A mong issues of research ethics, informed consent has historically received the greatest attention. Nonetheless, a significant gap persists between the spirit of informed consent and what it actually means in practice. Ideally, informed consent would reflect an agreement between researcher and participant, entailing ongoing dialogue to improve the conduct of research. Yet in reality, informed consent is often something far different—largely a series of legalistic measures to conform to regulatory requirements. Too often, informed consent is a one-way, one-time communication, a hurdle so that researchers can move on to the next stage of their research protocol.

**Elements of informed consent and emerging agreements**

Agreement is widespread on the principal components of informed consent: disclosure of information, comprehension, decision-making capacity, voluntariness, and an explicit declaration to participate or refuse. Historically, informed consent has emphasized disclosure, especially in the United States where informed consent is often driven by fear of litigation. As a matter of self-protection, researchers and sponsors provide mountains of information, which may or may not contribute to anyone’s understanding of what participation actually entails. Recent discussion has stressed the difference between information to improve the quality of participants’ understanding and informational overkill to nominally cover bases.

Among Consultation participants and the ethical community, the critiques of informed consent have converged on several points of general agreement:

- Informed consent is a process, not a single action or moment in time.
- Emphasis should be on comprehension and choice, not merely disclosure.
- The amount of information should not be overwhelming or work against comprehension, and it must be conveyed in understandable language.
- Persons who choose to consent need to take some explicit action to indicate their decision.
- Reimbursements should be appropriate to the setting and circumstances.


2 Research sponsored by the US Government must also conform to Health and Human Services regulations governing the protection of human subjects (46 CFR 45), which detail up to 14 elements of information that must be imparted to participants during the informed consent process.

3 The amount and nature of information should be sufficient so that a "reasonable person" can weigh the risks and benefits of participation and make a fair decision. Exhaustive detail on pharmacology or research design is seldom essential to this process.
Informed consent as a process

Informed consent is a process with multiple stages and multiple levels that requires ongoing effort and renewal. In microbicide trials, informed consent begins at an early stage with community education about HIV and the nature of the proposed research. With that said, one Consultation participant also cautioned that "community education" can easily veer across the line into marketing and recruitment. Educating does not mean selling. Individual prerogative is not served if a village chief or church leader decides to sanction a trial, thereby pressuring some community members to join.

Informed consent should be phased. The explicit action that indicates consent should not be required when the information is provided. Participants should be able to absorb, think about the information, discuss it with friends and family, ask questions, and then return with a decision.

Community consultation

Most terminology used in research—including the notion of research itself—is unfamiliar and not easy to translate in the typical settings where HIV prevention research takes place. Serious community consultation provides the basis for communication, first by helping researchers to understand how a community interprets rarefied concepts such as confidentiality and free choice. With discussion and patience, a community can find its own terminology to interpret and explain the study concepts, thus making individual consent meaningful.

Confidentiality

Confidentiality on who is and isn't participating in the trial is utterly essential, especially if community pressure develops either against or in favor of the study. Generally, only HIV-negative women can be enrolled in a Phase 3 microbicide effectiveness trial. Being "screened out" can therefore imply a serious message about a woman's serostatus to friends, family, and male partners. If others interpret being screened out to mean that a woman is probably HIV-positive, the negative consequences can be severe. Thus, every effort must be made not to signal who is participating—for example, if blood is drawn from those who test HIV-negative, even those who are HIV-positive should leave the test location with a bandage on their arm.

Ensuring understanding

At the time of enrollment, participants should consent individually. Several methods can improve and confirm each person's understanding of what's involved—for example, the use of check lists, focus groups, exit interviews, flip charts, and videos. In response to participants' suggestions from a Phase 2 trial in South Africa, the Population Council produced a video for its Phase 3 trial. The video explained difficult concepts in a dynamic, graphically appealing fashion. The Medical Research Council (MRC) has similarly adapted materials across sites—flip charts in South Africa, a video in Uganda, and discussion groups elsewhere.

Comprehension tests should be repeated from time to time, with participants being periodically asked to reaffirm their consent. The HPTN has developed a preenrollment bank of questions for all prospective participants. As the trial unfolds, researchers draw upon the questions to

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retest a sample of participants. Other research institutions pose questions to participants at regular intervals—for example, every three months.

Consultation participants agreed that qualitative and quantitative methods each offer advantages and can be combined. Open-ended questions allow women to speak in their own language. The point is whether a woman understands key concepts, not whether she can repeat language verbatim from consent forms. Research staff can use open-ended questioning along side a checklist that probes for comprehension. When a participant fails to touch upon an important point, the researcher can ascertain understanding by posing additional questions on that topic.

It is not always clear how to proceed if a participant apparently does not understand all the information that investigators and ethicists deem as appropriate. Should she be encouraged to withdraw, or at least be strongly reminded that she can do so? Or should the information be provided again but in a different way?

More training of research teams and new approaches to conveying sophisticated information are clearly required. Hard data on the quality of informed consent in prevention trials is scarce. Most importantly, research sponsors and investigators must commit to conducting exploratory research prior to trial initiation to guide the process of informed consent. Experience is proving that informed consent in HIV prevention trials will not be achieved without concentrated effort to identify which words, concepts, and communication techniques make sense locally.

Admittedly, pretrial research on informed consent and ongoing monitoring is yet another expense that adds to the cost of trials. Yet for sponsors and researchers, there are tangible benefits beyond the obligation to meet ethical standards. If carried out well, the process of informed consent helps to minimize participant dropout. Moreover, a high-quality informed consent process improves overall adherence to the trial regimen and thus produces better data in the end.