

MODULE 5

Ethical issues

In this module we discuss important ethical issues in HIV vaccine research and development.

In this module we look at:

1. What is ethics and which ethical principles should guide research?
2. Why is it important to balance the ethical principles?
3. What are the key requirements for ethical research?
4. What is informed consent?
5. Are there any controversial issues in HIV vaccine research?





WORD BOX

Ethics:

Ethics is about the principles and rules that we use to decide which actions are acceptable and which are not, and that help to guide our behaviour in our relationships with others.

1. WHAT IS ETHICS AND WHICH ETHICAL PRINCIPLES SHOULD GUIDE RESEARCH?

What is ethics?

Ethics is about the principles and rules that we use to decide which actions are acceptable and which are not. It includes rules that we use to guide our relationships with others. These rules and principles are about what is good, right, fair and just.

When we do research into human health issues, our main aim is to develop knowledge that we can use to improve the health of people in general, and/or to improve our understanding of how the body works. But we also need to follow what we call biomedical ethics.

Biomedical ethics are the principles and rules we use to decide what is acceptable or ethical when we do medical research in humans. They help us ensure that in this research:

- we treat people with dignity and respect;
- we protect their rights and welfare; and
- we protect and improve their well-being and safety.



Trial participants are people with feelings, relationships and lives of their own. They are not simply a way of achieving our scientific aims.

DID YOU KNOW?

Throughout history terrible experiments have been carried out on human beings. For example, during World War II, the German Nazis carried out abusive experiments on many different people. To make sure that these abuses would never happen again, countries around the world committed themselves to ethical principles to guide all research and experiments that involve human beings. Researchers wrote these principles up in international documents like: the *Declaration of Helsinki*, and the *International ethical guidelines for biomedical research involving human subjects*. Some countries have also written these principles into their national documents. In South Africa an example is *The Department of Health Guidelines on ethics in health research: principles, structures and processes*.



What are the main ethical principles?

There are three main principles researchers use to guide research in humans. These are: respect for autonomy, beneficence and justice.

Principle 1: Respect for autonomy

The word 'autonomy' means 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 this. In research, autonomy means that researchers must respect and encourage each volunteer's right and freedom to choose whether or not to take part in the study, by giving them enough information about the trial.

Let's look at an example: People must have the freedom to decide whether or not to become a trial participant in the HIV vaccine trials. They must also have the freedom to leave the trials at any time. No one can force them to participate. This is especially important when it comes to women. At no point should a woman's decision to participate in a trial be left up to her partner, husband or community leader. Women must freely make their own decisions after they have all the important information and know all their rights.



A patient has the right to choose who to consult.

Respect for autonomy also means that researchers must take special measures to protect people who are **vulnerable**. This includes people who do not have the capacity or ability to choose for themselves, for example, children or the intellectually challenged. They must also protect people who have less independence to choose for themselves because of their circumstances, for example, they live in poverty or they are **marginalised** and they have no power.

WORD BOX

Vulnerable:

Those who are more likely to be harmed.

Marginalised:

Those people who usually do not have a 'voice' because they are the poorest or most uneducated or most disempowered. This may include people living with HIV and/or AIDS, disabled people, elderly people, gay people, the unemployed, the homeless, etc.



Principle 2: Beneficence

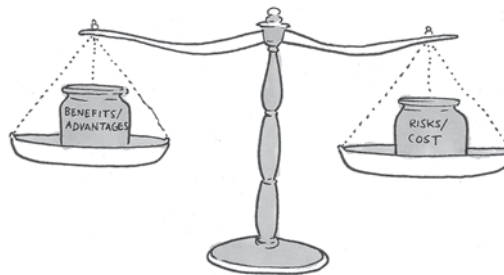
The word 'beneficence' comes from the word 'benefit', which means an advantage or improvement. Charity is an example of beneficence. Those who give to charity give help or advantages to those who have less. In research, beneficence means that those with the ability or power, for example, the researchers, must take steps to increase the benefits of the research and reduce the risks of the research. Research often benefits society by the knowledge that is gained. It can also give personal benefits to trial participants. Researchers must make sure that participants are never deliberately harmed or injured in any way through the research. This is called the principle of 'do no harm'. Researchers must also see that there is a good balance between the benefits and risks.

WORD BOX

Beneficence:
Some advantage or improvement.

DID YOU KNOW?

In our everyday lives, we often weigh up the benefits and risks of our actions. We may feel like throwing a rubbish packet on the street. The benefit is we do not need to find a rubbish bin. This saves time. But, the cost is that we litter the street and set a bad example. Here the cost is higher than the benefit.



Researchers must see that there is a balance between the benefits and risks of research.

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 outweighed by the benefits to the individual and/or society.

Principle 3: Justice

This principle means distributing benefits and risks fairly. It means that all people should be treated according to what is right, fair and just, and that each person should get what is owing to him or her. It also means that marginalised people should not be further exploited. For example, rich people get taxed more because they can afford more than poor people. This money can then be redistributed to the poor. If poor people were taxed the same as rich people, then we would be right to say: "But that is not fair!"

In research, this principle of justice means that the risks and benefits of research should be shared in a fair way, between all parties involved, for example, 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 research, for example, because it is convenient for the researchers to ask them;



- select participants in a way that lowers the risks involved. For example, researchers should choose those who are less vulnerable; and
- ask a person to take the risks of research, as long as they or the population that they represent, have a chance to benefit from the research. Anyone who stands to benefit should also take on some of the risks.

An injustice can happen when:

- a risk is unfairly forced onto trial participants. For example, it is unfair for a group of people (e.g. the poor) to take the risks of the research so that others can benefit (e.g. the wealthy), but they (the poor) do not; and/or
- a benefit is unfairly denied to a trial participant or a group of people. For example, if a specific group (e.g. women) is not included in the research for no good reason, then they cannot benefit from the research or the results.

Do you have similar concerns to the people below?

How will communities benefit from the HIV vaccine trials? Will they get anything out of participating?



How will the HIV vaccine be tested? Will participants be injected with HIV? Will they be encouraged to have unsafe sex?

Will illiterate participants really understand and be able to give proper consent?



Will participants be paid money as a reward for taking part? Will they be paid their expenses, e.g. bus fare?





Some of these questions show that the ethical principles of respect for autonomy, beneficence and justice may be in conflict with each other. When this happens, researchers must try to balance these principles.

2. WHY IS IT IMPORTANT TO BALANCE THE ETHICAL PRINCIPLES?



Researchers need to balance ethical principles.

Read through the following case study and think about the questions at the end of it.

CASE STUDY: A BALANCING ACT

A preventative HIV vaccine trial is starting in a poor community. The trial participants will take on some risks in the research. For example, they might have some discomfort after being vaccinated, or they may be stressed because of going for regular HIV tests.

Because of these risks, researchers want to offer trial participants a package of health care services, e.g. regular health checks, good HIV counselling and referral to a programme that will give ARVs if participants become HIV infected while on the trial. In other words, researchers want to take active steps to make sure that participants remain healthy. They want to fulfill the principle of beneficence – reduce risks, increase benefits, and balance the two.

But researchers must also think about the principle of autonomy – respect for the person's right to independently choose and act.

The questions are:

Is the package of health care services so good that it would actually encourage people to take part in the trials, when they would normally choose not to take part? Or, will it encourage them to accept risks that they would not normally accept? In other words, do the benefits take away the participants' independence or autonomy?



Sometimes a benefit is so great or such an **inducement**, that it takes away or reduces a volunteer's autonomy. **Undue inducement** is when a benefit is so great that it influences volunteers to take **excessive** risks that they would not normally take, which could lead to serious, harmful consequences for them.

Remember that researchers make sure that trial participants are never deliberately harmed or injured in any way through the research. This is called the principle of 'do no harm' and falls under the principle of beneficence.

In the case study on page 86 because the participants are poor and are being offered health care services, this does not automatically mean that this is undue inducement. If the ethics committees make sure that the procedures used in the HIV vaccine trial will not lead to serious harm to anyone, then it may be quite reasonable for participants to choose to accept the offer, as they will benefit from it. What the case study does show us is that researchers must always balance the ethical principles against each other to make sure that they are not in conflict.

3. WHAT ARE THE KEY REQUIREMENTS FOR ETHICAL RESEARCH?

According to an article by EJ Emanuel, D Wendler and C Grady published in 2000 in the *Journal of the American Medical Association* or JAMA, there are seven basic requirements for research to be ethical. Let's look at each one.

a) The research must be socially valuable for the country and must be scientifically sound

The principle of beneficence means we can only justify the inconvenience and risk of harm to trial participants if the research has possible benefits to 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.

I think HIV vaccine trials are valuable to society because HIV is responsible for more deaths in adults than any other disease.



WORD BOX

Inducement:
Incentive, bribe.

Undue inducement:
A reward that is so big 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.

Excessive:
Too much, extreme.

DID YOU KNOW?

HIV vaccine trials can benefit society because researchers will gain knowledge about:

- the safety of HIV vaccines;
- whether the vaccines cause an immune response; and
- whether they work to prevent infection or slow HIV disease progression.

The trials can also lead to the discovery of a successful HIV vaccine.



WORD BOX

Relied on:

Can be depended on or trusted.

HIV antibody-positive:

The person has antibodies to HIV when tested.

False-positive result:

When an HIV vaccine design triggers HIV antibodies, this can cause a positive test result on an HIV antibody test. But no test HIV vaccine can give a person HIV. So unless the person has got HIV through natural means, he or she will not be infected with HIV.

The researcher must also make sure that participants are not exposed to inconvenience and potential harm for no good reason, for example, just because a researcher is interested in a topic. To avoid these problems, the MCC and the RECs review the protocols for HIV vaccine trials. They check that the trial is designed properly and that it answers questions that will help us with the health problem of HIV that affects our society. They also ensure that the research is properly carried out so that it gives meaningful information that can be **relied on**, and so the research can be repeated.

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 risks to individual participants must be outweighed by the benefits to the individual or society

Researchers must identify and then decrease the risks and increase the benefits of research.

What kind of risks can there be?

Giving the test HIV vaccine may include the following risks:

- It might cause expected adverse events, e.g. swelling of the skin where the vaccine is given.
- It might cause unexpected adverse events.
- The person might test false **HIV antibody-positive**. In an HIV preventative trial, a trial participant may test positive when given an HIV antibody test, even though he or she does not have HIV. This is called a **false-positive result**. It happens because the test picks up the antibodies created by the immune system in response to the HIV vaccine. In this case the trial participant would need to have another test to check for the presence of the HI virus itself.



Risks of the research are explained to volunteers.



- The person may increase his or her risk behaviour. In a preventative HIV vaccine trial, participants might think that they are getting the HIV vaccine when, in fact, they are getting the placebo. They might think that the vaccine will protect them against HIV infection even though it is still being tested. This might lead them to have unsafe sex.
- During a preventative HIV vaccine trial, participants will be regularly tested for HIV infection. This may be stressful.

To decrease these risks, researchers should monitor the trial participants and provide them with education, accurate information that is easy to understand, as well as access to counselling and other support.

In South Africa, it has been recommended that trial participants receive an identity card or certificate to show that they are participating in an HIV vaccine trial. If they are then asked by a life insurance company to have an HIV test for insurance purposes, they can show their card or certificate. The insurance company can then do a test to check for the presence of the virus itself, if the standard HIV antibody tests shows a positive result.

What kinds of benefits are there in a trial?

- Trial participants get regular counselling to lessen the risk of HIV infection and to discuss other stresses they feel about the trial.
- They are given access to HIV-prevention methods, e.g. condoms.
- Trial participants have medical check ups and other regular tests that they may not normally receive.
- In later phases of the clinical trials, an effective HIV vaccine could benefit trial participants and have a huge impact on controlling the HIV epidemic.

RECs, CAGs and trial participants should all be involved in deciding if the benefits are greater than the risks.

d) There must be an independent ethical review

A committee that is independent and separate from the researchers must **review**, and inspect the research to make sure it is ethical and that trial participants will be treated with dignity and respect. In South Africa independent ethical reviews are done by the RECs and by other international RECs if the research is international.

e) There must be true informed consent

Informed consent is based on respect for autonomy. In research, it refers to a person's right to decide whether they will participate in the research or not. To give consent the person must have and understand all the necessary information, and must make their decision without too much pressure, control or influence from others.

WORD BOX

Review:
Critically evaluate.



WORD BOX

Explicit:

Stated or shown fully or clearly.



DID YOU KNOW?

In some cultures, it is respectful for volunteers to consult their husbands, wives, partners, or community leaders about their decision to participate in a trial. Researchers must allow this to happen. However, because of the ethical principle of autonomy, the decision to participate must be made and consent must be given by the individual.

NOTE:

For more information on how the researchers do the informed consent, please see page 131 in Module 7.

What must informed consent include?

- **Information:** Researchers must give volunteers enough information about the research. They must also give them time to think through the information so that they can make a good decision.
- **Understanding:** The information should be presented to the volunteers in a way that they understand.
- **Freedom:** Volunteers must not be forced, threatened, punished or put under undue influence to make a decision. They must choose freely.
- **Capacity:** Volunteers must have the legal capacity to agree to participate – they must be recognised by law as being old enough and capable enough to make the decision.
- **Explicit (usually written) consent:** Volunteers must show their agreement to participate fully or clearly, for example, by signing a written informed consent form. If some cannot or do not want to sign a consent form, then other procedures must be found to record their consent.



Researchers must give volunteers enough information and time to decide if they want to participate in the trial.

In an HIV vaccine trial, participants must be given and must understand the following information before they can give informed consent:

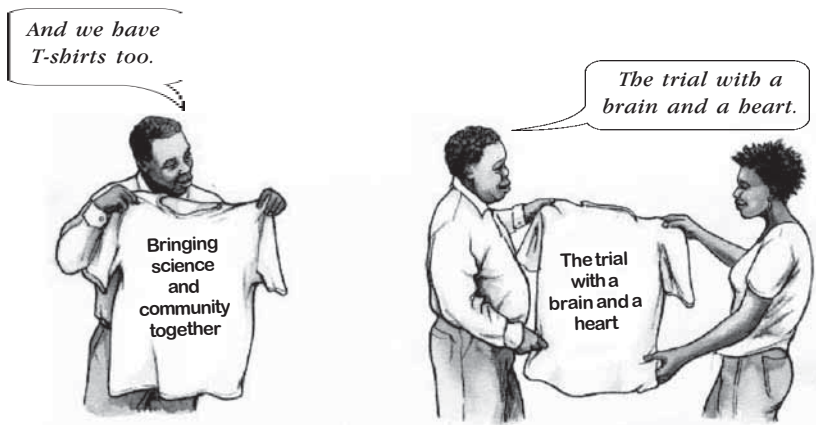
- the purpose of the HIV vaccine trial;
- the kind of procedures and tests they will go through;
- the possible risks and benefits of participating in the trial, e.g. the stress of having regular HIV tests;
- that the outcomes of the research are not known, e.g. that there is no guarantee that the test HIV vaccine will protect them against HIV infection or slow down HIV disease progression;
- what research design will be used, e.g. use of placebo and randomisation;
- the confidentiality they can expect; and
- that they are free to leave the trial at any time.

Information should be given in a way that is easily understood. Researchers must make an extra effort to ensure that volunteers understand information, including complicated information. They might need to translate information into a volunteer's home language or have an interpreter sitting in on sessions with volunteers.



f) There must be full and meaningful community involvement and participation

People have a right to participate in decisions that can affect their community. They need all the information about the trials to make good decisions about how and whether to be involved. Community members can play an important role in making sure that 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). This is a group of people who represent the interests of the different subgroups in the community and contribute to decision making around trial-related issues affecting the community.



NOTE:
You can read more about CAGs in Module 7.



Through groups like the CAG, communities can help to advise the researchers on recruitment, selection and informed consent in the HIV vaccine trials. They can advise the researchers on:

- possible risks of doing the HIV vaccine research in the community;
- ways to recruit trial participants that are fair, culturally right, and that include many different groups but do not unfairly target any one group;
- ways to try to protect vulnerable trial participants;
- how the community sees these processes (e.g. are they seen as fair?);
- how to reimburse trial participants fairly, or to ensure fair benefits from the research;
- informed consent that is culturally correct; and
- how to give information about the trials that is easy to understand, for example, by using drama.

g) There must be ongoing respect for volunteers and trial participants

- Researchers must protect the privacy of trial participants, for example, by only asking questions needed to answer the research question.
- Researchers must also respect and protect a trial participant's right to confidentiality, for example, by training staff not to tell anyone who is participating in the trial.
- Researchers must regularly check on the well-being of trial participants.
- They must make sure that they arrange ways for trial participants to get new information and research results.
- They must tell trial participants that they have the right to leave the trial at any time.



4. ARE THERE ANY CONTROVERSIAL ISSUES IN HIV VACCINE RESEARCH?

Often HIV vaccine trials bring up complex ethical issues. Here is one of the debates that could occur when a sponsor comes from a rich country with many resources, and does the research with poorer countries who have a lot less resources.

The debate: In a preventative HIV vaccine trial, are sponsors responsible for providing trial participants with treatment (including ARVs) for HIV infection?

Remember, HIV infection will not happen because of the test HIV vaccine, but because participants take risks in their sexual activities even though counsellors explain how to prevent HIV infection (this is called HIV risk-reduction counselling).

Some people say that trial participants are responsible for their own behaviour. They say that the sponsor and researchers are not responsible for providing treatment for these participants because the HIV infection is not related to the trial. It is because of unsafe sex. So these participants should get treatment through the clinics or hospitals.



Other people argue that sponsors and researchers are responsible and must make sure that all trial participants can get treatment. Some say that the trial participants may believe that the preventative test HIV vaccine is very effective. This false belief may lead them to not practise safer sex and put them at increased risk of getting HIV.

Think about or discuss:

- Do you think that sponsors and researchers should provide ARVs to trial participants who are infected with HIV during a preventative HIV vaccine trial? Why or why not?



TO SUM UP

- Ethics is about the principles and rules that we use to decide which actions are acceptable and which are not. It includes rules that we use to guide our relationships with others. These rules and principles are about what is good, right, fair and just.
- The three ethical principles involved in human research are:
 - respect for autonomy;
 - beneficence; and
 - justice.
- Often these ethical principles are in conflict with each other and need to be balanced against each other, so that we make the most ethical decision.
- There are seven basic requirements for ethical research:
 - a) The research must be socially valuable for the country and must be scientifically sound.
 - b) There must be a fair selection of trial participants.
 - c) The benefits to the individual and/or society must outweigh the risks to individuals.
 - d) There must be an independent ethical review.
 - e) There must be true informed consent.
 - f) There must be full and meaningful community involvement and participation.
 - g) There must be ongoing respect for volunteers and trial participants.
- Informed consent refers to a person's right to decide whether they will participate in the research or not. It is based on respect for autonomy. To give consent:
 - The person must receive and understand all the necessary information.
 - They must have capacity – they must be recognised by the law as being old enough and capable enough to make the decision.
 - They must have the freedom to decide whether or not to participate without too much pressure from others.
 - Their agreement must be explicit – they need to show their agreement to participate fully and clearly by signing a written informed consent document.