent is the cornerstone of ethically conducted research and is explicitly discussed in guidance documents that address the overall ethical conduct of research, such as the Declaration of Helsinki,[5] CIOMS guidelines,[7] the Belmont Report,[6] good clinical practice,[2] the World Health Organization *Handbook for good clinical research practice*,[3] the Nuremberg Code,[18] the Nuffield Council guidance on health research in developing countries,[8, 9] and UNAIDS/WHO *Ethical considerations in biomedical HIV prevention trials.*[10]

2. There are extensive literature and resources on the development of informed consent processes in multiple contexts,

including a range of innovative approaches to measure and assess participant understanding, to address literacy issues, and to accommodate the desire of participants to consult with families and friends. [19, 20, 21,22,23]

3.10. Standard of HIV prevention

3.10.A. Definition

The term 'standard of HIV prevention' refers to the package of comprehensive counselling and state-of-the-art HIV risk reduction methods provided or made available to participants in biomedical HIV prevention trials.

3.10.B. Relevance to good participatory practice

Helping trial participants reduce their risk of acquiring HIV is a key ethical obligation of research teams. Trial sponsors and implementers must work with relevant stakeholders in establishing the type, scope, and process by which participants are provided with, or given access to, the full HIV prevention package. How trial sites help participants prevent HIV acquisition is often at the forefront of community concerns, thus successful negotiation with community stakeholders of the prevention package to be provided to trial participants is likely to have a significant influence on community perceptions of the trial.

3.10.C. Special considerations

1. The full prevention package determined appropriate for the mode of transmission being studied is expected to be available to all trial participants. Differences from the standard of prevention package at a trial site or between trial sites in multisite studies may be caused by national legal restrictions. When funding-body restrictions limit which prevention methods can be paid for by trial funds, trial sites have the responsibility to find other ways to provide these methods, such as through alternative funding streams or linkages with nongovernmental organizations and community-based organizations.

2. The HIV prevention package is reviewed taking into consideration new HIV counselling models and risk reduction methods that are being scientifically validated and, when appropriate, approved for use by national bodies.
3. To improve relevant stakeholder understanding of the prevention package offered and the clinical trial process, research teams can describe the trial as comparing the investigational product plus the HIV prevention package with the placebo (or comparator arm) plus the HIV prevention package.

3.10.D. Good participatory practice concerning standard of HIV prevention

1. Research teams and relevant stakeholders negotiate the HIV prevention package during the protocol development phase of the trial.
2. Research teams determine which stakeholders already provide HIV prevention services, what types of services they provide, and their capacity to provide adequate services. This will enable research teams to provide appropriate referrals and make linkages when necessary.
3. Research teams and relevant stakeholders discuss and negotiate the comprehensive HIV prevention package and consult local HIV prevention service providers when appropriate. All scientifically validated methods are discussed and the appropriateness for the trial design and population assessed, including:
    a. Risk assessment and risk reduction counselling—including partner and couple counselling.
    b. Male and female condoms—with appropriate instructions and demonstrations.
    c. Testing for and treatment of sexually transmitted infections.
    d. Sterile injecting equipment and drug substitution treatment.
    e. Medical male circumcision.
    f. Post-exposure prophylaxis.

g. Other novel HIV risk reduction strategies as they become available (see Section 3.16).

4. Research teams and relevant stakeholders discuss and negotiate the comprehensive HIV prevention package, taking account of the following:
   a. The HIV prevention package required as a minimum for the trial protocol.
   b. Current HIV prevention standards and services available nationally and in the local area.
   c. Current national laws on HIV prevention technologies and services.
   d. The trial's funding source, any implications this may have for the prevention package, and how these will be overcome to ensure participants are offered a comprehensive package.
   e. The HIV prevention services and technologies that will be offered through referral mechanisms;
   f. The HIV prevention services that will be available to partners of trial participants.
   g. The impact that any services offered by the trial, as well as those that participants will be referred to by the trial, could have on local services.
5. Research teams and relevant stakeholders discuss how the HIV prevention package will be implemented and monitored, including uptake and standards of referral services.
6. Research teams maintain clear written records of all discussions and agreements. This includes recommendations, actions taken by the research team, and any unresolved issues that require further follow-up.
7. Trial sponsors ensure sites receive sufficient funding to deliver the complete prevention package. Research teams create a budget and allocate sufficient funds to ensure provision of the comprehensive HIV prevention package.

3.10.E. Additional guidance

1. *Ethical considerations in biomedical HIV prevention trials* (guidance point 13, page 45, standard of HIV prevention).[10]
2. *Ethical considerations in biomedical HIV prevention trials* (page 13, selected circumstances in which biomedical HIV prevention trials should not be conducted).[10]
3. *Mapping the standards of care at microbicide clinical trial sites, global campaign for microbicides*.[24]
4. *Standards of prevention at HIV prevention trials, global campaign for microbicides*.[25]

3.11. Access to HIV care and treatment

3.11.A. Definition

Access to comprehensive HIV care and treatment refers to care and treatment services made available to individuals who are identified as HIV-positive during the screening process and to trial participants who acquire HIV during the trial. Comprehensive HIV care includes all preventive, psychosocial, psychological, and clinical components of HIV care. HIV treatment refers to antiretroviral therapy internationally recognized as optimal for the management of HIV.

3.11.B. Relevance to good participatory practice

Now that antiretroviral drugs are widely available globally, trial sponsors and implementers are ethically obligated to ensure that participants who acquire HIV during trial participation have access to HIV care and treatment. This issue is often at the forefront of community concerns, thus how access to HIV care and treatment is negotiated with relevant stakeholders and how it is provided to trial participants are likely to have a significant influence on community perception of the trial.

3.11.C. Special considerations

1. HIV care and treatment guidelines vary by country.

2. Treatment options may improve over time, and research teams may need to modify their HIV care and treatment access plans in line with updated national guidelines.
3. Mechanisms to provide HIV care and treatment packages require long-term logistics planning, as people living with HIV require lifelong care and treatment, and, for some participants, HIV treatment may begin after trial exit or completion.

3.11.D. Good participatory practice standards for access to HIV care and treatment

1. Research teams identify the existence and capacity of local HIV care and treatment services, local HIV nongovernmental organizations or community-based organizations, and HIV support groups. This will enable research teams to consult with providers to help to design appropriate referral mechanisms.
2. Research teams and relevant stakeholders discuss during protocol development access to HIV care and treatment under the following circumstances:
   a. Access to HIV care and treatment for individuals who are identified as HIV-positive during the screening process.
   b. Access to HIV care and treatment for individuals who become HIV-positive during the trial.
   c. Information about, or access to, prevention of mother-to-child-transmission services for women who are identified as HIV-positive during the screening process or who acquire HIV during the trial; provision of information about the benefits of prevention of mother-to-child-transmission to HIV-positive men, when appropriate.
3. Research teams and relevant stakeholders discuss the HIV care and treatment package, taking account of the following:
   a. The HIV care and treatment package required as a minimum for the trial protocol.
   b. Current national HIV care and treatment guidelines and policies and local provision of HIV care and treatment services.

c. The anticipated numbers of people likely to be found HIV-positive during screening and the anticipated numbers of participants likely to seroconvert during the trial.

d. The current national laws that could affect a person's right or ability to access HIV care and treatment.

e. The HIV care and treatment services that will be offered through referral mechanisms.

f. The possibility of negotiating priority access to national care and treatment programmes for individuals who are identified as HIV-positive during the screening process or who become HIV-positive during the trial.

g. Treatment regimens that will be available if the technology under study has the potential to give rise to antiretroviral resistance.

h. Local health institution responsibilities and proposed trial sponsor and implementer commitments regarding:

   i. Who will finance and who will deliver specific HIV care and treatment services.

   ii. The duration of HIV care and treatment services being provided by each partnering stakeholder.

i. The impact that any services offered by the trial, or to which participants will be referred, could have on local services.

4. Research teams and relevant stakeholders discuss the most appropriate way to ensure that all individuals screened and enrolled are aware of how to access the HIV care and treatment services.

5. Research teams and relevant stakeholders discuss and negotiate the gathering of information on how HIV care and treatment services are accessed throughout the course of the trial and beyond, such as numbers of seroconverters who access HIV care, barriers to accessing care at referral centres, or other issues that may arise.

6. Research teams maintain clear written records of all discussions and agreements. This includes relevant stakeholder

recommendations, actions taken by the research team, and any unresolved issues that require further follow-up.

7. Trial sponsors ensure that sites receive sufficient funding to deliver local agreements regarding access to HIV care and treatment. Research teams create a budget and allocate sufficient funds to ensure that the locally agreed HIV care and treatment package can be effectively delivered.

3.11.E. Additional guidance

1. *Ethical principles for medical research involving human subjects*.[5]
2. *Ethical considerations in biomedical HIV prevention trials* (guidance point 14, page 48, care and treatment).[10]
3. *Ethical considerations in biomedical HIV prevention trials* (page 13, selected circumstances in which biomedical HIV prevention trials should not be conducted).[10]
4. *Mapping the standards of care at microbicide clinical trial sites*.[24]

3.12. Non-HIV-related care

3.12.A. Definition

Non-HIV-related care refers to any health and social care services that are provided or made available to trial participants and that are not directly related to HIV prevention, HIV care and treatment, or research-related harm. The non-HIV-related care services appropriate for trial participants will depend on the trial population and the local health priorities. Examples could include provision of female or male sexual and reproductive health care, management of infectious diseases, nutritional health, psychiatric care, and psychological or psychosocial services.

3.12.B. Relevance to good participatory practice

Access to non-HIV-related care can provide benefits for participants and improve clinical trial outcomes. The provision of such services can contribute to the welfare of trial participants. Negotiating the range of non-HIV-related services available to participants at the trial site or via referral will assist in ensuring

that relevant stakeholders clearly understand the breadth of services available and reasons for inclusion and exclusion of certain services.

3.12.C. Special considerations

Non-HIV-related care packages may vary from site to site depending on local health priorities and local standards of care.

3.12.D. Good participatory practice standards for non-HIV-related care

1. Research teams identify the existence and capacity of local social care and primary health-care services, as well as secondary and tertiary diagnostic and treatment services. This enables appropriate referrals and linkages to be made should the need arise.
2. Research teams and relevant stakeholders discuss access to non-HIV care services during the trial's protocol development phase.
3. Research teams and relevant stakeholders discuss non-HIV-related care services to be offered to participants and consult with local social and health-care service providers when appropriate. Discussions take account of the following:
    a. Non-HIV-related care services that the trial protocol requires.
    b. Additional non-HIV-related care services that community stakeholders would like to see the trial site offer participants.
    c. Services that will be offered through referral mechanisms.
    d. Whether any non-HIV-related services will be available to partners of trial participants.
    e. The impact that any services offered or referred to by the trial could have on local services.
4. Research teams maintain clear written records of all discussions and agreements. This includes relevant stakeholder

recommendations, actions taken by the research team, and any unresolved issues.

5. Research teams create a budget and allocate sufficient funds to ensure provision of the locally discussed non-HIV-related care package.

3.12.E. Additional guidance

For additional guidance, see *Mapping the standards of care at microbicide clinical trial sites*.[24]

3.13 Policies on research-related harms

3.13.A. Definition

Policies on research-related harms describe how research teams will treat and compensate trial participants should they experience physical or social harms that are determined to be associated with trial participation, as well as how such harms will be addressed and mitigated.

3.13.B. Relevance to good participatory practice

Beneficence, or doing no harm, is a key ethical obligation of research teams. Relevant stakeholders can provide valuable input into discussions with research teams about possible social harms of trial participation. They can also provide advice about community expectations around the research team's obligations for research-related physical and social harms. Discussing with stakeholders before a trial starts and clearly explaining how research-related harms will be addressed and mitigated can significantly influence community perceptions of the trial and how well community stakeholder concerns are being addressed.

3.13.C. Special considerations

Sponsors typically give specific and binding guidance to research teams on how to determine and report physical harms as adverse events. It is good practice to define similarly stringent procedures for the determination, documentation, reporting, and manage-

ment of social harms that trial participants may experience. Examples of social harms due to trial participation may include stigma, discrimination, or bullying, as well as verbal, emotional, physical, or sexual abuse.

3.13.D. Good participatory practice standards for policies on research-related harms

1. Research teams create lists of anticipated physical and social harms that might occur due to trial participation.
2. Research teams and relevant stakeholders discuss and develop policies on research-related physical and social harms, considering the following issues:
    a. Strategies to prevent or reduce the risk of research-related harms.
    b. Procedures to actively probe participants and to encourage reporting of social harms.
    c. Procedures to investigate events that have been reported indirectly, such as through a third party, taking account of confidentiality issues.
    d. Procedures for reporting social harms, and whether these are to be reported to sponsors, ethics committees, and regulatory bodies if not specifically required by them.
    e. Compensation or insurance policies, when applicable, for specific research-related harms, coverage provided by the policies, how claims are made, and how participants are informed of their rights in relation to the policies.
3. Research teams and relevant stakeholders review follow-up strategies to reduce research-related physical and social harms over the course of the trial.
4. Research teams maintain clear written records of all discussions and agreements. This includes recommendations, actions taken by the research team, and any unresolved issues that require further follow-up.
5. Research teams create a budget and allocate sufficient funds to ensure effective management of physical and social harms related to research.

3.13.E. Additional guidance

1. *Ethical considerations in biomedical HIV prevention trials* (guidance point 11, page 40, potential harms).[10]
2. *International ethical guidelines for biomedical research involving human subjects* (guideline 19, right of injured subjects to treatment and compensation).[7]

3.14. Study accrual, follow-up and exit

3.14.A. Definition

Study accrual, follow-up, and exit activities include the recruitment, screening, enrolment, follow-up, and exit of trial participants in biomedical HIV prevention trials.

3.14.B. Relevance to good participatory practice

Community stakeholders can provide the best intelligence on how to design socially and culturally acceptable strategies for recruitment, screening, enrolment, follow-up, and exit. Community stakeholders included in the process of developing these strategies can play an important role in identifying and mitigating study-related stigma, misconceptions, or miscommunications.

3.14.C. Special considerations

1. While the processes of study recruitment and of stakeholder education are related, they are distinct (see Section 3.4).
2. Follow-up of participants after missed visits must respect agreements between the participant and research team about how to contact the participant.
3. Exiting a study may present changes in what participants have become accustomed to with regard to clinical care and the impact the study has had on their social relationships. Anticipation and discussion of these issues between research teams and community stakeholders will help in the development of appropriate strategies to support participants upon study exit.

3.14.D. Good participatory practice standards for study accrual, follow-up and exit

1. Research teams consult with relevant stakeholders about the accrual, follow-up, and exit processes, taking account of the following:
    a. Strategies and messages that are socially and culturally appropriate, meet the needs of specific stakeholders in terms of language and literacy level, and draw on a range of communication modes, including written, oral, and visual.
    b. Procedures to anticipate, monitor and mitigate trial-related stigma resulting from ineligibility to enrol or from enrolment itself.
    c. Strategies to ensure the confidentiality of participants at study visits, while following-up participants outside of the study clinic, and after study exit;
    d. Strategies to ensure that participants have the opportunity to receive study results and their study product assignment, when these become available.
    e. Procedures for transfer of care at the end of follow-up or study closure, such as providing participants with referrals to HIV counselling and testing and other supportive services.
2. Research teams provide relevant stakeholders with ongoing updates on trial accrual, follow-up and study exit.
3. Research teams seek advice from relevant stakeholders on how to improve accrual, follow-up, and exit processes and messages.
4. Research teams maintain clear written records of all discussions and agreements, as well as ongoing discussions about ways to modify strategies.

3.15. Trial closure and results dissemination

3.15.A. Definition

Trial closure occurs when all participants have exited from the trial and all study procedures are completed. Results dissemination

involves dissemination of study results to participants, community stakeholders, and the public at large, and the unblinding of participants to product assignment.

3.15.B. Relevance to good participatory practice

Community stakeholders in biomedical HIV prevention trials must be kept informed about when a trial ends and be among the first to be informed of the trial results. In the event that a trial is stopped early or unexpectedly, research team-initiated dialogue with relevant stakeholders will minimize the risk of misinformation. Effectively engaging relevant stakeholders about study closure and result dissemination in a transparent process is essential in building community trust and laying a positive foundation for future research.

3.15.C. Special considerations

1. Trials may run to completion per protocol, or they may be stopped early. Reasons for stopping early may be due to evidence of a clear protective effect, evidence of harm, or due to futility. Trials may also stop early due to other unforeseen circumstances, such as administrative or financial reasons, community objection, or sudden social unrest.
2. In multicountry or multisite trials, sites might complete participant follow-up at different times. Thus, while some sites might be closed for participant follow-up, research teams at other locations may continue to see participants.
3. Where trial product manufacturers are publicly traded companies, there may be legal requirements that affect the timing of and methods by which public announcement of a trial closure occurs.
4. Ownership of data, issues of publication, and release of trial results vary by trial and may be strictly delineated in non-negotiable terms by sponsors or product manufacturers.

3.15.D. Good participatory practice standards for trial closure and results dissemination

1. Research teams consult with relevant stakeholders to develop a trial closure plan. The plan addresses a range of possible closure scenarios, including:
    a. Early closure due to evidence of harm, futility, or clear protective benefit from interim analyses of trial data.
    b. Early closure because of evidence of harm or clear protective benefit from a different trial evaluating the same product.
    c. Early closure due to unforeseen circumstances, such as administrative or financial reasons, stakeholder objection, or sudden social unrest.
    d. Study closure as scheduled per protocol.
2. Research teams consult with relevant stakeholders to develop a results dissemination plan, detailing the following issues:
    a. Strategies to manage expectations about trial results by preparing participants and relevant stakeholders for all possible outcomes.
    b. Timelines for study closure at the site and at other sites, completion of data analysis, and availability of results.
    c. Procedures and timelines for who will be informed of trial results in confidence prior to public release and how results will be disseminated publically.
    d. Development and piloting of key messages, how the messages will be finalized when the results are known, and the range of communication methods to be used.
    e. How the messages will explain implications of the results for the local community, limitations of the trial, and its ability to generalize findings for specific aspects, such as by sex, behaviours, or location.
    f. Whether and how to disseminate additional findings that are not related to the primary trial question but that may be of interest to some stakeholders, for example reported

patterns of sexual networks, rates of various infections, or demographic data.

g. How participants will be informed of their product assignment at the time the results are released and beyond.

h. How community stakeholder responses to the results will be systematically collected and documented. Although community stakeholder agreement is not a prerequisite for publishing or sharing research in a scientific forum, it is important that community stakeholder interpretations be noted, particularly if they differ from the predominant scientific analysis.

i. Issues around ownership of the data, data access, and publication, including how the research team will facilitate community stakeholder access to published results of the trial.

3. Research teams maintain clear written records of all discussions regarding trial closure and dissemination messages, as well as documentation of responses to the results.

4. Research teams create a budget and allocate sufficient funds to ensure comprehensive dissemination of results for participants, the community, and other stakeholders.

3.16 Future access to new HIV prevention options

3.16.A. Definition

The term 'future access to new HIV prevention options' refers to the obligation to make the option tested available to trial participants and local communities should the new option be scientifically validated or approved by relevant authorities.

3.16.B. Relevance to good participatory practice

Ethical standards require that trial participants and local communities be among the first to gain access to new prevention options, should they be safe and effective. Community stakeholders must be made aware of this obligation and of the relevant issues concerning potential access to the option being tested.

3.16.C. Special considerations

1. Availability of newly identified options to trial participants and other community stakeholders will depend on the biomedical option being tested.
2. After a trial is completed, other trials may need to be completed to corroborate findings.
3. After results from all relevant trials are available, it may take time for normative agencies and appropriate regulatory authorities, including national governments, to approve the new option. Approval processes and timelines will differ by product.
4. National regulatory authorities make the ultimate decision about whether a new option will be approved for use within a particular country.
5. Availability and pricing of new options may be affected by product manufacturer parameters as well as by agreements with trial sponsors.

3.16.D. Good participatory practice standards for future access to new HIV prevention options

1. Research teams discuss with relevant stakeholders issues affecting future product availability, including the need for corroborated biomedical evidence, pursuit of licensure, production rights, and needs for additional marketing and distribution research.
2. Trial sponsors and research teams discuss, negotiate, and agree on responsibilities and funding requirements with national governments on licensure requirements and access issues, should the HIV prevention option under investigation be safe and effective.
3. Trial sponsors and research teams develop a clear strategy and funding mechanisms for how the HIV prevention option will be made available to participants (at a minimum) rapidly, affordably and sustainably, should the HIV prevention option be safe and effective. Sponsors and research teams can collaborate with multiple stakeholders, such as

UN organizations, development partners, local governments, and nongovernmental organizations, to design and support the overall strategy.

4. Research teams inform community stakeholders of their rights, the access plan, and the factors that could postpone or prevent their gaining access to the new prevention option, such as the need to secure regulatory approvals or parameters related to the product manufacturer. Research teams give community stakeholders updates as they are available.

3.16.E. Additional guidance

1. *Ethical considerations in biomedical HIV prevention trials* (guidance point 19, page 60, availability of outcomes).[10]
2. *Rethinking the ethical roadmap for clinical testing of microbicides: report on an international consultation* (chapter 10, after the trial: continued access and post-approval studies).[26]
3. *Ethical and policy issues in international research: clinical trials in developing countries* (recommendation 4.1).[27]

Conclusion

These GPP guidelines set global standards in stakeholder engagement. Adherence to good participatory practice standards is an investment that benefits the research process by facilitating the engagement of all stakeholders and achieving mutual gains in local capacity-building and biomedical HIV prevention research. Although the investment required is long-term, funding is generally bound by the implementation of specific trials and often ceases after trial completion. From the perspective of stakeholder engagement, it is highly beneficial to maintain and support key staff at trial sites and sustain relationships that have been developed with local partners. Ongoing engagement allows the fostering of relationships with local nongovernmental organizations and community-based organizations to improve research literacy and develop and expand the local research agenda between trials. Collaboration between trial funders, sponsors, and implementers with relevant stakeholders such as academic institutions, ministries of health and nongovernmental organizations, is key to securing such ongoing engagement to maintain new or less established trial sites which are in between funded trials.

Well-conducted biomedical HIV prevention trials are in everyone's best interest. They are essential to discover additional options to reduce new HIV infections worldwide. Good participatory practice during the entire life-cycle of a biomedical HIV prevention trial can enhance both the quality and outcomes of research. Developing participatory processes that balance the opinions of all stakeholders while serving to achieve the scientific goals of a trial can ensure that the needs of both the communities participating in a trial and the broader HIV prevention field are met.

In a forward-looking approach, it is important to gather and analyse stakeholders' experiences with the implementation of these GPP guidelines. Recommendations for modifications and refinements based on experience and reflection should be sent by email to gpp@unaids.org or avac@avac.org, where they will be gratefully received and considered in future updates of these guidelines.

Appendix 1: Acronyms

AIDS - Acquired Immune Deficiency Syndrome

AVAC - Global Advocacy for HIV Prevention

CAB - Community Advisory Board

CAG - Community Advisory Group

CBO - Community-Based Organisation

CIOMS - Council for International Organizations of Medical Science

GCLP - Good Clinical Laboratory Practice

GCP - Good Clinical Practice

GPP - Good Participatory Practice

HIV – Human Immunodeficiency Virus

NGO - Non-governmental organisation

PEP - Post-exposure prophylaxis

PrEP - Pre-exposure prophylaxis

PMTCT - Prevention of mother-to-child-transmission

UNAIDS - The Joint United Nations Programme on HIV/AIDS

WHO - World Health Organisation

Appendix 2. Glossary

accrual. The process of recruiting participants into a trial to reach target participant numbers.

acquired immune deficiency syndrome (AIDS). The late stage of HIV disease, characterized by deterioration of the immune system and a susceptibility to a range of opportunistic infections and cancers.

activist. A person or group that is usually from outside of the system and that works to bring about change in the system.

adverse event. An unwanted effect reported by a participant in a clinical trial. This may or may not be related to the product being studied.

advocate. A person or group that acts on behalf of individuals or groups.

antiretroviral drugs. Medications that control HIV by interrupting the ability of HIV to make copies of itself.

AVAC: Global Advocacy for HIV Prevention. An international, non-profit organization that uses education, policy analysis, advocacy, and community mobilization to accelerate the ethical development and eventual global delivery of AIDS vaccines and other new HIV prevention options as part of a comprehensive response to the pandemic.

blinded trial. A randomized trial designed to prevent the participants, research teams, or both from knowing which participants are in the experimental group and which are in the control group of the study, in order to reduce bias.

clinical trial. A research study or experiment in humans (as opposed to animals) that is designed to answer specific questions.

community (per the GPP guidelines). People living in the trial catchment area.

community advisory boards, also referred to as **community advisory groups.** A formal stakeholder advisory mechanism composed of community members or representatives that meet regularly with research team representatives. Community advisory boards or groups

inform community stakeholders about proposed and ongoing research. As an independent advisory voice, a community advisory board provides feedback to research teams about community norms and beliefs, as well as community views and concerns around specific trials.

community-cased organizations. Civil society, non-profit organizations that operate within a local community. Community-based organizations are distinct from non-governmental organizations in that a community-based organization tends to be a membership organization aimed at furthering the interests of its own members, whereas a non-governmental organization tends to have a broader scope of activities that might assist community-based organizations and pursue commitments that do not directly benefit nongovernmental organization members.

confidentiality. Refers to the right of trial participants to protection from unauthorized disclosure of personal information to third parties during data collection, storage, transfer, and use.

control group. The standard by which experimental observations are evaluated. In many clinical trials, one group of participants is given an experimental product, while the control group is given either a standard treatment or a placebo.

data and safety monitoring boards. An independent committee established by the sponsor to review data while a clinical trial is in progress to ensure that participants are not exposed to undue risk. A data and safety monitoring board may recommend that a trial be stopped or modified if there are safety concerns or if the trial objectives have been achieved.

ethics committee. An independent body made up of medical, scientific, and non-scientific members whose responsibility is to ensure the protection of the rights, safety, and well-being of human participants involved in a trial. Ethics committees review, approve, and provide continuing review of the trial protocol and amendments and of the methods and materials to be used in obtaining and documenting informed consent of the trial participants. Generally the United States of America uses the term 'institutional review board' and other countries use the term 'ethics committee' or 'independent ethics committee'.

experimental group. The group in the trial that receives the product being studied, while the control group is given either a standard treatment or a placebo.

female condoms. A strong, soft, transparent polyurethane sheath that, when inserted in the vagina, or onto the penis in the case of anal sex, before vaginal or anal intercourse, provides protection against most sexually transmitted infections, including HIV, and pregnancy. Currently made of polyurethane (female condom 1) or a synthetic latex (female condom 2), it is stronger than the natural latex used in male condoms, odourless, non-allergenic, and usable with oil-based and water-based lubricants. It can be inserted vaginally prior to intercourse, is not dependent on male erection, and does not require immediate withdrawal after ejaculation.

formative research activities. Activities that enable research teams to gain an informed understanding of the local population, sociocultural norms and practices, local power dynamics, community perceptions, channels of communication and decision-making, and history of research in the area, as well as an informed understanding of the needs and priorities of the people living in the trial catchment area.

futility. Refers to the expected inability of a clinical trial to achieve its objectives. This determination may be suggested during an interim analysis of the trial.

good clinical laboratory practice. Guidelines that set a standard for compliance by laboratories involved in the analysis of samples from clinical trials. These guidelines were written to ensure that trial laboratory data are repeatable, reliable, auditable, and easily reconstructed in a research setting.

good clinical practice. Internationally recognized guidelines for designing, conducting, recording, and reporting clinical trials in which humans participate. These guidelines were issued by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use and adherence is required by law in the European Union. Following the guidelines helps to ensure that the participants are protected and that the data collected are accurate.

human immunodeficiency virus (HIV). The virus that weakens the immune system, ultimately leading to AIDS.

implementers. See 'trial implementer'.

informed consent. A process by which a participant voluntarily confirms his or her willingness to participate in a particular study after having been informed of all aspects of the trial that are relevant to the participant's decision to participate. Informed consent is a continuing process throughout the study life-cycle.

institutional review board. See 'ethics committee'.

medical male circumcision. The surgical removal of the entire foreskin of the penis. Reasons for male circumcision include both hygienic concerns as well as religious indications, and male circumcision's prevalence is geographically dependent on the cultural practices of the local populations. Three clinical trials conducted in sub-Saharan Africa have shown that medically performed circumcision is safe and can reduce men's risk of HIV infection during vaginal sex by about 60%.

men who have sex with men. Men who report sexual contact with other men, regardless of whether or not they have sex with women or have a personal or social gay or bisexual identity. This concept is useful because it also includes men who self-identify as heterosexual but have sex with other men. There is clear evidence that men who have sex with men and transgender people are disproportionately at risk of HIV infection.

microbicides. A range of products that could be used vaginally or rectally (such as a gel or cream) that are being tested and may reduce or prevent the transmission of HIV and other disease-causing organisms during sex. Microbicides might also take other forms, including films, suppositories, and slow-releasing sponges or vaginal rings. The development of safe and effective microbicides could help many women and men who have sex with men substantially lower their risk of HIV infection.

network, or **research network.** A cooperative of research institutions or centres conducting clinical trials under a common research agenda.

nongovernmental organizations. Legally constituted, non-profit organizations with specific missions and goals that operate outside of

government, often in the private sector. While some receive government funding, their decisions are independent of government. Nongovernmental organizations may be local, national, or international. They often assist local non-profit organizations with specific projects consistent with the mission of the nongovernmental organization.

placebo. An inactive substance designed to resemble the product being studied that is administered to some study participants while others receive the active agent under evaluation in order to provide a basis for comparison of effects.

post-exposure prophylaxis. Antiretroviral medicines prescribed and taken after exposure or possible exposure to HIV. The exposure may be occupational, as in a needle stick injury, or non-occupational, as in the case of rape.

pre-exposure prophylaxis (PrEP). An experimental approach that would use antiretroviral medications (which are normally used to treat people living with HIV) to reduce the risk of HIV infection in HIV-negative people. In this intervention, HIV-negative people would take a single drug or a combination of drugs with the hope that it would lower their risk of infection if exposed to HIV. PrEP trials are ongoing around the world.

preventive HIV vaccine (or AIDS vaccine). A vaccine designed to prevent HIV infection or AIDS.

protocol. A document that details the goals, design, methodology, statistical considerations, and organization of a study or clinical trial. The clinical trial protocol will have a study plan that describes what types of people may participate in the trial, the schedule of tests, procedures, medications and dosages, and the length of the study. The plan is carefully designed to safeguard the health of the participants as well as to answer specific research questions.

randomization. A process by which trial participants are assigned to a study arm to assure that the different treatment arms are 'statistically equivalent'. Randomization minimizes the differences among groups by equally distributing people with particular characteristics among all the trial arms.

randomized trial. A study in which participants are assigned by chance to one of the study arms. Also referred to as a 'randomized-controlled trial'.

regulatory authorities. Government agencies charged with carrying out the intent of legislation that constrains the actions of private individuals, businesses, or government bodies. In most countries, one or more regulatory agency may be responsible for ensuring the safety and effectiveness of health products and of clinical trials.

research network. See 'network'.

research team. The group of investigators and staff involved in implementing biomedical HIV prevention trials. Research teams can include investigators and staff at a specific trial site as well as investigators and staff working at coordinating centres or central agencies.

scientific process. A recognized systematic way to form and test hypotheses by designing controlled experiments to collect data, analyse results and make conclusions to acquire new knowledge, or correct and integrate previous knowledge.

seroconversion. The development of detectable antibodies in the blood directed against an infectious agent. When an individual who was HIV-negative becomes infected with HIV, their body produces antibodies against the infection.

sexually transmitted infections. Infections that are often or usually passed from one person to another during sexual or intimate contact.

stakeholders. Individuals, groups, organizations, governments, or other entities that are affected by the outcome of a biomedical HIV prevention trial or that can influence the outcome of proposed research through their input and actions.

standard operating procedure. A document that gives step-by-step instructions for how to do a procedure, in order to ensure that everyone can perform the procedure in the same way.

stigma. AIDS-related stigma refers to a pattern of prejudice, discounting, discrediting, and discrimination directed at people perceived to have HIV or AIDS, their significant others and close associates, and their social groups and communities.

therapeutic HIV vaccine. A vaccine designed to boost the immune response to HIV in a person already infected with the virus. Also referred to as an immunotherapeutic vaccine.

trial funder. An individual or entity responsible for financing the cost of a trial.

trial implementer. Investigators, research staff, and all others specifically responsible for executing biomedical HIV prevention trials. Implementers may be employed by governments, government-sponsored networks, non-governmental organizations, academic institutions, the pharmaceutical industry, and other companies, foundations, or public–private partnerships.

trial life-cycle. The entire process of the trial, starting from developing the concept and continuing through to the completion of the trial and dissemination of results.

trial sponsor. An entity that is responsible for a trial but that does not actually conduct the investigation. The sponsor may be a pharmaceutical company, governmental agency, academic institution, or private or other organization.

UNAIDS (Joint United Nations Programme on HIV/AIDS). A joint venture of 10 UN organizations in the AIDS response to help prevent new HIV infections, care for people living with HIV, and mitigate the impact of the epidemic. UNAIDS is the main advocate for accelerated, comprehensive and coordinated global action on the HIV epidemic.

unblinding. The notification of each participant following a 'blinded trial' as to their study product assignment.

vaccine. A substance that stimulates the body's immune response in order to prevent or control an infection. A vaccine is typically made up of some part of a bacteria or virus that cannot itself cause an infection.

The internet is a rich source of additional information about HIV generally. The following links to glossaries may be useful:

http://www.sfaf.org/glossary
http://www.aidsinfo.nih.gov
http://www.aegis.com/ni/topics

Appendix 3. Additional guidance

International reference guidelines

Belmont Report, 1979

This report was written by the US National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, which was established after the US public learned about the Tuskegee Syphilis Study.

Citation: National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. *The Belmont Report: ethical principles and guidelines for the protection of human subjects of research*. Washington, DC, Department of Health, Education, and Welfare, 1979.

http://ohsr.od.nih.gov/guidelines/belmont.html

Declaration of Helsinki, 1964

This declaration of the World Medical Association is often considered to be the first document to set world standards for research on human participants.

Citation: World Medical Association. *World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects*. Helsinki, World Medical Association General Assembly, 1964; latest amendment at the 59th WMA General Assembly, Seoul, 2008.

http://www.wma.net/en/30publications/10policies/b3/17c.pdf

Ethical considerations in biomedical HIV prevention trials, 2007

This is an ethical guidance document, issued by UNAIDS and WHO, for biomedical HIV prevention research. This document is a revision of the *Ethical considerations in HIV preventive vaccine research*. UNAIDS guidance document. Geneva, UNAIDS, World Health Organization, 2000.

Citation: *Ethical considerations in biomedical HIV prevention trials.* UNAIDS guidance document. Geneva, UNAIDS, World Health Organization, 2007.

http://data.unaids.org/pub/Report/2007/jc1399_ethical_considerations_en.pdf

Guideline for good clinical practice, 1996

These guidelines were issued by the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use and outline an international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve human subjects.

Citation: *Guideline for good clinical practice*. ICH harmonised tripartite guideline. Geneva, International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use, 2006.

http://www.ich.org/LOB/media/MEDIA482.pdf

***International ethical guidelines for biomedical research involving human subjects,* 1993**

These guidelines were published by the Council for International Organizations of Medical Science (CIOMS) and added guidance around conducting research in developing countries to the body of ethical guidelines. The 2002 version supersedes the 1982 and 1993 guidelines.

Citation: *International ethical guidelines for biomedical research involving human subjects*. Geneva, Council for International Organizations of Medical Sciences, 2002.

http://www.cioms.ch/frame_guidelines_nov_2002.htm

Nuffield Council on Bioethics, 2002

The 2002 Nuffield Council on Bioethics report on the ethics of research related to health care in developing countries provided an ethical framework for designing or conducting externally sponsored research in the developing world. The 2004 follow-up report, co-hosted with the Medical Research Council of South Africa, discussed how

the guidelines could be applied in practice, particularly in light of conflicting ethical advice.

Citation: *The ethics of research related to healthcare in developing countries*. London, Nuffield Council on Bioethics, 2002, and *The ethics of healthcare related research in developing countries: a follow-up discussion paper.* London, Nuffield Council on Bioethics, 2005.

http://www.nuffieldbioethics.org/fileLibrary/pdf/errhdc_fullreport001.pdf

Nuremberg Code, 1949

This code of research ethics came out of the ruling of the International Military Tribunal at the end of the Second World War, which prosecuted Nazi war criminals.

Citation: *Trials of war criminals before the Nuremberg Military Tribunals under Control Council Law No. 10.* Washington, DC, US Government Printing Office, 1949.

http://ohsr.od.nih.gov/guidelines/nuremberg.html

Ethical and policy issues in international research: clinical trials in developing countries, 2001

A report and set of recommendations of the US National Bioethics Advisory Commission for US policy regarding conducting clinical trials in developing countries.

Citation: US National Bioethics Advisory Commission. *Ethical and policy issues in international research: clinical trials in developing countries. Volume I: report and recommendations of the National Bioethics Advisory Commission*, 2001.

http://bioethics.georgetown.edu/nbac/pubs.html

Other references

***Communications handbook for clinical trials: strategies, tips, and tools to manage controversy, convey your message, and disseminate results,* 2010**

The *Communications handbook for clinical trials* is a practical guide developed for site-level researchers, communicators, advocates, and others working on HIV prevention trials in developing countries. It provides guidance on how to anticipate and respond to the special communications challenges posed by the conduct of clinical research.

Citation: Robinson ET et al. *Communications handbook for clinical trials: strategies, tips, and tools to manage controversy, convey your message, and disseminate results*. Microbicides Media Communications Initiative and FHI, 2010.

http://www.fhi.org/NR/rdonlyres/eojrbfqk5sxmkto7t7clepl445k-zisntxzccl7lmqvl5j7ferzdalabnow6gb5weccrn5utvueuphp/CommhandbkFrontMatter1.pdf

Mapping the standard of care at microbicide clinical trial sites, 2008

The Global Campaign for Microbicides mapped the standard of care being provided across various microbicide clinical trial sites. The report resulted in a set of recommendations relating to the standard of care that should be provided to participants in microbicide clinical trials.

Citation: Heise L, Shapiro K, West Slevin K. *Mapping the standards of care at microbicide clinical trial sites*. Washington, DC, Global Campaign for Microbicides, 2008.

http://www.global-campaign.org/clientfiles/SOC.pdf

***Recommendation for community involvement in national institute of allergy and infectious diseases, HIV/AIDS clinical trials research,* 2009**

The National Institute of Allergy and Infectious Diseases (NIAID) Division of AIDS (DAIDS) and Community Partners developed these recommendations as a tool for researchers and community representatives to further expand and deepen good community practice.

Citation: *Recommendation for community involvement in National Institute of Allergy and Infectious Diseases, HIV/AIDS clinical trials research*. Community recommendations. Working Group of Community Partners, 2009.

http://www.hanc.info/cp/resources/Pages/recommendationsInvolvement.aspx

***Rethinking the ethical roadmap for clinical testing of microbicides: report on an international consultation,* 2005**

In 2003, the Global Campaign for Microbicides held a consultation to rethink the issues and ethical dilemmas facing the field of microbicide development. The report addresses ethical issues such as informed consent, standards of care, and post-trial access.

Citation: *Rethinking the ethical roadmap for clinical testing of microbicides: report on an international consultation*. Washington, DC, Global Campaign for Microbicides, 2005.

http://www.global-campaign.org/researchethics.htm

***Standard of prevention in HIV prevention trials,* 2010**

In March 2009, the Global Campaign for Microbicides, UNAIDS, and the US Centers for Disease Control and Prevention jointly convened a consultation on the Standards of Prevention in HIV Prevention Trials in Kampala, Uganda. The resultant report summarizes the points of agreement and proposes a range of recommendations for standards of prevention in future HIV prevention clinical trials.

Citation: *Standards of prevention at HIV prevention trials: consultation report and recommendations*. Global Campaign for Microbicides, PATH, 2010.

http://www.global-campaign.org/clientfiles/SOP-report-FINAL-.pdf

Endnotes

1 Arnstein SR (1969). A ladder of citizen participation. *Journal of the American Institute of Planners*, 35:216–224.

2 *Guideline for good clinical practice* (2006). ICH harmonised tripartite guideline. Geneva, International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. Available at http://www.ich.org/LOB/media/MEDIA482.pdf.

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The Joint United Nations Programme on HIV/AIDS (UNAIDS) brings together ten UN agencies in a common effort to fight the epidemic: the Office of the United Nations High Commissioner for Refugees (UNHCR), the United Nations Children's Fund (UNICEF), the World Food Programme (WFP), the United Nations Development Programme (UNDP), the United Nations Population Fund (UNFPA), the United Nations Office on Drugs and Crime (UNODC), the International Labour Organization (ILO), the United Nations Educational, Scientific and Cultural Organization (UNESCO), the World Health Organization (WHO), and the World Bank.

Leveraging the AIDS response, UNAIDS works to build political action and promote the rights of all people for better global health and development results. Globally it sets policy and is the source of HIV-related data. In countries UNAIDS brings together the resources of the UNAIDS Secretariat and its 10 Cosponsors for a coordinated AIDS response.

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