

## informed consent in hiv vaccine trials

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**INFORMED CONSENT** is an essential part of any ethical research study involving human volunteers. When the horrific “experiments” conducted by Nazi doctors on concentration camp inmates came to light after World War II, doctors, ethicists and other concerned people worked to establish international standards for protecting the rights of people in *clinical studies*, while allowing research aimed at improving human health. Their efforts led to the *Nuremberg Code*, and since then, to other widely recognized international ethical regulations (see chapter 15 on research ethics).

*Clinical trials* of HIV vaccines raise most of the same ethical concerns and challenges as trials of other new medicines, and they follow the established regulations. But there are also new issues that arise when dealing with a stigmatized disease like HIV/AIDS, and when products developed in wealthy countries are tested in poor ones. For large-scale (*Phase III*) studies, there are also concerns about what is sometimes called the “double vulnerability” of participants, who are usually drawn from populations at high risk for HIV infection—a vulnerability that most often arises

from being poorer, having less formal education and/or being exposed to some form of discrimination, e.g. racial or anti-gay discrimination. For these reasons, a set of special guidelines was developed by the Joint United Nations Programme on HIV/AIDS (UNAIDS) to make sure that the specific needs of volunteers in HIV vaccine trials are met.<sup>①</sup> While these guidelines are not legally binding, in practice they have been widely adopted.

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### what is informed consent?

One of the core principles of bioethics is the right to autonomy or self-determination, which in practice means that volunteers for clinical studies must explicitly consent to participate after being fully informed about the research. The decision to participate should be made without any form of coercion, including subtle pressure such as offering rewards for participation. Autonomy also assumes “first person consent”—each volunteer must consent her/himself, rather than someone else consenting on their behalf (except for studies involving minors, where parents must give consent).

*Informed consent* is a process (and not just a piece of paper) that has both legal and ethical aspects. Legally, it is a formal record of a person's willingness to participate in a clinical trial. Ethically, it is a decision-making process during which a person who is thinking about volunteering collects and then weighs the available information.

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### the elements of informed consent

Genuine informed consent involves five key components: information, understanding, voluntariness, capacity to decide and formal consent.

### *Information*

Prospective volunteers must be fully informed about the purpose and procedures of the trial and about what participation entails. International guidelines specify the information that must be given to volunteers, which includes:

- › The aims of the trial, and its risks and benefits.
- › How many visits the trial involves for each volunteer and what procedures will be carried out (e.g., blood drawing, HIV testing, discussion of risk behaviours).
- › Policy regarding confidentiality of records and biological samples (such as blood).
- › What, if any, care and compensation will be given in the event of serious harm arising from trial participation.
- › Who to contact for more information about the study, or in the event of a research-related injury.

### *Understanding*

It is not enough for trial staff to simply provide information to volunteers. This information must use language and terms that are meaningful to the participants, who should be encouraged to ask questions. While this probably seems obvious, the reality is that researchers may have trouble explaining the study in easy-to-understand terms, and volunteers may feel uncomfortable questioning doctors or researchers who they sometimes see as more powerful than themselves. The trial site's *Community Advisory Board (CAB)* and perhaps other community organizations can help bridge this gap (for example, by helping to develop appropriate informational materials and consent procedures, and being available to answer volunteers' questions). The various committees charged with approving and monitoring trials also pay close attention to this issue. But ultimately it is the responsibility of the trial researchers to ensure that participants fully understand the essential information.

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### *Voluntariness*

Potential participants must feel free to decide about volunteering without pressure from researchers, family or others. Volunteers also have the right to change their minds about participation and withdraw at any stage of the trial, without having to explain their decision or suffering any penalty.

### *Capacity*

Each country stipulates the minimal age of consent. Volunteers must either be of legal age to consent or, for trials involving minors, have the consent of parents or legal guardians (except for specific circumstances, such as where married teenagers are considered legally emancipated). They must also have the mental capacity to understand the information about trial participation.

### *Formal consent*

Once both volunteer and researchers are satisfied that the volunteer understands the implications of trial participation and expresses willingness to enroll, he or she is usually required to sign a formal document to this effect in the presence of a witness. Separate consent may also be required for certain procedures, such as HIV testing. Where participants are illiterate, alternate arrangements (such as a record of thumbprints) can be made.

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## **culture and informed consent**

Although these principles of informed consent are widely recognized and practiced in health research, HIV vaccine trials in developing countries have also raised questions and controversy about the impact of culture on how consent is understood and implemented—for example, in countries where participants' beliefs about health and illness differ from those of medical researchers.<sup>②③④</sup>

This has led to calls for greater sensitivity to local beliefs, values and practices, which can involve approaches such as:

- › *Using language and concepts* appropriate to the local culture and social context. For example, trial staff are often asked why it is impossible to become HIV-infected from the vaccine. One site in South Africa answers as follows. “Maize seeds are planted in order to grow maize crops. But if a maize seed is taken and crushed, and a small portion of the powder planted in the ground, a maize plant would not grow. Something similar happens in making HIV vaccines.”<sup>5</sup> There may also be ways of sharing information that work well in particular communities (for instance, at times and places where people are most comfortable), and local taboos about sharing certain types of information.
- › *Incorporating locally relevant practices or traditions* into the informed consent. For example, assessments of how well volunteers have understood information about the trial can be done in ways that are culturally familiar—such as by asking people to tell stories about what the trial will involve, rather than by the conventional practice of posing test questions in writing. Trial staff with values and world views similar to those of the volunteers are also helpful, because they are better placed to understand the cultural issues that affect participants. For the same reason, community advisory groups can play a key role.

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But cultural sensitivity does *not* mean unquestioning acceptance of cultural norms, which may conflict with international standards for consent and raise the risk that important ethical protections may be ignored in the name of respect for local culture. An example of this would be cultures which require that men always make decisions on behalf of women.

This issue raises a deeper concern about applying informed consent in non-Western (or non-Westernised) settings. The emphasis on autonomy and self-determination is sometimes seen as a reflection of Western values, which focus strongly

on individual people and rights. But many other cultures, especially African and Eastern ones, emphasize communities, or the so-called “collective”—a perspective captured in the isiZulu saying in South Africa that “*Umuntu ngumuntu ngabantu*” (people are only people by reason of their relationship with other people). In these settings, requiring every trial participant to give consent can seem out of step with local norms, while getting consent from traditional leaders or other community representatives might seem more fitting. But this approach can lead to situations where individuals may not feel free to decide against participation if a decision to go forward has been made on their behalf by community leaders.

The debate over how to balance these sometimes-conflicting sets of values continues, but two guidelines are emerging. First, getting first person consent guarantees that the rights of individuals are always respected, and that there is no risk of enrolling people against their will. Second, as just mentioned, the consent process can incorporate practices that speak to the local culture and values. For example, trial staff in some regions routinely ask local leaders for permission before entering a community and beginning to discuss trials or seek volunteers. In preparation for community-based trials in South Africa it is a common custom for the local traditional leader (*Inkosi*) to call a public gathering (*imbiz*) that formally establishes a partnership of the local community, health care providers and researchers. Such solutions offer ways to combine respect for individual autonomy with respect for traditional community norms.<sup>③</sup>

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#### myths around cultural sensitivity and informed consent

It can be easy, especially for outsiders, to assume that everyone in a cultural group has the same beliefs and values. But there is often more variation *within* cultural groups than *between* them, which makes it important for trial staff to avoid generalizing about people from particular cultural groups. For example, trial staff working in rural South African communities with strong collective values have found that, contrary to these cultural

norms, many women express a strong desire for first-person consent rather than having this decision made for them by community leaders or representatives. There is also evidence from many countries that people in rural areas are likely to share traditional values, but that as they become urbanized there is more diversity of beliefs and practices within these same groups.

**INFORMED CONSENT IS A CRUCIAL PROTECTION** for study participants and researchers in HIV vaccine trials. But making it a truly ethical practice and not merely the fulfilment of a formal legal requirement is an ongoing effort, especially as trial sites are established in parts of the world that are new to clinical studies. Doing the right thing will continue to take research, creative thinking and comparing notes and experiences around the world.

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