What is a vaccine?
A vaccine is a substance that teaches the body to recognise and defend itself against bacteria and viruses that cause disease. A vaccine causes a response from the immune system (the body's defence system), preparing it to fight--and also remembering how to fight--if exposed to the virus at a later time. A successful vaccine can cause the body to stop or disable an invading virus. A vaccine is not a cure, but prevents infection or slows down disease progression.

What is the history of vaccines?
The first modern vaccine was developed in 1796 by Edward Jenner to prevent smallpox. Through vaccination, smallpox, which at the time killed about a million people per year in Europe, has been eradicated. Now, there are also vaccines to prevent many other diseases, including rabies, tetanus, measles, mumps and polio. These vaccines save millions of lives.

Why an AIDS vaccine?
The 2002 report by the United Nations Programme on HIV/AIDS (UNAIDS), estimated that about 42 million people are living with HIV/AIDS worldwide, including 4.7 million South Africans (one in every nine). According to the Medical Research Council's (MRC) 2001 report, The Impact of HIV/AIDS on adult mortality, AIDS accounted for about 25 percent of all deaths in 2000 and was the leading cause of death in South Africa. Development of a vaccine is the only long-term hope to control the HIV epidemic. However, it must be part of an overall strategy that includes prevention, treatment, care and support.

How would an AIDS vaccine work?
An effective AIDS vaccine would teach the body to recognise the human immunodeficiency virus (HIV) that causes AIDS, and would boost the immune system in slowing and neutralizing the virus if it enters the body. The information on how to defeat the virus would then becomes part of the immune system’s memory so that it would remember how to fight back if it encountered the virus again. An AIDS vaccine cannot cause a person to become infected with HIV.

Can an AIDS vaccine cause AIDS?
No, a vaccine cannot cause HIV infection or AIDS. AIDS vaccines do not contain any live virus that could spread and cause infection. AIDS vaccines generally contain only harmless particles or copies of particles of the virus, which cannot cause infection. A vaccine is a bit like a motor car with the engine removed – it is still recognisable as a car but it can’t drive.

Is there a preventative AIDS vaccine available?
Currently, there is no effective AIDS vaccine available. However, there are several possible vaccines that may work and will be tested in clinical trials. Testing a vaccine takes a long time to ensure that it is safe and effective. It normally takes 10 to 20 years to bring a vaccine to the market.

How do you test an AIDS vaccine?
Both vaccines and drugs are tested in stages taking a number of years. Initial laboratory work is followed by animal studies to establish overall safety and then human clinical trials. During the human trials the candidate AIDS vaccine is tested in volunteers to evaluate safety and establish
effectiveness There are three phases in these trials.

Phase I involves about a relatively small number of healthy, HIV-negative, adult volunteers at low risk of HIV infection and tests for safety. Phase II involves about 200 - 500 of healthy HIV-negative adult volunteers, some of whom are at higher risk of HIV infection and tests for safety, an immune system response, as well as early information on the required dose and route of administration. A Phase III trial involves several thousand adult volunteers at high risk of HIV infection to assess if the vaccine prevents infection with HIV.

All these phases usually make use of placebo groups - in other words, some of the participants receive a harmless substance that resembles the test vaccine. The ‘placebo’ group is then compared with the group that received the actual test vaccine. Use of placebo groups in Phase I and Phase II has nothing to do with protection. All volunteers receive extensive risk-reduction counselling throughout the trial and access to other prevention methods such as condoms.

Who participates?
Only adult volunteers who meet the criteria outlined above and understand the study and agree to give informed consent can participate.

How are people's rights safeguarded?
People's rights are safeguarded by:

- International guidelines for ethical vaccine and pharmaceutical trials;
- A sound constitutional and legal framework within South Africa;
- An independent system of ethical review based on ethical principles and guidelines for each trial site;
- Well-informed and mobilised communities that actively participate in the research;
- Ensuring 'informed consent'. This is the agreement free of coercion or undue influence, by volunteers to participate, based on a complete understanding of all the relevant information;
- Taking active steps to minimise potential harm to participants and to maximise the expected benefits of research;
- Ensuring that trial participants and research communities are chosen fairly;
- Employing competent and highly trained research staff; and,
- Protecting confidentiality.

What about vaccines in South Africa?
There are a number of potential candidate vaccines in development in South Africa. As of 25 August this year, two vaccines have been approved for human trials. The IAVI MVA.HIVA trial is the second to be approved. The first was the AlaphaVax AVX101 candidate vaccine, approved in June this year. Coordination of the development and testing of these candidate vaccines is the responsibility of the South African AIDS Vaccine Initiative (SAAVI). The Medicines Control Council (MCC) must approve all vaccine trials and institutional ethics review boards.

Why an HIV/AIDS vaccine for South Africa?
A vaccine that can prevent HIV/AIDS in South Africa is vital for reducing the country's incidence of HIV. Although it is important to develop vaccines based on the subtype C virus, the most common
HIV subtype in South Africa, vaccines based on other subtypes could also be tested as they may offer protection and could help resolve the outstanding scientific issue regarding the significance of the HIV virus subtype, or “clade” in vaccine development.

**Where will the vaccine trials be held?**

Two sites are ready to begin clinical trials - the AIDS Vaccine Division of the Perinatal HIV Research Unit (PHRU) of the University of the Witwatersrand at the Chris Hani Baragwanath Hospital in Johannesburg, and the SAAVI HIV Vaccine Research Unit at the MRC in Durban. Additional trial sites in other regions are in the early stages of development.

**Why are these trials being done in South Africa?**

With South Africa’s high rates of infection it is important to develop a vaccine that will work for the strains of the HIV virus circulating in the country. It is only possible to evaluate whether any candidate vaccines work in South Africa by testing them in South Africa.

**What about vaccines in other countries?**

The International AIDS Vaccine Initiative (IAVI), the US National Institutes of Health (NIH), the European Union (EU), the Centres for Disease Control and Prevention (CDC) in the US, and others, all support the development of AIDS vaccines. Clinical trials are under way in countries including the US, Thailand, Britain, Kenya, Uganda, India, Botswana, Haiti, Brazil and Peru. Several pharmaceutical companies are also involved in vaccine development. International efforts are focusing on vaccines that will be inexpensive to make and easy to access by both rich and poor countries. International collaboration will ensure that breakthroughs are shared to speed up the development of an effective AIDS vaccine.

**Why is it necessary to do many trials?**

As yet it isn’t known which approach will provide an immune system response that is sufficient to protect against the virus – so many different approaches may need to be tested. The testing process takes a long time (at least 7 to 10 years for each candidate vaccine) so it makes sense to run trials of different vaccines at the same time to develop a successful vaccine as quickly as possible.

**Why does it take so long to get to Phase III trials?**

Each phase involves monitoring the volunteers over a lengthy period. Until this has been completed, and the candidate vaccine has been shown to perform satisfactorily, a candidate cannot move on to the next trial phase.

**In Phase III trials, will volunteers be injected with HIV to test the efficacy of the vaccine?**

Definitely not. At no stage are volunteers injected with anything other than synthetic copies of portions of genes, which cannot cause HIV or AIDS.

**What is the quality of the research teams and the laboratory that will be analysing samples taken during these trials?**

The principal investigators (PIs) in charge of the Johannesburg and Durban validate trials units are highly respected, locally and internationally, for their work in this field. The South African Immunology Laboratory at the National Institute for Communicable Diseases in Johannesburg is a world-class and internationally validated facility, which is regularly audited by local and international organisations, to ensure it maintains this standard.

**Why must volunteers be HIV negative?**

A preventive vaccine is intended for people who are uninfected with HIV. Therefore the trials must be conducted among uninfected people.

**Why the focus on prevention and not a cure for HIV?**
Ultimately, a vaccine to prevent HIV infection represents the best hope for stopping AIDS. We are concentrating on vaccine research; other researchers will be seeking a cure. If we could stop new infections there would be fewer people needing treatment.

**Are the trials focusing only on black people?**

No, volunteers should reflect representative samples of the South African population. However, these are not exclusively South African trials-- they are part of a global effort to develop a vaccine against HIV/AIDS.

**Will there be enough volunteers for simultaneous trials?**

Each Phase 1 trial will enrol roughly 50 to 100 volunteers. More than enough candidate volunteers are ready. Both sites continue to interview and screen volunteers. If one site does not have sufficient volunteers, the number can be made up at the other site.

**How many volunteers can be expected to drop out of the trials?**

The interviews and counselling before the trials start are designed in part to ensure that volunteers will stay the course. While it is not unusual for a very small number not to drop out, in some trials there are no dropouts at all.

**How many volunteers are expected to contract HIV during these trials?**

Ideally, none. For the phase I trials, volunteers are healthy HIV-negative adults.

**If any do contract HIV during the trials, will they be provided with anti-retrovirals?**

Yes. The government of South Africa has recently established that participants in HIV vaccine trials who become HIV-infected during the period of the trial will be provided with anti-retrovirals. IAVI’s own guidelines support provision of anti-retrovirals as one component of comprehensive care. The detailed policy is not yet available from the government, but from what we understand, it is similar to IAVI’s own guidelines.