What is ethics?
Ethics is about the principles and rules we use to decide which actions are acceptable and which are not, and to guide our relationships with others. Ethics is based on what is good, right, fair and just.

Biomedical ethics is about the principles and rules we use to decide what is acceptable or ethical when doing medical research in humans. They ensure that:
- we treat people with dignity and respect;
- we protect their rights and welfare; and,
- we promote their well-being and safety.

Which ethical principles guide research?
The three ethical principles that guide human research are:

1. respect for autonomy;
   ‘Autonomy’ refers to a person’s right to independently choose and act. This principle means that where people can think or act for themselves (e.g. they are old enough and can understand the relevant facts), we must respect their choices and actions. It also means where people cannot act independently (e.g. young children), special measures should be taken to protect them. When we apply this principle to research like HIV vaccine trials, it means that researchers must respect and encourage a trial participant’s right to say ‘no’, or to say ‘yes’ to take part in a trial by giving them enough information, and the freedom to choose. It also means that a parent or guardian should be involved if children are ever asked to take part in such trials.

2. beneficence; and,
   The word ‘beneficence’ comes from the word ‘benefit’, which means an advantage or improvement. In research, beneficence means that those with the ability or power, e.g., the researcher, must take steps to increase the potential advantages and benefits of the research and to reduce its potential risks. Researchers must make sure that participants are never deliberately harmed or injured through the research. This is called the principle of ‘do no harm’. In HIV vaccine trials this means it would be unacceptable to deliberately harm participants by, e.g., injecting them with HIV or telling them to have unsafe sex.

Researchers must also see that there is a good balance between the benefits and risks. Some research has no obvious or direct benefits to the trial participants, but it benefits society as a whole.

In general, research should only be done if the risks to the individual are much lower than the benefits to the individual and/or society. Applied to HIV vaccine trials, this means that the possible risks of the research, like the side effects or adverse events, must be reduced to an acceptable minimum. This can be done through, e.g., excellent safety monitoring. It also means that the potential benefits of the research, like the knowledge to be gained, should be maximised through, e.g., explaining the research results to the participating communities.

Benefits/Advantages

Researchers must ensure a balance between the benefits and risks of research.

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3. justice
   The principle of justice means giving people what is due to them. This means that the risks and benefits of research should be shared in a fair way, between all parties involved, e.g. sponsors, trial participants and communities. So it is fair to:
- invite people and communities to take part in the research because it helps researchers achieve their scientific goals. But they should not be invited for reasons that have nothing to do with the research, e.g., because it is convenient for the researchers to ask them. For example, in phase III HIV vaccine trials, people at high-risk of HIV infection will be recruited.
- select participants in a way that lowers the risks involved. For example, researchers should choose those who are less vulnerable. So, adults should be involved in HIV vaccine trials first, then older adolescents, then younger adolescents and so on.
- ask a person to take on the risks of research, as long as they or the population or community they represent, have a chance to benefit from it. Anyone who stands to benefit should also take on some of the risks. For example, it would not be fair to ask poor participants living in Africa to take on the risks of
Ethical issues continued . . .

HIV vaccine research if only persons in the West will benefit. Similarly, if sponsors stand to benefit from a successful vaccine, they must take on some of the risks like the cost of making the vaccine.

Although these three ethical principles apply to most cultures and situations, they should always be used in ways that are most appropriate to the environment and community in which researchers are working.

Balancing ethical principles

At times ethical principles are in conflict with each other. Then they need to be balanced against each other to lead to the most ethical decision.

Researchers need to balance ethical principles.

What are the key requirements for ethical research?

According to an article by EJ Emanuel, D Wendler and C Grady in the Journal of the American Medical Association published in 2000, there are seven basic requirements for ethical research:

a) Research must be socially valuable for the country and must be scientifically sound.

We can only justify the inconvenience and risk of harm to trial participants if the research has the potential to benefit society. For example, society must gain the following kind of benefits from the research:

• important knowledge, e.g., on how the body responds to a new drug, and, or
• a new or better intervention, e.g., a new HIV vaccine.

Researchers must also ensure that participants are not likely to be inconvenienced or to experience potential harm for no good reason, e.g., just because the researcher is interested in a particular topic. To avoid this problem in South Africa, the Medicines Control Council (MCC) and the RECs review the protocols or research plans for HIV vaccine trials. They check that the trial is designed properly and that it answers questions to help us address the HIV epidemic in our society.

b) There must be a fair selection of trial participants.

Researchers must be guided by the ethical principle of justice when choosing trial sites and selecting trial participants. This means that their choices should be based on:

• the scientific aims or goals of the research. For example, for phase IIb or III trials they should choose communities where there is a high incidence rate of HIV and not merely because it is in a convenient place;
• the need to reduce risks – remember beneficence. For example, in HIV vaccine trials, researchers should first include individuals or groups who are less vulnerable rather than more vulnerable, such as adults before children; older adolescents before younger ones etc.; and,
• the need to ensure that those that assume the risks get access to benefits – remember the principle of justice. For example: if researchers find a successful preventative HIV vaccine during a phase III trial, it should be given to the trial participants who received the placebo, and other groups in the community who are at high risk of HIV infection. If the trial only develops knowledge, this benefit should be provided to participating communities.

c) The benefits to the individual and/or society must outweigh the risks to individuals.

Researchers must identify and then decrease the potential risks and increase the benefits of research. For example, one possible risk of the research is that participants in a preventative HIV vaccine trial may test false positive for HIV infection from some HIV vaccines. To minimise this risk, researchers should providing counselling to trial participants advising them to only test at the trial site, supporting them if there is stigma and discrimination, and providing them with long-term support. Another possible risk in HIV vaccine trials is that participants might lower their standards for safer sex. Researchers must reduce this risk by regular HIV risk-reduction counselling and by providing good methods to reduce the risks of unsafe sex, e.g., by treating STIs, providing condoms and so on.

d) There must be an independent ethical review.

A committee that is independent and separate from the researchers must review the research to make sure it is ethical. In South Africa, all research protocols or plans for HIV vaccine clinical trials must be submitted by the trial sponsor to the MCC for scientific review. Independent ethical reviews are done by the RECs of each institution that participates in the research, and by other international RECs if the HIV vaccine trial includes multi-country trial sites.
There must be full, meaningful community involvement and participation.

Undue inducement:
An incentive that is so great that it makes someone volunteer against their better judgement and accept risks that they would not normally agree to, which leads to serious, harmful consequences.

False-positive HIV test result:
When an HIV vaccine design for a preventative HIV vaccine trial triggers HIV antibodies, this can cause a positive test result on a standard HIV antibody test. But no test HIV vaccine can give a person HIV. So he or she will need another kind of HIV test that tests for the presence of the HIV virus itself.

Multi-country trial sites:
Trial sites in many different countries, but all involved in the same clinical trial.
RECs usually refer to international and national ethical guidelines including HIV prevention trial ethical considerations to guide their decisions. International documents are, for example: the Declaration of Helsinki (2001); the CIOMS (2002) International ethical guidelines for biomedical research involving human subjects; and, the UNAIDS (2007), Ethical considerations in biomedical HIV prevention trials. In South Africa, examples are: The Department of Health (2004), Guidelines on ethics in health research: principles, structures and processes; and the South African Medical Research Council’s (2001), Guidelines on Ethics in Medical Research: General Principles (Book 1) as well as the MRC (2003), Guidelines on ethics for medical research: HIV preventive vaccine research (Book 5). The MCC and the RECs also refer to Good Clinical Practice or GCP Guidelines.

Following the review, both the MCC and the RECs must give approval before an HIV vaccine clinical trial can begin. The trial must also be registered with the Department of Health (DoH).

e) There must be true informed consent.
Informed consent is based on respect for autonomy. This refers to a person’s right to decide whether they will participate in the research or not. For example, to give consent for an HIV vaccine trial:
• The person must receive and understand all the necessary information about the HIV vaccine research in a way that is easy to understand. They must also be told that they are free to withdraw from the trial at any time.
• The person must have capacity – this means they must be recognised by the law as being old enough and capable enough to make the decision to participate.
• The person must be free to decide whether or not to participate in the trial without too much pressure from others.
• The person’s agreement must be explicit – this means they need to show that they agree to participate in the trial fully and clearly by signing a written informed consent document.

You will find the Department of Health Guidelines on Ethics in Health research at: http://www.doh.gov.za/docs/factsheets. It is listed under Norms, standards, instructions.
You will find the UNAIDS Ethical considerations in biomedical HIV prevention trials at: http://www.unaids.org/en/default.asp
You will find the MRC Guidelines for medical research: Book 1 and Book 5 at: http://www.sahealthinfo.org/ethics/index.htm

f) There must be meaningful community involvement and participation.
People have a right to participate in decisions that can affect their community. For example, they need all the necessary information about the HIV vaccine trials to make good decisions about how and whether to be involved. Community members can play an important role in making sure that HIV vaccine research is carried out in a way that protects and promotes the legal, ethical and human rights of people in their communities. One way to do this is to develop a Community Advisory Group (CAG) – a group of people who represent the interests of the community and contribute to decision making about trial-related issues affecting the community.

g) There must be ongoing respect for volunteers and trial participants.
Researchers must protect the privacy of trial participants, e.g., by only asking questions relevant to the HIV vaccine research. Researchers must also respect and protect a trial participant’s right to confidentiality, e.g., by training staff not to tell anyone who is participating in the trial. Researchers must regularly check on the well-being of HIV vaccine trial participants. They must arrange ways for trial participants to get new information and research results about the trial. They must tell trial participants that they have the right to leave the trial at any time. At the end of the trial, they should unblind participants (tell them whether they got the HIV vaccine or the placebo).

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