



An AIDS vaccine with 50% efficacy provided to just one-third of the population would cut the number of new HIV infections in the developing world by more than half in 15 years.

The background is a solid orange color with a pattern of semi-transparent orange circles of varying sizes scattered across the top and middle sections. A white rectangular bar is located in the bottom right corner.

FAQs about AIDS Vaccines

What is a vaccine and how does it work?

Millions of lives, across the world, are saved each year because of a small but powerful collection of 10-20 different vaccines. These protect both children and adults from a whole range of otherwise life-threatening diseases like diphtheria, tetanus, measles, rabies, hepatitis, influenza, meningitis and yellow fever. Without vaccines, we would still be battling polio on a global scale and living in fear of small pox across India. Vaccines are among the safest and most cost-effective public health tools that have shaped human well-being as we know it today.

A vaccine works in a seemingly simple manner. In normal course, an individual's immune system learns how to protect him/her against a disease only after the body is exposed to the disease or infection once. But a vaccine stimulates the immune system to recognise the disease/infection in advance, by teaching the immune cells to identify certain invaders, such as germs, that cause disease. These lessons of being able to distinguish invaders are then stored by the memory of the immune system, so that it quickly responds the next time the body is exposed to the same risk. Thus, vaccines prime the human body in advance to take charge and keep dangerous diseases at bay.

Is there a vaccine against AIDS?

Currently, there is no effective AIDS vaccine available, but the need for one is urgent because it remains the best long-term hope to bring an end to the AIDS epidemic. The scientific search for such a vaccine is almost as old as the discovery of HIV/AIDS, but developing a safe and effective AIDS vaccine is turning out to be a bigger challenge than other vaccines.

Many common vaccines are based on killed or weakened versions of the germ which causes the disease against which they build protection. No one is looking at vaccines of this type against HIV. All the AIDS vaccines which are being tested in humans are based on a new way of making vaccines: scientists take tiny, harmless bits of HIV and hide them inside common germs that we know the body can recognise. There is no way that such vaccines can cause infection. Researchers hope that the body will find the hidden fragments and then learn to recognise HIV if it tries to attack the body.

Several candidate AIDS vaccines are in various stages of being tested in the laboratory, animals and humans. It is a long and tedious process but there is sufficient evidence to believe that an effective AIDS vaccine is a scientific possibility.

Most vaccines in use today are designed to protect humans from disease or infection, i.e. they are preventive vaccines. Most scientific efforts in the search for an AIDS vaccine are also focussed on finding a preventive AIDS vaccine. A preventive AIDS vaccine will be meant only for people who are not infected with HIV, for it will prepare the immune system to respond in case of exposure to the virus. All references in this document are to a preventive AIDS vaccine.

An AIDS vaccine, once available will be integrated into existing HIV/AIDS prevention programmes that encourage condom use, safe blood practices, behaviour change and possibly other new prevention technologies such as microbicides. An effective AIDS vaccine will always remain one of the multiple options to fight HIV/AIDS. Over the long term, as more and more people become vaccinated, a vaccine could help bring an end to the epidemic.

How is an AIDS vaccine developed?

AIDS vaccines are tested in various stages over several years, as with most other vaccines. Initial laboratory work is followed by animal studies and then human clinical trials. Many of the modern, licensed vaccines that are used today have taken several decades before they cleared the many complicated stages of their development. Experts believe a safe and effective AIDS vaccine may be found within the

decade, but there are others who feel it may take much longer than that.

The detailed plan or roadmap for a clinical trial is called a **protocol**. This is the official trial guideline - an outline of all the procedures involved in the trial. For example, it contains information on who can participate, how the vaccine will be given, the schedule for clinical examination and blood tests, how long the study will last, how results will be assessed etc. A protocol should follow the highest international standards and ethical guidelines for the conduct of clinical trials.

The AIDS vaccine trials in India have been approved by the appropriate Ethics Committees and by the Drugs Controller General of India.

Vaccine development and clinical trials

There are many steps involved in the development of any vaccine before it can be licensed and used in humans. After a vaccine is designed or developed in the laboratory and is tested in animals for safety, immune response and toxicity, it must go through a series of clinical trials in humans. A **clinical trial** is a study done in humans to answer specific questions about a new vaccine or drug. While undergoing testing, new vaccines or drugs are referred to as 'candidate' vaccines or drugs. A series of carefully conducted trials is the fastest way to see if a new vaccine can protect people from

Infection or disease. This series involves three or more phases and several trials before an application for licensure to distribute the vaccine is made.

Phase I

These trials are the first human tests of an experimental vaccine. They measure the safety and ability to stimulate immune responses (immunogenicity) in a small group of 20-60 healthy volunteers. Several Phase I trials may be conducted to obtain this information, possibly involving different routes of injection (mode to give vaccine-mouth/skin/in muscle) or doses (how much to give). If a vaccine is immunogenic, this means that immune responses have been observed in volunteers' blood after they receive the vaccine. It is not known whether this immune response will protect a person against infection or disease. Phase I trials often last 12-18 months.

Phase II

These trials measure safety and immunogenicity in a larger group of 50-500 healthy volunteers. Here the goal is also to find the best dose and regimen. Phase II trials may last up to two years or longer. In some cases, a larger group of volunteers that represent the population at risk for the disease is asked to join a trial; these trials are known as Phase II b trials. These trials can provide important data about safety of the vaccine and may give some information about whether the vaccine truly works, or has efficacy.

Phase III

Phase III trials evaluate the safety and measure efficacy of the vaccine in a much larger number of people (for HIV vaccines, estimates range from 2,000 to 20,000, depending on the number of infections per year in the population) who are at significant risk of infection. The ability of the experimental vaccine to stimulate immune responses may be measured

in some or all volunteers to ensure that the vaccine is inducing the same immune response it did in earlier trials. This is particularly important if the same vaccine is from a different manufacturing batch or has been made in larger quantities. Phase III trials can last for several (3-5) years. The whole process, including all phases of testing, can take 10 years or more. A vaccine must be proven safe and efficacious before it can be reviewed and approved for licensure by regulatory agencies, licensed and distributed to the community.

Phase IV

One type of Phase IV study, called an expanded access study, is usually conducted during the interval between the end of the efficacy trials and approval of the product. This allows for the collection of safety data in a larger population of people as well as access to the candidate vaccine before it is fully approved and licensed. Phase IV studies may also look at the safety and effectiveness of the vaccine after it is licensed and in use by large populations. These studies examine how the vaccine performs under real-life conditions, as opposed to the controlled conditions of a clinical trial. These studies are sometimes called post-marketing surveillance studies or field studies. Collection of safety data and data on rare adverse events are primary goals of Phase IV studies.

'Safety' in the context of an AIDS vaccine trial means that researchers are testing to make sure the vaccine does not cause side effects in a significant number of people or to a significant or severe degree in any person. Testing for safety does not mean testing to see if the vaccine causes HIV infection. Before a vaccine goes into clinical trials, researchers already know that there is no chance it will cause HIV infection in humans. No vaccine that could cause HIV infection would be put into preventive AIDS vaccine trials in humans.

People who join a clinical trial should never count on the experimental product protecting them. When the degree of protection the vaccine provides in the trial is being tested, this concept is referred to as 'efficacy'.

Questions Asked :

Does it cause side-effects in humans?

Does the human immune system respond to it?

What is the ideal dose of the vaccine?



Phase I

Number of participants : 20 - 60

Healthy HIV-uninfected people who are unlikely to be exposed to HIV (they practise low-risk behaviour)

Duration of trial : 12 - 18 months

Objective : Safety, dose, regimen, route

Does it cause side-effects in humans?

Does the human immune system respond to it?

What is the ideal dosage and the vaccination schedule?



Phase II

Number of participants : 50 - 500

Healthy HIV-uninfected people

Duration of trial : 2 years

Objective : Safety and immunogenicity with selected dose, region, route

Does it cause side-effects?

Is the vaccine effective?
Meaning does it prevent HIV infection or does it delay progression to disease?



Phase III

Number of participants : 2000 - 20,000

HIV-uninfected people who are at risk

Duration of trial : 3 - 4 years

Objective : Safety, efficacy



If the vaccine is found to be safe and effective, it may be licensed for widespread public use by the Drugs Controller General of India and be made available to the community.

Source: AIDS Vaccine Literacy Toolkit, IAVI, 2005
Graphic Design: Deepak Harichandan, Courtesy TOI.

Is it necessary to test an AIDS vaccine in humans?

After initial laboratory work and animal testing, a vaccine has to be tested in humans to make sure that it is successful in protecting against the infection or disease and poses no danger to the human body. The necessity of testing AIDS vaccines in humans is even stronger because:

- HIV exclusively infects and causes disease in human beings
- there are no good animal models that can mimic what happens in the human body because our immune system is very different
- although animal model data provide insights into vaccine concept and design, and reassurance about safety, only human clinical trials can determine whether the vaccine actually works the way it is supposed to (vaccine efficacy).

Why does India need to participate in AIDS vaccine trials?

India today is a strong partner in the global search for a safe and effective AIDS vaccine. Scientists and top medical research institutions from India are collaborating with international partners to develop a preventive AIDS vaccine.

Multiple vaccine candidates are being considered for testing in India.

Are there other countries conducting AIDS vaccine trials?

Since 1987, more than 40 different AIDS vaccines have already been tested in over a 100 clinical trials. These trials have taken place or are ongoing in many countries across the world including Australia, Belgium, Botswana, Brazil, Canada, China, Cuba, Finland, France, Germany, Haiti, Kenya, Malawi, Peru, Puerto Rico, South Africa, Switzerland, Thailand, the United Kingdom, Trinidad and Tobago, Uganda and USA. More than 15,000 volunteers have participated in such clinical trials worldwide.

Have any AIDS vaccine trials been conducted in India?

Yes. India's first Phase I trial was initiated in 2005 at the National AIDS Research Institute (NARI), Pune. The trial enrolled 30 volunteers and was completed in December 2006. A second Phase I trial to test another candidate vaccine is underway at the Tuberculosis Research Centre (TRC), Chennai, where 32 volunteers have been enrolled. It is planned to initiate a third Phase I trial at NARI and TRC.

Has the Government of India approved of these AIDS vaccine trials?

Yes. This AIDS vaccine programme is governed by a Memorandum of Understanding (MoU) between the Government of India and the International AIDS Vaccine Initiative (IAVI). The Government of India is represented by the National AIDS Control Organization (NACO) in the Ministry of Health and Family Welfare and the Indian Council of Medical Research (ICMR). All approvals for the two Phase I trials being conducted at NARI and TRC have been obtained from the office of the Drugs Controller General of India (which approves all clinical research with new drugs or vaccines).

What are Prime-boost studies?

Prime-boost is a series of immunisations meant to 'prime' or prepare the immune system with the first vaccination and 'boost' the immune system with the next vaccination(s). The same or different types of vaccine may be used for the prime and boost.

The intent of the vaccination regimen is to induce stronger immune responses than those obtained by using either

vaccine alone. The decision of a prime-boost study is taken on the basis of the safety and immunogenicity data generated in Phase I clinical trials of each vaccine separately.

Managing expectations

Generally, when people learn of an AIDS vaccine trial being conducted in their community, expectations are raised about the outcome of the trial. People may assume, for example, that a highly efficacious vaccine will become available quickly after the trial is over. However, if the vaccine is only in Phase I or II testing, it will need to go through further phases of testing, which takes many years. Sometimes, after testing, data analysis may reveal that the vaccine was not efficacious and /or safe enough to be used in the general population. Finally, if the vaccine was shown to be effective and efficacious through the process of all phases of testing, regulatory approval to license a vaccine will take additional time.