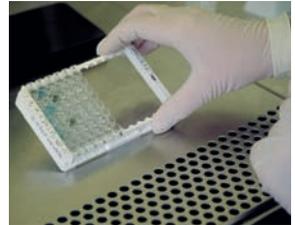


Good participatory practice guidelines for biomedical HIV prevention trials



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Cover photos: S Noorani/UNAIDS, L Gubb/UNAIDS,
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UNAIDS/07.30E / JC1364E (English original, November 2007)

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WHO Library Cataloguing-in-Publication Data

Good participatory practice : guidelines for biomedical HIV
prevention trials.

« UNAIDS / 07.30E ».

1.HIV infections - prevention and control. 2.Acquired immuno-
deficiency syndrome - prevention and control. 3.Biomedical
research. 4.Consumer participation. 5.Community networks.
I.UNAIDS.

ISBN 978 92 9 173634 8 (NLM classification: WC 503.6)

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Printed in France

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Acknowledgements

UNAIDS and AVAC gratefully acknowledge the contribution of the Working Group which oversaw the creation of *Good participatory practice guidelines for biomedical HIV prevention trials*, providing comments and suggested wording as well as keeping the editorial group focused.

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We would also like to express our sincere appreciation to Emily Bass who conducted interviews and drew comments together into working drafts; Charles Wiysonge, Tania Lemay, Jolene Nakao and Constance Kponvi who assisted with logistics and editing of various drafts; Jennifer Sarché, Anne-Christine d'Adesky, and Elizabeth McGrory who conducted additional interviews, and Lon Rahn who did the layout.

These guidelines were refined with assistance from many individuals who responded to requests for comments via interviews, through email requests and following listserv postings. We would like to warmly thank them for the practical and useful feedback they provided on a prior draft of this document. These individuals and their organizations represented a diverse range of perspectives, geography and expertise. They included researchers, policy makers, industry representatives, research funders and sponsors, clinical trial investigators, trial site staff, community liaison officers, community advisory board members and advocates.

These guidelines are intended to complement the companion document Ethical considerations in biomedical HIV prevention trials published in 2007 by UNAIDS and WHO. Both documents are available initially in English, Spanish, French, Russian, Chinese, Arabic, Portuguese, Thai, Khmer and Vietnamese.

In the coming months and years, it is expected that these Good participatory practice guidelines for biomedical HIV prevention trials will be applied, validated, and revised through field-based use, consultation and discussion. Comments and feedback are welcomed by email at gpp@unaids.org.

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PROLOGUE

In 2005, a series of regional consultations convened by the Joint United Nations Programme on HIV/AIDS (UNAIDS) in Abuja, Nigeria; Pattaya, Thailand; and Durban, South Africa culminated in an international consultation in Geneva of investigators, ethicists, community stakeholders, government representatives, and advocates drawn from all regions. These meetings focused on defining the key elements needed for creating effective partnerships for HIV prevention trials and addressing lessons learned during the cancellation or closure of pre-exposure prophylaxis (PrEP) trials in Cambodia and Cameroon. Consensus was achieved on a number of recommendations¹ including one on the need for guidelines on good community practice. A working group was formed by UNAIDS, assisted by the AIDS Vaccine Advocacy Coalition (AVAC), to shepherd the drafting of guidelines. The draft guidelines were then further refined through broad consultation involving a wide range of stakeholders.

These Good Participatory Practice guidelines aim to provide systematic guidance on the *roles and responsibilities* of entities funding and conducting biomedical HIV prevention trials towards participants and their communities. Such entities include investigators, research staff, pharmaceutical industry sponsors, foundations, government-supported research networks, non-governmental research sponsors, and all others involved in designing, financing, and executing clinical trials research. The implementation of these guidelines would be facilitated by the inclusion of individuals on the research team who are trained in community literacy and skilled in effective and appropriate community mobilisation. The trials in question test interventions and products for reducing HIV risk such as vaccines, microbicides, oral chemoprophylaxis, vaginal barrier methods, herpes simplex virus-2 (HSV-2) suppression or treatment, index patient treatment, and other strategies. They also

can include implementation trials of biomedical interventions such as male circumcision which have been found to be effective.

Effective *community* engagement during the entire life-cycle of a biomedical HIV prevention trial, and beyond, through genuine, transparent, meaningful participatory processes enhances both the quality and outcome of research.² Well-conducted biomedical HIV prevention trials are essential to discover the additional risk reduction options that are urgently required to expand efforts to stem the tide of new HIV infections worldwide.

Although this guidance document seeks first and foremost to provide a foundation for systematizing the engagement with communities that research entities should strive for, communities themselves have roles and responsibilities too. Models for community participation exist in other disciplines and areas of health promotion³ and there is an expanding literature on participatory approaches and their results.^{4,5} Additional materials with a primary focus on the roles and responsibilities of potential trial participants, activists, advocates, non-governmental organisations (NGO) and other community members may emerge as these guidelines are discussed and implemented.

These *Good participatory practice guidelines for biomedical HIV prevention trials* will be of use to civil society groups in their advocacy for well-conducted clinical trials. Although not addressed specifically, those engaged in trials of new therapeutics, such as antiretroviral medications for treating HIV-related disease, or in HIV prevention trials assessing behavioural or other HIV prevention modalities may find them relevant.

INTRODUCTION

Great strides have been made in reaching communities affected by biomedical HIV prevention trials with information, discussion fora and skills-building that effectively empower them to work as partners with researchers in critical aspects of trial design and conduct. However, there is no existing, standard and internationally recognized guidance that primarily addresses ‘*Good participatory practice*’ and community engagement in biomedical HIV prevention trials.

Increasing the awareness of researchers, funders, trial participants, and community stakeholders of essential good practices for community engagement through these guidelines can help reduce unnecessary conflict, confusion, or non-constructive criticism and ensure that research is meaningful, applicable, and correctly interpreted. Serving as a reference for negotiating agreements about basic Good Participatory Practice elements for optimum trial conduct and related investments of necessary human and financial resources, this guidance document for those who conduct, fund, participate in and assess trial conduct can act as a positive incentive for all parties to strive for effective community involvement.

Essential practices for other aspects of clinical trials conduct are found in guidance documents such as the Good Clinical Practice (GCP) standards⁶ of the International Conference on Harmonisation, the standards for Good Clinical Laboratory Practice (GCLP)⁷, and others.^{8,9} Clinical trial sites use these standards to guide practice and independent monitors verify that sites meet them, ensuring consistency in practice regardless of where the trial takes place. National governments also regulate the conduct of clinical trials, with many countries having well-developed guidance. A number of documents addressing the ethical aspects of HIV prevention trials touch on standards of community engagement but do not provide much detail on mechanisms for achieving them.^{10, 11, 12, 13} The UNAIDS/WHO 2007 ‘*Ethical considerations in biomedical HIV prevention trials*’¹⁴ contains explicit guidance on community participation, capacity building,

monitoring informed consent, standard of prevention, and other key ethical issues in 19 guidance points.

Well-conducted biomedical HIV prevention trials are both scientifically rigorous and include active community involvement expediting ethical research conduct. These Good Participatory Practice guidelines for biomedical HIV prevention trials are grounded in the mutual objectives of all stakeholders to expand safe, effective prevention choices within comprehensive, combination HIV prevention programming.

Questions and concerns arise about how to protect the rights of trial participants and their surrounding communities in light of the tremendous disparities in power, wealth, education and literacy which often exist between the individuals proposing to conduct research and those who are hardest hit by the HIV epidemic. Such concerns in placebo-controlled and other randomised controlled trials play out under the close scrutiny of ethicists, advocates, and activists.^{15,16} Planned trials may be cancelled while trials underway may be closed prematurely¹⁷ when it is perceived that affected communities have not been adequately involved in trial design and conduct.

International guidance documents on research ethics such as the Declaration of Helsinki⁸ and the guidelines of the Council for International Organizations of Medical Sciences (CIOMS)¹⁸ provide a broad framework for participants' rights such as the right to bodily integrity, to participate in research which is asking a legitimate scientific question, to have access to interventions which prove effective, and other rights. These documents do not directly address issues such as whether trial sponsors should make treatment and care available to trial participants who become HIV infected during the course of a trial, nor do they set minimum expectations regarding such instances.

Guidance point 2 of the 2007 UNAIDS document *Ethical considerations in biomedical HIV prevention trials*¹⁴ emphasises the importance of community involvement:

‘To ensure the ethical and scientific quality and outcome of proposed research, its relevance to the affected community, and its acceptance by the affected community, researchers and trial sponsors should consult communities through a transparent and meaningful participatory process which involves them in an early and sustained manner in the design, development, implementation, monitoring and distribution of results of biomedical HIV prevention trials.’

Following the appearance of the first edition of similar UNAIDS guidelines in 2000¹³, trials of HIV vaccine candidates and other HIV prevention modalities widely adopted a community engagement approach. Multiple HIV prevention trials in a wide range of contexts have now documented context-specific questions about ethical trial conduct, community engagement and specific trial experiences in rich descriptive accounts of work in the field.^{1, 19, 20, 21, 22} These valuable reports reflect the ways in which HIV prevention trial stakeholders have developed together donor-, network-, site-, or institutional-level approaches to community engagement. The crux of the challenge in defining the “community engagement” approach arises from the broad terms “community”²³ and “engagement”, the meaning of which may shift depending on the audience.

If in the process of answering questions about the ethics of biomedical HIV prevention trials a trial is delayed or stopped, this may be the result of a system of checks and balances, protective for researchers, sponsors, trial participants and communities alike, which is intended to ensure that research is neither perceived as being or is in fact exploitative of individuals or communities. Finding mutual solutions in a timely fashion is critical to meeting the goal of discovering new ways to prevent HIV, including providing additional protection against HIV acquisition to community members as soon as possible. The demand for new HIV risk reduction measures is high and efforts to find new strategies for HIV prevention must proceed at a speed that is commensurate with the gravity of the epidemic.

Although communities clearly can and should have a voice in whether a trial takes place, what optimal products or interventions should be studied, and how the trial is conducted, there are limitations on the extent to which trial protocols can be altered while staying true to their scientific goals. Standard trial procedures start with small safety studies (phase I), progressing to expanded safety (and immunogenicity, in the case of vaccines) investigations (phase II) and then to large-scale efficacy trials (phase III). Preparing for the conduct of phase I and II trials can build community research literacy and test mechanisms for community engagement; the design and conduct of phase III trials, however, require effective community engagement at all stages. Phase IV trials assess the effectiveness during roll-out under real world conditions of an intervention already proven to be efficacious in a Phase III trial.

Communities or groups of individuals may be poor, marginalized and even criminalized or may lack the information, skills or power to raise concerns about research. Identifying the critical elements of best practices for building relationships with various communities, particularly with these communities, as part of the research process is the objective of these Good Participatory Practice guidelines. Standardized core principles, roles and responsibilities of research entities, and activities related to community engagement in the context of biomedical HIV prevention trials laid out in this document can provide a foundation for discussions and conflict resolution between various groups, enhancing the innovative, often groundbreaking HIV prevention research taking place in communities worldwide. While recognizing that social, political, and economic structural issues may create significant challenges to the full implementation of these guidelines, documenting and sharing experiences in implementing these guidelines will contribute significantly to the constructive evolution of research policy and practice around the world.

CORE PRINCIPLES

Ten fundamental principles for Good Participatory Practice underpin this guidance for researchers, trial sponsors, and research site staff on how to work toward achieving adequate standards of community engagement, participation and input throughout the life-cycle of a biomedical HIV prevention trial. These core principles, referenced throughout the document, form a foundation for evaluating existing community engagement efforts and creating new approaches.

1. Scientific and ethical integrity
2. Respect
3. Clarity in roles and responsibilities
4. Towards shared responsibility
5. Participatory management
6. Autonomy
7. More transparency
8. Standard of prevention
9. Access to care
10. Building research literacy

Scientific and ethical integrity

Maintaining the highest standards of scientific and ethical integrity, including adherence to the universal ethical principles of respect for persons, beneficence and justice, is fundamental to achieve the scientific goals of a biomedical HIV prevention trial, maximise the benefits for the trial community, and advance science in the interests of global HIV prevention.

Respect

Mutual respect among all stakeholders is key to effectively communicating, fostering trust,²⁴ and developing partnerships to achieve mutual goals. Respect for communities includes respect for communal values; protecting and empowering social institutions; and, where applicable, abiding by the decisions of legitimate communal authority²⁵. Respect for research includes respect for the scientific method and for the importance of maintaining scientific and ethical integrity in order to achieve valid trial results.

Clarity in roles and responsibilities

Articulating expectations and negotiating to achieve a clear understanding of the diverse roles and responsibilities of all biomedical HIV prevention trial stakeholders is the first step in creating an effective framework for community engagement. Mechanisms for monitoring these roles and responsibilities together through the research life cycle, evaluating the need for changes, and making any required mid-course modifications should be defined from the start.

Towards shared responsibility

Researchers, trial funders, research site staff, local authorities (including health authorities), and the community of people affected by a trial (including trial participants, family members, community leaders, and related advocacy groups) should work jointly to develop and conduct ethical biomedical HIV prevention trials whose goals, risks, and benefits are clearly understood and supported by all stakeholders. Shared responsibility commits all stakeholders to work in partnership towards the achievement of study goals and to honour the commitments that they have made to one another throughout the research lifecycle, from initial outreach to dissemination of research results.

Participatory management

Communities of people affected by research should play an active, informed role, working throughout trial conduct with site research staff and the principal investigator who is responsible for all aspects of a trial, including efforts to enhance community participation. Acknowledging structural power imbalances and striving to overcome these is an overarching concern for all parties. Participatory management requires that communities strive for the best possible representation in terms of inclusivity and parity for the values, norms, and behaviours of those affected by the research process.²⁶ Participatory management benefits all parties; helps ensure smooth trial functioning; and builds community capacity to understand and inform the research process, raise concerns, and help find solutions to unexpected issues that may emerge once the trial is underway.

Autonomy

The principle of autonomy highlights the importance of the independence of established community advisory mechanisms. Researchers and trial site staff must pay close attention to possible conflicts of interest that may inhibit collective critical input of participating community members and strive to create conditions to minimise these.

More transparency

Open and honest communication is fundamental to Good Participatory Practices. The principal investigator and research staff should strive to provide clear, comprehensible, and timely access to trial-related information for communities affected by research. Protocols, communications plans, community education materials, and deliberations related to a trial that are public knowledge should be made readily available for community partners in appropriate formats, summarized and translated when appropriate. Decisions taken at other levels which might affect site trial conduct should be communicated in a timely

fashion. Plans for data analysis, interpretation of findings and dissemination of results should to be discussed and agreed upon at the onset, taking into account, when necessary, the need to maintain confidentiality of proprietary and other information prior to official public release of findings. Communities have a responsibility to raise issues with researchers and propose constructive suggestions for solutions to improve trial conduct. Communication should be multi-directional, continually feeding back from site to community and community to site, from local site level to international network and back, etc.

Standard of prevention

Researchers, research site staff, and trial sponsors have an ethical responsibility to ensure that appropriate risk-reduction counselling and access to proven HIV prevention methods are provided to all biomedical HIV prevention trial participants throughout the duration of the trial as an integral component of the research protocol.

Access to care

This principle reinforces core tenets of the Declaration of Helsinki and CIOMS guidelines stating that trial participants have the right to access medical care for trial-related injuries and harm, and to the experimental product under investigation should it prove effective. In the specific context of biomedical HIV prevention trials, participants who acquire HIV infection during the conduct of the trial have the right to access a comprehensive package of care, including eventual antiretroviral treatment, which is negotiated before trial conduct and defined in terms of components and timeframe.²⁶

Building research literacy

Researchers, trial sponsors, research site staff, and community representatives have a responsibility to contribute to strengthening community research literacy, not only in the interest of improved study

conduct but as a broader contribution to development. National and local host governments should facilitate the conduct of biomedical HIV prevention trials by creating a framework for HIV prevention research within country plans for comprehensive HIV prevention, using processes which build research literacy at all levels.

Box 1) Defining Community

There are many different definitions for “community” and different understandings of “community” with respect to research. In this guidance document, the word “community” is used to describe separate and overlapping groups of people who are infected and affected by HIV in various ways, e.g., “the community of people living with HIV”, “the community of men who have sex with men”, “the community of sex workers”, “the research community”, “the activist community”, etc. In this case, community not only refers to the specific groups of people who are united around an identity, activity, or function, but it also refers to different sectors of society that are part of a larger social structure, all of which have a stake in a biomedical HIV prevention trial and its outcomes. In many instances, individuals will belong to more than one community. The term “community” is also used in other more specific ways in discussions of clinical trials. For example, “community” could be the term used to describe the specific locations for research, such as the neighbourhoods or sections of town where key populations¹ live or congregate and from which research participants are recruited.

¹ Key populations are defined as populations that are both key to the dynamics of the epidemic in a community and key to the response. Often they may be highly vulnerable to HIV exposure or already infected or may be affected by HIV.

PART 1

ESSENTIAL ISSUES AND ACTIVITIES

IN THIS SECTION:

The following sub-sections present a core set of topics which should be addressed by every trial site in partnership with communities affected by the research.

Introduction

This section (Part I) describes good practices as they relate to a set of activities of fundamental importance to the clinical trials process and to communities affected by research. These activities are:

- ➔ formative research involving the community concerning trial relevance and design prior to initiation of a biomedical HIV prevention trial;
- ➔ development of community advisory, outreach and education plans and ongoing plans for community engagement;
- ➔ development of informed consent documents;
- ➔ development of standards of prevention, treatment, and care for enrolled participants and individuals screened out during the enrolment process;
- ➔ development of policy on coverage for research-related harm;
- ➔ development of communications and results dissemination plans;
- ➔ development of plans for care, treatment, and if possible, introduction of new interventions after the trial has ended, recognizing that there may be a significant delay between study closure and introduction of new interventions based on trial results.

Formative research with the community

Meaningful engagement with communities affected by research is predicated on researchers having an informed understanding of how the community in question is constituted, including an understanding of the power dynamics, local perceptions of and history with research, and cultural norms and practices. Failure to invest in pre-trial activities to develop this understanding can lead to inaccurate assumptions on the part of trial planners about community boundaries, demographics, resources, culture and networks for disseminating information. Investment of time, resources and staff hours in these activities builds trust with the community, increasing the likelihood that the trial will be able to answer the key questions of the study.

Formative research involves a comprehensive exploration of the services, needs, and priorities of people living in the environs of the trial catchment area and improves understanding of how people access services and information and what are effective ways to deliver information. Since the community is integral to trial conduct, community members should be actively engaged in the process of devising questions, gathering information, and analyzing results.

Various techniques have been used to help research teams develop context-specific definitions of “community” which incorporate geographic, cultural, political, economic, and other factors which affect perceptions and definitions of collective identity. These include community transect walks, in which members or key informants of the community take representatives of the research team through the community, and map-drawing exercises, in which community members illustrate for the research team the community’s borders, constituents (who is an insider; who is an outsider), and focal points of history, memory, and gathering. Working with local residents in conducting formative research helps ensure that community members’ expertise and understanding of community perceptions, culture, and traditions inform subsequent stages of trial design.

Minimum elements of good practice in relation to formative research with communities are:

- ➔ written plans articulating the goals and methodology of formative research, including a list of community partners;
- ➔ budget lines and dedicated staff time for executing these plans;
- ➔ records of meetings and contacts with community members during this formative phase;
- ➔ a written report of the results of the formative research which specifies the questions that were asked (cf. Box 2), answers gathered, areas where clarification or particular attention is needed, potential barriers, and subsequent clinical research;
- ➔ results dissemination activities such as focus group meetings, one-on-one discussions, and Community Advisory Board (CAB) meetings (when such an entity or similar advisory groups exist) to analyse and validate the results.

Box 2) Issues to consider in formative research

- How do people define “community” in the research setting? Are there different kinds of communities that people identify with or to which they feel a sense of belonging? Is there a lack of a sense of community? Do some people feel excluded from the community?
- What are the existing mechanisms by which the community is organized?
- Are there organizations that represent the communities around the trial site and seek to protect their interests and rights? Do such organizations work together effectively or is there a sense of competition? Do they share common goals?
- Are there civil society organizations, including NGOs and community-based organizations (CBOs), working to empower communities to actively engage in research-related activities? What is the history of their experience?

- Is the key population that will be included in the trial represented by existing structures and organizations in the community? Are its members actively excluded by, exploited by or discriminated against by existing structures and organizations?
- Are there any vulnerable groups within the community that may need special protection within this and subsequent research?
- How are decisions about representation made within the community? Are leaders representative of the populations to be engaged in the trial? Who is speaking for whom? How do representatives stay informed about what members of the community think about issues? How do they ensure community members are informed about important issues?
- What are specific needs of the community that the trial might address and who determines these needs?
- Will trial conduct increase the vulnerability of the communities being considered for research?
- Are there other past and ongoing HIV prevention trials in the community? What are the lessons learned and potentials for overlap and impact? Will any existing studies be negatively affected by new research or this formative research?
- What health and other needs of the community should be addressed in order to ensure adequate conduct of the trial?
- What are the programmes and referral mechanisms that currently exist within the community offering HIV treatment, care, and support, as well other health services? What additional systems can be set up to address needs identified during trial conduct, including during screening for eligibility? Are existing programmes willing and able to provide the needed support?
- How could sustainable community systems be strengthened as part of the research?
- What barriers exist to future research and how could the community help to overcome these?

Protocol development

Opportunities for protocol review and input vary by trial. In some circumstances, particularly international or multi-site trials, the protocol may have been drafted, revised, and almost finalized by the time it reaches the site for consideration. In other circumstances, there may be opportunities for community input on specific language or revisions to the protocol. Best practices build in mechanisms for input from both local investigators and communities prior to trial protocol finalization and for participation of local investigators and community representatives on the protocol team. The following are essential steps in all circumstances:

- ➔ Clear, transparent communication about the types of input that the community can and cannot have incorporated into a protocol based on circumstances particular to the trial: Is there an opportunity to make changes prior to finalization? What is the timeframe for making changes? If the protocol is already finalized, how will concerns be addressed?
- ➔ Translation and simplification of the trial protocol for discussion with the CAB or other community advisory mechanisms prior to study launch, with time to raise and address concerns should they arise.
- ➔ Opportunities created – and facilitated – for community advisory groups and/or mechanisms to provide input into study design issues such as selection criteria, recruitment, follow-up plans, appropriate incentives for participants, informed consent, counselling approaches, and outreach to the broader community.
- ➔ Consideration of the utility and desirability of the formation of a formal community advisory mechanism if a CAB does not exist.
- ➔ Mechanisms included for arbitration when agreement cannot be reached.

Institutional review boards, ethics committees and other regulatory mechanisms

Institutional review boards (IRB's), ethics committees, drug regulatory bodies, and other structures play an essential role in reviewing and evaluating biomedical HIV prevention trial protocols prior to approval. These approval processes should be transparent to community representatives. Wherever possible, these bodies should include community representatives who have some training in trial monitoring. Sites may not be able to influence the composition of institutional review boards in all instances. Whether or not community inclusion does occur, the following are essential:

- ➔ provision of public information to community partners about the general purpose and function of the various statutory review mechanisms – IRBs, ethics committees, and Data and Safety Monitoring Boards (DSMBs) – and about the specific qualifications and expertise of institutional review board members and ad hoc reviewers involved in the assessment of a given trial protocol;
- ➔ communication with community members and community advisory mechanisms about how local statutory review structures operate, including that they meet in private sessions without release of information;
- ➔ freely-available information on IRB and ethics committee consultations and findings, including the input and concerns raised by IRBs considering the same protocol at different sites.

Informed Consent

Informed consent is a cornerstone of ethical research on human subjects. These principles are addressed in international documents on research on human subjects such as The Declaration of Helsinki and the CIOMS guidelines, and are further explored in the World Health Organization *Handbook for Good Clinical Research Practice*²⁷ and *Guidelines for the development of culturally sensitive approaches to obtaining informed consent for participation in HIV vaccine related trials*²⁸ among other documents.

Around the world, trial sites have used a range of innovative approaches to measure and assess participant understanding,²⁹ address literacy issues, and accommodate participants' desire to consult with family and friends. There is extensive literature on the development of informed consent processes in multiple contexts.

Given the importance of local context, it is not realistic to make specific prescriptions about how to design programmes or processes. Rather this guidance focuses on describing good practices for engaging the community in the development and evaluation of the informed consent process.

Minimum elements of good practice in relation to informed consent are:

- ➔ Capacity building within communities to assemble a group of advocates who sufficiently understand the structure of clinical trials, the purpose of informed consent, and the nature of the proposed study question to participate in the following process. This applies particularly to communities where no clinical trials have taken place before or where there are no records of previous capacity-building efforts. Whether these community advocates are volunteers or are reimbursed for their work, and if so by whom, needs to be carefully considered in order to preserve their independence, both perceived and real, from the research team.
- ➔ Discussion with community representatives and groups prior to finalization of the informed consent provisions of a trial protocol regarding:
 - strategies to be used to ensure comprehension of critical trial-related terms and concepts – including translation into and use of visual and metaphorical formats to build understanding;
 - decision-making structures and hierarchies within the community that may affect individual ability to give informed consent;
 - policies showing respect for participants time, effort, travel or other needs and detailing reimbursements that may be offered to trial participants;
 - participant rights and responsibilities, including voluntariness of participation and the possibility of withdrawal from participation at any point, without losing one's rights;

- discussion and negotiation of the level and provision of medical care and other services to cover infections and illnesses that are identified in trial participants during the study but are not directly related to the study drug, vaccine or intervention, and provisions for post-trial care;
- discussion and negotiation of any potential trial-related harm and provisions for how harm will be determined and accommodated;
- formats for assuring individual comprehension of critical topics at the time that the consent form is signed and throughout the trial's duration;
- procedures for ascertaining participant understanding and providing informed consent in the participant's preferred language;
- exploration of community norms concerning who should be consulted before an individual provides consent to trial participation, and discussion of how these norms would affect autonomy and confidentiality;³⁰
- considerations and requirements for illiterate participants, including specification of who may serve as a participant advocate (witness) to the informed consent process;
- considerations and requirements for minors as participants, including specification of who may serve to give informed consent (witness) to the informed assent process with the minor;
- consideration of the timing and number of consent forms;
- explanation of trial procedures with reference to local standards of care and available alternatives;
- explanation and understanding of when verbal informed consent is adequate or preferred to reduce potential harm;
- exploration of preferred ways for participants to make contact to ask questions or express concerns – whether by phone, email or other means of access;
- exploration of ways to pre-test the informed consent materials.

- ➔ Written records of the discussions described above specifying the participants, community recommendations, actions taken by the research team, and any unresolved issues or issues requiring follow-up.
- ➔ Ensuring funding and plans for ongoing review of participants' understanding of key study concepts (such as placebo, randomization) and participant rights (such as confidentiality, right to withdraw from the trial, access to treatment and care), as well as for procedures for re-consenting participants during trial conduct.
- ➔ Reports on and discussions of findings of these reviews with community partners and advisers.

Completion of these activities will help to ensure that the informed consent process of the trial is fully understood and endorsed by communities that will be affected by the research—a critical prerequisite for fulfilment of the core principles of shared ownership and participatory management and for smooth trial conduct.

Box 3) Defining informed consent for biomedical HIV prevention trials

The principle of informed consent³¹ is recognised both in ethics and human rights. It is based upon respect for the dignity and autonomy of each person.

In a medical setting, it requires that a person is fully informed about both the benefits and possible risks of a medical procedure or treatment, as well as the risks of the absence of the procedure or treatment. Experts on informed consent say that the principle creates the following duties for health professionals:

- provision of accurate, understandable, and complete information to the patient
- assessment of a patient's understanding of the information that is conveyed
- assessment of the capacity of the patient to make the necessary informed decision
- assurance that the patient has the freedom to choose without coercion or manipulation
- assurance that all questions have been answered to the participant's satisfaction.

In the clinical trial setting, the participant must learn about the process, the risks, and the benefits of study participation so that he or she can make an informed, voluntary, and knowledgeable choice about enrolling in a trial. The informed consent process should assist the potential study participant to make a decision which is in their own interest after the information that is conveyed has been clearly understood.

Standard of prevention and access to care

Meaningful community involvement in establishing the type, scope, and duration of prevention, treatment, and care that will be available to participants and communities affected by research is essential. As discussed in the introductory section of this guidance document, standards of prevention and care have been central to debates, controversies, and consultations related to biomedical HIV prevention trials virtually since their inception. Consensus has emerged around some specific questions, but others remain and may grow more complicated over time. Among the latter are:

- ➔ How to ensure that antiretroviral treatment will be provided to a trial participant when he or she needs it, generally years after the end of a trial, and how to determine the duration of care and treatment?
- ➔ How to define the standard of prevention – when, where, and how to incorporate newly proven interventions, such as male circumcision?
- ➔ Who provides and funds the treatment and care of people who are diagnosed with HIV during the screening process for a trial?
- ➔ Who provides and funds the treatment and care of people in the community where the trial is taking place?
- ➔ Does the offer of free treatment or services unduly induce trial participants in a negative way?¹⁸

Research sites should work to answer these and other questions in partnership with communities affected by research, including those geographically contiguous with the trial catchment area and communities of advocates, activists and others affected by the research. This work should be thorough and carefully documented in order to protect the rights of the people being asked to endorse and participate in the trial, to provide a clear record of what has been agreed, and to safeguard the trial itself from potential controversy or confusion which can emerge at any point in the trial life-cycle.

Various international trial networks and sponsors have developed policies which affect their work in multiple countries. These over-arching policies are critical and may affect what individual sites can offer to their participants in current and future trials. However, these over-arching policies may not meet the needs of all participants and communities, and the opportunity for incorporating context-specific concerns should be explored.

By the same token, trial sponsors should ensure that the core elements of the package of prevention and care offered are consistent across trials and networks. This includes ensuring agreements for access, for a specified amount of time, to antiretroviral treatment for volunteers who become infected during the trial and ensuring availability of a package of prevention options including male and female condoms, risk reduction counselling, sterile injecting equipment, treatment of sexually transmitted infections, and, where applicable, male circumcision and other novel HIV risk reduction strategies.

Local Ministries of Health, ethics committees and regulatory bodies may also impose or require certain actions with respect to the standard of prevention and access to treatment within trials. Trial sponsors and sites must, therefore, work with communities to reach a consensus on a standard of prevention, treatment and care that encompasses minimum core elements and additional context-specific elements.

Minimum elements of good practice in relation to standards of prevention and care are:

- ➔ Capacity building within communities to build or sustain a group of advocates who understand the design of biomedical HIV prevention trials, and the nature of the proposed study question.
- ➔ Discussion with community representatives and other stakeholders before the trial begins regarding:
 - Decision-making structures for determining policies: Which elements of policy are determined at network level or above the level of the trial site, and therefore are likely to remain fixed, and which elements are determined at a local level?
 - Community expectations, local public health institution responsibilities, and proposed sponsor and trial site commitments regarding:
 - provision of antiretroviral therapy and access to care for individuals who become infected with HIV during the trial, including duration of coverage, proposed referral networks, and regimens that will be available if the intervention under study has the potential to give rise to antiretroviral resistance;
 - access to clinical assessment, counselling and provision of antiretroviral treatment for individuals who are identified as HIV-infected during the screening process;
 - access to medical care and services for family members of trial participants and the broader community.
 - Proposed approaches to build capacity and/or ensure quality of referral mechanisms so that individuals receive the needed services that are not offered at the trial site.
- ➔ Written records of these discussions including participant names, community recommendations, actions taken by the research team, and any unresolved issues requiring further follow-up.
- ➔ Capacity and needs assessment of organizations in the community that will support the site in providing prevention, treatment and care services including support groups, groups of people living with HIV, treatment clinics, voluntary counselling and testing centres, etc.

- ➔ Written and funded plans to build capacity where needed, based on needs assessments.
- ➔ A funded plan to gather information on how treatment, prevention and care services are accessed throughout the course of the trial, such as numbers of seroconverters who access care, barriers to accessing care at referral centres, quality of care, etc. The involvement of civil society groups and other stakeholders in information gathering can help provide an independent perspective.
- ➔ Inclusion of information on implementation of standard of prevention and access to care and treatment as part of the results dissemination package at the close of the trial.

Policy on coverage for research-related harm

As per Good Clinical Practice guidelines,^{6, 27} every trial must have specific provisions for how volunteers will be treated for injuries or illness that are determined to be associated with trial participation. These policies must be clearly laid out in simple, comprehensible language and should be presented to community partners with the opportunity for questions to be raised and concerns addressed before the trial starts. Trial staff, sponsors, and communities should also consider possible policies for both minimizing and mitigating potential social harms, such as stigmatization of research participants, discrimination in employment and housing, and risk of domestic violence.

Community engagement/Involvement/Education plan

Community outreach and education are critical components of clinical trials conduct. Educating communities about the purpose and goals of the trial is a critical first step and should precede any screening and recruitment process. Given that many communities around the world lack general research literacy and specific knowledge about the design and conduct of biomedical HIV prevention trials, outreach and education efforts are key to build capacity and contribute to the empowerment of these communities as decision-making agents and

advocates in the research process. Furthermore, community education and outreach can lay the foundation for a supportive environment for research that extends beyond the lifespan of a specific biomedical HIV prevention trial.

A critical tool for trial sites and community partners, the plan laying out the outreach and education needs and objectives for every stage of the research process should be informed by consultations with key stakeholders. The plan should include staffing commitments, lists of community partners, proposed activities, and budgetary information. It should specify the types of formal consultative mechanisms for communication between the site and the surrounding community.

In implementing a range of activities, it is important to review and revise the plan as issues, needs and new audiences arise.

Minimum elements of good practice in relation to the community engagement/involvement/education plan are:

- ➔ Research teams should include at least one individual with the responsibility of overseeing community interactions. Sponsors should mandate and fund this community liaison officer or community educator.
- ➔ Principal investigators and sponsors must include a budget line for the community involvement and education activities laid out in an agreed community outreach and education plan. This should include – but not be limited to – resources to support a CAB or other community advisory mechanism.
- ➔ Key informed stakeholders from the community should be involved in designing the broader outreach and education plan, including discussions of key messages that will be communicated; channels of communication that will be used to convey these messages; and mechanisms for gathering and responding to feedback from the community; and evaluating success.

- ➔ The CAB chairpersons and principal investigators of the trial should sign off on the community education plan to indicate their respective endorsement and support.
- ➔ Principal investigators and sponsors should undertake to support and participate in activities which aim to build research literacy in the community, independent of a given trial. Governments, NGOs, and other entities may provide technical and financial resources to support these activities, with trial sites and research sponsors assisting in their implementation.
- ➔ Plans should cover the complete life-cycle of the trial and should be subject to regular review, eliciting views of participants and study staff on an ongoing basis.

Communications plan

A communications plan lays out the strategies that will be used for providing information to various stakeholders involved in a biomedical HIV prevention trial. Beyond trial participants, their families, and immediate community these may include the media, policy makers, public health officials, medical professionals, religious leaders, major employers, labour unions, and opinion leaders in the trial communities. Such a document includes key messages about the trial and plans for their dissemination at various stages of the research life-cycle (see Part II) from early phases of outreach, recruitment and enrolment to trial closure and dissemination of results.

A communications plan assesses and addresses media training needs at trial site level for staff and community advocates who have been designated to respond to questions from the media and the general public. The plan maps out the audiences, defines core messages and specifies trial representatives who will be involved at various stages.

National governments in developing countries where research is taking place should be regularly informed of new developments and trial progress, and should be immediately informed of significant changes to trial design or procedures, including the possibility of

unanticipated trial closure (see related section in Part II). Strategies for communicating with policy makers and relevant government officials should be detailed in the communications plan.

The plan should describe media training needs at the trial site level and include a clear protocol for dealing with inquiries about the trial from the general public. It should reference site strategies for dealing with potential stigma related to participation (either of individuals who enrol or those who are found during initial recruitment screening procedures to be ineligible for trial participation).

A crisis plan should be in place for managing unexpected developments including negative rumours about the trial, unexpected findings such as evidence of harm among study participants, developments in other HIV prevention trials, and premature closure of a trial for reasons of harm, futility or proven efficacy in interim analyses.

These plans must be resourced accordingly, with funds committed to media training, information sessions, and the development and testing of messages, as well as to dedicated staffing for monitoring and responding to communications issues as they arise.

Audience segmentation is part of standard communications practice, and the plan should consider the needs and messages required at a local, national, and global level. The goals of communications are to increase broad awareness of the trial, to facilitate dissemination and understanding of correct information, and to create a supportive and conducive environment for trial implementation .

Minimum elements of good practice in relation to the communication plan are:

- ➔ A written communications plan that is developed in consultation with community partners and is reviewed regularly and revised as necessary. The plan identifies policies and procedures for coordinating internal and external communication between

the research team, key stakeholders, the media, and the public. These should delineate:

- key audiences and information needs at site, local, and national levels;
 - focal people who can be resources for answering questions, providing correct information, and addressing concerns;
 - processes for swiftly addressing issues which may require input from the sponsor level, or from other entities outside the trial site itself;
 - core messages that the trial site or NGOs and CBOs will be communicating about the purpose, risks, and benefits of the study;
 - training for trial staff and community partners.
- ➔ Staffing for implementation of the communications plan.
- ➔ Mechanisms for measuring the adequacy and implementation of the plan.

Monitoring and issues management plan

Every trial site should have a plan for monitoring community engagement and partnership processes, and for managing issues that arise. This plan should be in place at the outset of the trial, since concerns can emerge even before a trial protocol has begun to be implemented; it may need to evolve as issues emerge. The plan can be included as an element of the community outreach and education plan described above. One component should be a risk analysis to identify potential vulnerabilities and concerns that could limit the success of the trial. This could include anticipating how study information may be misinterpreted or misunderstood, and developing potential responses in advance. The plan, which should include input from researchers, sponsors, and other trial stakeholders, should have clearly delineated content and roles for its implementation.

Community advisory mechanisms

The core principles of shared ownership and participatory management cannot be fulfilled in the absence of ongoing, agreed mechanisms for community input. Establishment and maintenance of these mechanisms throughout the research process helps to ensure that trial sites and networks participate in a robust and continuous dialogue with community members who serve as partners, advisors, critics, and allies. These mechanisms should ensure bi-directional input, with the researchers learning from the community and the community learning from the researchers.

One such mechanism is a CAB,³² or community advisory group (CAG) which meets on a regular basis and is composed of representatives from various constituencies such as people living with HIV, religious leaders, members of the media, women, youth, traditional health practitioners and others as determined by the location of the trial. For simplicity, the term CAB will be used here to refer to this entity which meets regularly.

Some sites include study participants on the CAB and/or people who have previously participated in similar trials. Other CABs include representatives of the target population of the trial. Including various constituencies and perspectives is helpful in creating broad-based support for the trial.

CABs were first developed in the context of the USA and European HIV epidemics and have become a standard element of HIV research over the past two decades in both high-income and low- and middle-income countries. CAB members volunteer their time and are not trial staff.

CABs can serve many functions, including advising site staff on protocol and materials design, serving as a two-way information conduit between the site and the broader community, acting as advocates for

the community involved in the trial, and acting as ambassadors for HIV prevention research.

Establishing and maintaining an active CAB is not without its challenges. Work responsibilities and personal demands on volunteers may lead to high turnover rates. Lack of infrastructure and support, combined with training needs pose challenges for the research team and for the CAB. In addition, CAB members are sometimes regarded as elders who are not approachable by other members of the community.

Minimum elements of good practice in relation to community advisory mechanisms (CAM) include:

- ➔ Establishment of (or partnering with) a community advisory board or group² with the following characteristics:
 - Has terms of reference, including specific roles, responsibilities, and duration of service for each member, reimbursement policies, procedures for conflict resolution, etc.
 - Meets regularly.
 - Has the ability to provide voluntary and independent input.
 - Receives logistical support from the site or through a different, existing technical or funding institution.
 - Represents multiple constituencies in the surrounding community.
 - Is knowledgeable about essential elements of the research process including HIV prevention research, and is empowered and knowledgeable to provide meaningful input into the development and conduct of trial and trial-related activities.

² In some instances sites may use a pre-existing community advisory mechanism such as a CAB which has already been established for a different trial. A useful principle to help guide when to use a pre-existing mechanism is to examine the CABs current agreements or terms of reference; to perform a feasibility assessment of the existing CAB and its members; and to identify conflicts, or potential conflicts, with their existing activities. This process should help identify whether or not the existing arrangement will be easily transferable or expandable to align the operational nature of the existing CAB with the interests and goals of the new trial or study.

- Is knowledgeable on local culture including norms, priorities, and vulnerabilities of various key populations.
 - Does not play a direct role in trial recruitment.
 - Has a diverse membership and includes representatives of populations likely to be recruited for trials, socially vulnerable groups and locally-identified political, traditional and religious leadership in the community.
 - Is able to communicate with broader communities including those not in geographic proximity to the research catchment area but who may be affected by the research.
 - Rotates members regularly after they have served for a specified period.
 - Documents discussions and recommendations.
 - Has a chair person to lead the group and provide coordination with other groups and the sponsor.
- ➔ Funding for capacity building of CAB members to build and maintain understanding of clinical trials conduct, HIV prevention research, ethics, and relevant scientific issues and other topics. At least one training session should be provided at the establishment of the CAB followed by supplemental trainings on at least an annual basis.
- ➔ Written CAB by-laws, specific terms of reference or other guiding documents which delineate roles and responsibilities of CAB members and describe mechanisms by which CAB members can raise concerns with trial staff and with trial sponsors who are not on site, in the event that a concern related to the site emerges. These guiding documents should also include a process to elicit views of trial participants and study staff on an ongoing basis.
- ➔ Funding for regular CAB meetings and written records of the minutes from these meetings, including participants present, issues discussed and proposed actions.

The CAB fulfils important functions and is both an expected and a highly-desirable structure in most instances in a biomedical HIV prevention trial. However, a CAB should not be the sole mechanism for community input. In most settings, a CAB is set up and financed

by the research entity; CAB members may not be perceived by other community members as having independence from the research site—and these perceptions may be accurate. Hence, it is important to have alternative mechanisms for input. A CAB is therefore an often-necessary but seldom-sufficient element of a site's community advisory structure.

Developing a formal coherent CAB may not be feasible for all sites. In areas where CABs cannot be formed, researchers will need to assess existing community-based, political, cultural, media, and health organizations to determine who the stakeholders are and how best to engage them to ensure smooth conduct of the trial.

Other channels for input include open community or town-hall meetings, door-to-door campaigns, trial participants' groups, call-in radio shows in which community members can raise questions and hear from trial staff, and suggestion boxes. Formal qualitative social science research methods, including focus groups discussions and in-depth interviews, can also be channels for obtaining useful feedback from the community.

Minimum elements of good practice with respect to the establishment of additional community advisory mechanisms include:

- ➔ Development of additional mechanisms must be developed to facilitate bi-directional input with researchers and the community learning from each other.
- ➔ Discussion and adaption to site characteristics of a range of consultative and feedback processes.
- ➔ Establishment of a schedule and budget for conducting activities which facilitate dialogue between the site and participants and/or the broader community.
- ➔ Documentation of these activities, including analysis of issues and concerns, actions taken, additional recommendations made, and evidence of feedback and input from the wider community.

PART II

GOOD PARTICIPATORY PRACTICE AND THE RESEARCH LIFE-CYCLE

IN THIS SECTION:

The following sub-sections describe Good Participatory Practice at different stages of the research life-cycle, from site selection through study initiation to study closure. The size of the study, the number of sites nationally and internationally and the phase of research will all affect the interpretation of these recommendations.

Site Selection

Site selection refers to the process of identifying and evaluating sites for a planned biomedical HIV prevention trial or in some instances, for inclusion in an HIV prevention trials network. For the purposes of this guidance document, site selection refers to the earliest stages of identifying a site to conduct clinical research.

At this stage, trial sponsors frequently use a site assessment tool which gathers a range of information on topics such as infrastructure, epidemiology, human resources capacity, and other dimensions.

Indicators of site capacity for and experience with community engagement should be incorporated routinely into these site assessment tools, since their findings form the basis of decision-making on site selection.

At the outset of the research process, sites that are in the process of applying for funding for a specific HIV prevention trial or for support through a network and sites that are planning to launch studies independently will not in every instance have the full complement of

community advisory mechanisms and processes in place. However, research teams should be able to demonstrate that the basic elements for an effective community programme exist or are being actively developed through participatory processes.

Site assessments should evaluate the state of development and adequacy of:

- ➔ Draft communications strategies for sharing information about the research programme and about HIV prevention research in general with various core constituencies and communities in appropriate languages, formats, fora, etc.
- ➔ Plans for developing community advisory and consultative mechanisms and for creating a communication channel for input from individuals and groups not represented on the CAB.
- ➔ Plan, budget, and timeline for completing community mapping exercises or other comparable initial exploration.
- ➔ Site level staffing and funding plans for community outreach and education activities, all of which are conducted under the oversight of the principal investigator. Documentation might include: job descriptions for community outreach officers and staff and plans for training and capacity-building of staff concerning community issues.
- ➔ Demonstrated relationships or plans to develop relationships with community and public opinion leaders, health care providers in geographical proximity to the site, and broader civil society stakeholders working and living in the area where the trial site is planned.
- ➔ Demonstrated relationships or plans to develop relationships with NGOs, CBOs, advocates and other associations working with key populations from which trial participants will be drawn (e.g. sex workers, adolescents, injecting drug users), or representing the perspectives of broader civil society stakeholders.
- ➔ Demonstrated awareness and evaluation of human rights issues which may be raised by the trial, particularly as they relate to vulnerable, marginalized, or criminalized groups.

The conduct of biomedical HIV prevention trials in low-and-middle-income settings may frequently involve partnerships between personnel from high-income countries who may be involved in funding the trial, staffing central data analysis facilities, drafting the protocol, and other activities at a central level. Local staff from the country will have varying degrees of input into and control over the HIV prevention trial that they are asked to conduct. Good practices in community engagement include open communication and shared responsibility between international and local investigators. All trial staff are responsible for adhering to international standards.

Over the course of the site assessment and selection process, the following questions should be addressed by relevant stakeholders, including site investigators and research staff, trial sponsors, international partners, etc:

- Are the national and local governments supportive of the trial and are there punitive laws or guidelines which violate confidentiality or other instruments which would complicate the participation of key populations from which trial participants will be drawn?
- What is the history of research in the community?
- What is local researchers' experience with this type of trial; what are their needs and priorities in terms of capacity building and scientific agenda setting?
- Have previous consultations about HIV prevention research occurred with the community in which the trial is to take place?
- What community interest and concerns about involvement in the trial have been expressed? What views are held on past HIV-related and non HIV-related research projects in the community, where applicable?
- Why is this specific site being considered for inclusion in the trial?
- How was the protocol developed and what is its ethical and scientific basis?
- What is current state of the protocol and what are the opportunities and deadlines for local input into the final document?
- What are the anticipated benefits and risks to the individuals and the community during and after the trial?

Box 4) Defining stakeholders

Stakeholders are those people or organisations affected by the outcome of a biomedical HIV prevention trial, negatively or positively, or those who can affect the outcome of proposed research. This includes the population that will be approached to participate in the trial, as well as communities and individuals who are not physically located where the research takes place, including advocates, activists, groups representing specific constituencies such as sex workers, drug users, treatment activists and others. In addition, key stakeholders can potentially include educators, medical professionals, media professionals, and, in the immediate community, family members, and people whose age and/or gender make them ineligible for study participation. Policy makers and leaders of countries where research is taking place are critically important to the research process. All of these groups can provide important input on how to build support for and conduct an ethical, scientifically sound, and successful trial.

Site development

Site development is a preparatory phase for clinical trials which may include training laboratory technicians, validating standard operating procedures, and expanding infrastructure to meet the needs of the proposed HIV prevention trial, as well as any anticipated requirements for upcoming research projects.

Site development includes critical work on strengthening and deepening the relationship between the site and the surrounding community prior to the launch of the study protocol. Relevant activities include formative research, communications and education plans, and establishment of community advisory mechanisms, all described in Part I. Together, these activities may constitute an initial phase of community outreach and mobilization prior to or in conjunction with protocol review and planning for specific biomedical HIV prevention trials.

The precise nature of these activities will be determined at the local level, but should include elements of the following:

- ➔ Drafting and piloting of informational materials.
- ➔ Needs assessment for and capacity-building of scientific and HIV prevention research literacy among all audiences, with specific focus on potential CAB members and other key stakeholders that will be called upon to inform subsequent plans.
- ➔ Formative research that identifies community priorities and concerns with regard to HIV treatment and prevention along with existing capacity to address these priorities, as well as community concerns and priorities around prevention research. This information should be fed back to investigators to inform the trial protocol and preparations for study implementation.
- ➔ General information sessions on HIV prevention research and on specific study information for key stakeholders in the media, medical professions, government and other sectors.
- ➔ Outreach to local NGOs, CBOs and health facilities with the goal of developing written agreements such as Memoranda of Understanding to solidify partnerships and build sustainable improvements to capacities of all services and groups.
- ➔ Elaboration of community engagement plans for the duration of the study, including longer term engagement with participants who may complete their study visits well before the trial ends.

These activities establish an on-going dialogue between community and research staff; they promote a collaborative relationship between community members and researchers, as community members see their input acknowledged and informing the research process.

Study initiation

This section addresses activities which take place during trial recruitment including the launch of pre-screening, screening, and enrolment—all of which may continue for the first year(s) of the study. By the time these activities are set to begin, partnerships between the

site and the communities affected by the research will already be in place, guided by the essential activities described in Part I and elaborated upon in the preceding section on site development.

Messaging

Partnerships developed with community stakeholders during site development efforts will have informed the messages to be used in recruitment efforts. These messages will be conveyed in different ways depending on the target audience. It may be difficult to develop consensus across all stakeholders on all of the messages. Instead, the trial team should document discussion of and note points of dissent on the following topics:

- Why the trial is happening
- Overview of trial
- Who is the sponsor and who is performing the study
- Where the trial is being conducted (local, national and international)
- Who has approved the trial to be conducted
- Who the target populations of volunteers are (and are not)
- Strategies and support available at the site level for minimizing the potential for trial-related stigma for both enrolled participants and individuals who are found to be ineligible during initial recruitment screening procedures
- Risks and benefits of trial participation to the individual
- Levels and form of community support
- Ways that the trial will (and will not) benefit the community during and after the trial
- Community advisory structures in place
- Anticipated duration of the trial and potential scenarios in which the study could be stopped unexpectedly or extended beyond the scheduled stop date
- Future plans, including further research and/or future access to a product

Materials and outreach

Sites can use a range of strategies to reach out to potential volunteers, such as videos, skits, music, community forums, newspaper advertisements, and informed recruiters based in clinics, bars, truck stops or other locations relevant to trial recruitment. These methods will have been discussed and, ideally, field-tested during the site development stage. Minimum elements of good practice include documented community input on:

- ➔ Outlining the best strategies for reaching the target population while minimizing harm and protecting participant confidentiality. This step may include such activities as working with existing NGOs or social networks, hiring or finding volunteer outreach workers, purchasing advertisements in various media, hosting public events or others;
- ➔ Developing culturally appropriate recruitment messages, perhaps using focus groups or other kinds of community consultation with those who are less familiar with research terminology than CAB members;
- ➔ Developing culturally appropriate recruitment materials, with consideration to perceptions of HIV and HIV risk, HIV-related stigma, language, and literacy level;
- ➔ Obtaining ethics committee and MOH approval for materials.

Monitoring and evaluation of recruitment and enrolment efforts

A monitoring plan developed in consultation with the community should be finalised as part of the research protocol and in place prior to the start of a trial. With the commencement of recruitment, pre-screening, screening and enrolment, the principles of transparency and accountability become increasingly important. As plans are executed, they must be monitored, evaluated and revised accordingly. Minimum elements of good practice at this stage include:

- ➔ Launch of a site-level monitoring and feedback mechanism which can gather information on community responses to recruitment strategies and pre-screening, screening and enrolment processes, including, where possible, the experience of individuals who are found to be ineligible for participation during the screening process.

- ➔ Use of above feedback mechanism to learn about the motivations for enrolment of eligible participants who enrolled; to identify any misconceptions and miscommunication; and to learn from participants found to be eligible who nevertheless decline to enrol, as this information can help evaluate individual and community perceptions of voluntariness of enrolment.
- ➔ Conduct of periodic focus groups or other consultations to learn about community perceptions of the recruitment methods and messages, and to discuss possible barriers and alternative strategies in the event that recruitment goals are not met.

Pre-screening

Depending on the structure of the trial site and the methods for recruitment, some research sites may conduct a pre-screening visit, during which site staff can quickly determine whether a participant meets certain eligibility criteria for the study, such as age, sex, HIV risk factors, residence, intention to remain in the geographic area for the expected trial duration, and other criteria.

Minimum elements of good practice include:

- ➔ A simple, culturally appropriate tool developed with community input that explains the pre-screening purpose and process as well as the pre-screening questions.
- ➔ Clear, written guidelines or standard operating procedures (SOPs) which have been shared with the community advisory mechanism prior to study initiation. They should explain reasons for ineligibility at this pre-screening stage and at subsequent stages of enrolment, such that failure to enrol in the trial is not stigmatized or interpreted as an indication of serostatus.

Screening

During the screening process, individuals who have been pre-screened undergo a more in-depth evaluation, to determine whether they fit all of the eligibility criteria. This stage may include medical histories and blood chemistry analyses, and HIV testing, as well as a more detailed discussion of trial-related issues including the research

question, participants' rights and responsibilities, study demands, and informed consent. The principles of participatory management and transparency should underpin the screening process.

Screening may detect a range of health conditions including HIV infection, laboratory abnormalities, pregnancy, etc. that may preclude study participation. Depending on the study, blood chemistry and haematology analyses may be conducted to identify individuals with results outside established reference ranges. Wherever possible, it is desirable that these reference ranges be informed by local or regional data, rather than standards from other regions. Significant geographical differences in reference ranges can potentially lead to unnecessary exclusion of potential volunteers.

Study-related stigma resulting either from ineligibility to enrol or enrolment itself should be anticipated and strategies to prevent and mitigate it implemented and carefully monitored. Individuals who are not eligible for HIV prevention trial participation due to HIV positive serostatus should be counselled about strategies they can use to explain why they are not participating in the trial while protecting their confidentiality. Counselling approaches to reduce potential stigma should be evaluated and fine-tuned.

Previously-established referral networks should be activated to provide care and treatment to people who are ineligible for trial participation as a result of HIV infection or other medical conditions. These referral networks should be monitored as they are activated to ensure that promised services are delivered.

Community advisory mechanisms and other partners, where relevant, should receive progress reports and contribute to troubleshooting sessions related to screening and enrolment.

Many communities have identified as a priority the assessment of the experiences of stigma, disclosure and access to care and treatment

services of individuals newly-diagnosed with HIV during the course of trial screening. Trial sponsors and sites should consider the feasibility of addressing this issue in light of confidentiality concerns. Options for further exploration include development of a separate protocol, potentially in collaboration with groups of people living with HIV who could conduct interviews and other forms of community outreach to gauge effectiveness of referral mechanisms. A similar approach could be used to learn about reasons for non-participation among people who decline to participate during the screening process.

Enrolment

Individuals often give informed consent for pre-screening, screening and again for enrolment in a trial once they are found to be eligible. Good participatory practices for community input into the informed consent processes are described in Part I.

Ensuring that informed consent is conducted according to the site's informed consent standard operating procedure is a part of the clinical monitoring of the site and the responsibility of the principal investigator and research sponsor.^{6,27}

Study conduct

During this phase of study visits and follow-up of trial participants, mechanisms for ongoing information-sharing, monitoring, evaluation, adjustments, and trouble-shooting are essential.

Study visits and follow-up of volunteers

At the interim visits laid out in the study design and protocol, activities vary and are specific to each trial protocol. These visits are important both in terms of ensuring participant safety and welfare and collecting data for the study, as well as for developing and maintaining relationships with study participants.

Once the site is operational, sites may want to engage community partners in discussions on the following topics:

- ➔ methods for ongoing HIV testing and counselling, ensuring confidentiality of test results, and accessing services;
- ➔ on-site treatment and/or referrals for mental and physical health results unrelated to the study;
- ➔ methods for tracing trial participants who miss study visits;
- ➔ information about emerging data from other related HIV prevention studies, including implications for the ongoing study;
- ➔ retention activities, gifts, or reimbursement for time, effort, or travel expenses;
- ➔ ideas and suggestions emerging from study participants if such information can be shared without breaching confidentiality;
- ➔ public release of interim findings and assessment of community information needs, following consultation with the CAB, sponsor, IRBs, Ministry of Health, local health(MOH) authorities, and DSMB;
- ➔ recruitment progress;
- ➔ identification of unknown/new health trends and social concerns;
- ➔ identification of ways for the community to provide better support to the participants and the trial.

Site staff are best placed to gather and analyze much of this data, particularly where confidentiality is concerned. It may be desirable to collaborate with a community group not funded by the site, which can interview site staff and solicit input on emerging concerns from the community. Community advisory mechanisms and other community stakeholders may also request opportunities to visit the study site to observe its operations.

Monitoring scientific conduct

As the study progresses, monitoring of site practices and data collection occurs on a regular basis, as required by sponsors and the standards

for Good Clinical Practice. Though the community may not have the opportunity to participate in this aspect of overall trial monitoring to protect both the confidentiality of participants and the data, the process of monitoring should be transparent. It should include explanations of the roles that clinical monitoring boards and DSMBs play in ensuring the safety of study participants and the quality of data produced. Summaries of IRB and regulatory body reports may be made available throughout the trial. Community advisory mechanisms should also be informed about the planned schedule for DSMB reviews; as the trial proceeds, this information should be updated and potential scenarios such as a DSMB recommendation to stop the study prematurely should be discussed.

Broad issues that result in protocol amendments or changes to informed consent should be shared with the community advisory mechanisms, in addition to the IRB and the MOH.

Responding to emerging issues

A range of issues not anticipated during preparatory activities may emerge during trial conduct. Examples include protocol changes, recruitment challenges, lower-than-expected HIV incidence, and negative media coverage of the trial or the site.

Communications plans and crisis management tools described in Part I are indispensable for addressing these issues. Good practices in putting these plans into action include sharing information, seeking community input to solving problems, and producing clear, timely statements about decisions which have been made at the sponsor level.

Study closure

Trials run until their scheduled completion dates, may be prolonged or may be stopped early. The latter may be due to findings of clear protective effect, evidence of harm or recognition of futility (the study will not be able to prove or disprove the trial hypotheses in a reasonable amount of time). Discussion of and planning for various

scenarios should occur in a phased approach throughout the trial so that response strategies are in place in advance of milestones such as DSMB sessions reviewing the trial data. Regardless of the scenario—early closure, scheduled closure, etc.—the following are elements of good practice:

- ➔ dissemination of regularly-updated trial timelines to key audiences including study participants, community partners, and stakeholders;
- ➔ creation and documentation of an activity plan, with staffing and budget, for results dissemination in the community;
- ➔ clear communication plans addressing trial participants, communities, and other stakeholders as the trial comes to a close.

Scenario: Planned trial closure

As participants finish their study visits and research sites prepare the data for analysis, research sites should actively communicate with study participants, community partners, and agencies about when results can be expected, how the results will be communicated, and potential next steps. Where appropriate, plans should be made at this stage for community meetings or fora to facilitate broad discussion of the trial.

Scenario: Unexpected trial closure

Normal study activities may be affected by unanticipated events such as a DSMB review identifying a clear protective effect, potential harm to participants or futility of continuing the trial. Site-initiated dialogue about this issue will minimize confusion, disappointment and feelings of mistrust which can emerge when a study is unexpectedly recommended to halt its activities.

Specific elements of good practice around unanticipated trial closure include:

- ➔ Trial sponsors and sites should ensure that appropriate health officials, ethics committees, participants, local research partners, policy makers, and study participants are informed as soon as practicable. In some cases, where study product manufacturers

are publicly traded companies, there may be legal requirements that public announcement of a study closure is implemented in specific ways, often within defined time parameters. These regulations need to be followed, with study and other direct stakeholders quickly informed of the closure. Every effort should be made to inform relevant health professionals and key community stakeholders about the study closure before media broadcast the news locally and internationally. Stakeholders in the country where the trial is taking place should not learn of results from the international press.

- ➔ Sponsors and sites should work together to ensure that appropriate staffing and communications capacity exist to handle media queries related to unexpected closures and to address questions which may emerge from participants and the broader community.
- ➔ In the event of a trial closure due to evidence of potential harm for a self-administered product such as a microbicide, sponsors and sites should take immediate steps to recall the product from all participants and provide appropriate care.
- ➔ In the event of a trial closure due to evidence of clear protective benefit, sites and sponsors should take immediate steps to communicate the benefits and limitations of the finding to the community, and to communicate the timing of steps that will be taken to make the intervention available to all control group participants.
- ➔ In the event of a trial closure due to futility, sites and sponsors should take immediate steps to communicate the reasons that the trial is being stopped and the implications for both the community and for further trials.

Termination of participants from the study

Some studies last for a few months and others last for years; in either case, it is important to acknowledge the time spent with participants and the relationship that has been established.

Participants' final study visits should be carefully planned. Good practice for the termination process includes conversations that address the following issues:

- ➔ Services and care that have been available to the participants through the study, such as HIV counselling and testing or supportive counselling from trial staff, may have become a part of the participants' routine expectations. As much as possible, trial sites need to find ways to link participants with this sort of care in the surrounding community after the study is completed and to explore financing mechanisms which will permit this.
- ➔ The focus and length of the follow-up programme defined in the protocol for trial participants following trial termination should be shared with them as study visits near completion.
- ➔ Referrals to rollover studies for similar products or other kinds of prevention and to different research studies may be offered.
- ➔ Participants complete their study visits at different times depending on when they were enrolled. As each individual comes close to completing planned study visits, the timeline for unblinding should be explained. Participants must have a clear idea of when they can return to the site for this information. Because, the unblinding visit can potentially happen several years after a participant's final study visit, sites should ask for as much contact information as possible to ensure that the participant can be reached with this information; the site should also provide the contact details for an ongoing point of contact at the trial site, should the participant have questions or concerns.

Data analysis, validation, dissemination and publication

Ownership of and responsibility for analyzing the data vary by trial. The roles of sponsors, principal investigators, and site level researchers should be clearly defined and documented at the outset of the process. It is important for research staff, trial participants, and community partners to understand their involvement in data analysis, validation, and dissemination of results.

Researchers frequently plan to present preliminary findings at a scientific meeting, followed by submission of an article for peer review. Dissemination meetings which present the findings to various stakeholders in country, including trial participants, surrounding commu-

nities, medical professionals, policy makers, and others must also be conducted, both as an obligation and as an opportunity to validate the findings and explore their potential implications.

The precise steps that will be taken depend on the type of trial that has been conducted. It is important that staff, trial participants, and community partners understand the proposed sequence; that their endorsement is sought; and that dissent is noted where the plans do not meet with unanimous approval.

Minimum elements of good practice include:

- ➔ Development of a plan for results dissemination in simple, culturally appropriate language for the surrounding communities.
- ➔ Convening the community advisory mechanism to reflect on the validity of the data and, in particular, whether the findings reflect the lived experience of the target population.
- ➔ Reporting results of the trial to study participants and surrounding communities in clear, understandable language. Critical topics to address include:
 - key study findings, whether positive, negative, or indeterminate;
 - who will have access to the data set apart from the immediate research team;
 - additional findings which are not related to the primary study question, but which may be of interest to the community, for example, reported patterns of sexual networks, rates of various infections, demographic data, etc;
 - implications for the community – how these data could affect people’s lives in the surrounding area;
 - limitations of the study – extent to which the data are generalisable, e.g. by age, gender, locale, behaviours, etc;
 - implications for follow-up work, including additional trials and access to strategies which prove effective;
 - additional plans for disseminating the research – where it will be published and presented;

- future plans at the trial site.

Once these topics have been addressed in clear and simple terms by site staff, the community should have the opportunity to discuss some or all of the following questions:

- Do these findings make sense to you?
 - In what way do these results reflect (or not) your experience?
 - Is there any aspect of your experience that is not represented by these findings?
- ➔ Community views on the trial findings should be documented, as should opinions about their validity and about dissemination. While community assent is not a prerequisite for publishing or sharing research in a scientific forum, it is important that community interpretations be noted in these contexts, particularly if they differ from the predominant scientific analysis.
- ➔ Communities should have access to the published results of the study. When study results are published in journals that are not open access, sites should provide ready access for the community to hard copies of the papers as well as to copies of conference posters.

Discussion of follow-up research

Community groups and local researchers should discuss opportunities for research stemming from the trial process or results. For example, can the study prevention package be implemented at a public clinic as part of an operational research study? Is there a specific population which emerged as particularly vulnerable or hard to reach during recruitment? If so, is there a follow-up project that can be tailored for this population? These discussions can take place in the context of data analysis and during the site maintenance phase between trials (see following).

Site maintenance between trials

Site maintenance between individual trials refers to core activities which continue between trials. Among these, community activities should be a key consideration. A programme of site maintenance supported by funding from research networks and/or linkages with academic and research establishments will lead to better returns on investment in research.

From the perspective of community engagement, it is highly beneficial for the trial site to sustain the relationships that have been developed with community partners and networks during the research process, maintain and support key staff at the trial site, and engage in ongoing activities to develop and expand the local research agenda. This provides a strong base for future activities and may lead to greater efficiency in the launch of future studies.

Potential elements of good practice related to inter-trial activities include:

- ➔ ensuring that support and referrals offered to past study participants in the trial context continue to be available and conducting follow-up with the providers, clinics, etc. with which the site has developed partnerships to ensure quality and availability of care;
- ➔ consulting with community groups about research questions which meet their own prevention needs and concerns, which can then guide the development of future grants and research proposals;
- ➔ offering ongoing education about methods and processes of biomedical HIV prevention trials and related prevention activities happening elsewhere in the world;
- ➔ staying involved with and responsive to other community efforts related to HIV prevention;
- ➔ building local NGO, CBO, and site staff capacity to be partners in the HIV prevention research process.

Future access to HIV prevention technologies

Good practice activities concerning study participants' and communities' access to the HIV prevention technologies tested in clinical trials will depend on the biomedical intervention being tested.

Future access policies

When a biomedical intervention is being tested, trial sponsors should have a clear strategy, negotiated with the national government and local partners, in place for ensuring rapid, affordable, and sustainable access to the intervention for trial participants at a minimum, should it prove effective. This plan should be shared with the community during study preparation. In addition to being made aware of their rights, communities must also be made aware of the factors which could postpone or even prevent them from realizing their entitlements in the immediate post-trial phase, such as the need to secure regulatory approvals and adequate supplies of the intervention.

Sponsors should also have a clear plan for funding implementation or additional operational research. Partners such as United Nations agencies, government ministries, local authorities, NGOs, development partners, and others can assist in plan development, as can communities which possess specific knowledge that is invaluable in the design of programmes to effectively deliver new and existing interventions.

Access in the interval prior to approval

When a biomedical intervention shows efficacy in a single trial, it may take some time before approval is secured and the product is licensed in country and widely available. In fact, normative UN agencies may wait for corroboration from additional trials before recommending the addition of a product or intervention to the combination HIV prevention package. During initial community education activities, sites and sponsors should clearly explain the plans for access. This information should be re-visited on an ongoing basis, and, once the trial is completed, detail on plans for expanded access such as

compassionate use programmes, off label use, accelerated regulatory approval, etc. should be discussed with the community.

New product interactions

Positive results from an efficacy trial may lead to licensure, large-scale manufacturing, and distribution of a new product. It might also lead to modifying or adapting a candidate product that is still under trial. These decisions should be clearly and transparently articulated to trial participants and representatives, as should the implications for future trial design. It will be important to consider whether and under what conditions the first product licensed would then be used as standard of prevention in future HIV prevention trials.

Conclusion

This document on *Good participatory practice guidelines for biomedical HIV prevention trials* has been created as supplementary guidance to the conduct of such trials and as reference for standards in community engagement. While not exhaustive, this guidance document is pragmatic in laying out basic standards for community engagement and providing a reference framework for assessing how successful community engagement has been prior to, during, and following completion of biomedical HIV prevention trials.

Most importantly, this document outlines the development of participatory processes that are meaningful, sustainable and proactive, seeking to balance the opinions of all stakeholders while serving to achieve the goals of the research enterprise, the communities participating in trials, and the broader HIV prevention field.

In a forward-looking approach, it is important to gather and analyse experiences that research stakeholders have with the implementation of these *Good participatory practice guidelines for biomedical HIV prevention trials*. Recommendations for modifications and refinements based on field experience and reflection should be sent by email to gpp@unaids.org where they will be gratefully received and considered in future updates of these guidelines.

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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.

UNAIDS, as a cosponsored programme, unites the responses to the epidemic of its ten cosponsoring organizations and supplements these efforts with special initiatives. Its purpose is to lead and assist an expansion of the international response to AIDS on all fronts. UNAIDS works with a broad range of partners – governmental and nongovernmental, business, scientific and lay – to share knowledge, skills and best practices across boundaries.



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