



# How HIV Drugs Get Approved

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## WHY DOES IT TAKE SO LONG TO APPROVE NEW HIV DRUGS?

Developing a new drug can take 10 years or more. First, drug companies must find substances that are active against HIV. Most HIV drugs are identified by testing existing drugs for anti-HIV activity (screening). A newer method is rational drug design. In this process, scientists build drug molecules to fight HIV in specific ways.

When a promising drug is identified, it goes through pre-clinical testing. This involves test-tube and animal studies. These show whether the drug works against HIV and how it works. They also show how it can be manufactured and make sure it is not too toxic (poisonous).

If pre-clinical results are good enough, the drug company files an Investigational New Drug (IND) application. Then it starts testing the drug in humans (clinical trials). Only about one candidate drug in 1,000 makes it into clinical trials. When enough clinical trials are completed, the manufacturer submits a New Drug Application (NDA). If the Food & Drug Administration (FDA) approves the NDA, the drug can be sold to treat specific medical conditions.

## WHAT ARE THE PHASES OF CLINICAL TRIALS?

There are four phases of human clinical trials. These apply to all drugs, not just drugs for HIV/AIDS. If the results from any phase of testing are not good enough, the company will stop developing the drug.

**Phase I** trials test the safety of new drugs by giving them to humans for the first time. People who participate in Phase I trials face the highest risks compared to possible benefits. These trials record the [side effects](#) that occur at different dosages of the drug. All participants in a Phase I trial receive the new drug, but different participants may get different dosages. Phase I trials usually study less than 100 people and take less than a year.

**Phase II** trials typically enroll several hundred people and take 1-2 years. They study what dose of drug may work best against HIV. They also collect more information about side effects. Only about 1 drug candidate in 3 makes it through Phase II trials.

Phase II trials are usually randomized. This means that trial participants are divided into two groups that are similar in terms of age, sex, and health. One group receives the study drug and the other group is the reference or control group. People in the control group get standard treatment (called standard of care). If there is no standard treatment, they may get a dummy medication (called a placebo).

In some Phase II trials, neither the participants or the researchers know who is getting the study drug or the placebo. This is called a blinded study. Studies are blinded so that the researchers will be totally objective

when they evaluate the health of patients in the study.

**Phase III trials** collect more data on a drug's effectiveness and side effects, using the dose selected in the Phase II trial. Phase III trials can study up to a few thousand people and often last for 2 years or more.

Phase III trials are normally randomized and often blinded. Participants may or may not receive the study drug for free. With good results in Phase III trials, a manufacturer can apply for FDA approval to sell the new drug.

**Phase IV** trials are called post-marketing studies. Phase IV trials monitor a new drug's long-term effectiveness and side effects, in new combinations, or how cost-effective it is. They can also compare the new drug to other drugs approved for the same condition.

### **HOW DO WE KNOW IF A DRUG WORKS?**

The FDA used to require trials that measured clinical endpoints before approving a new HIV drug. These trials analyze how many people get sicker, develop [opportunistic infections \(OIs\)](#), or die.

However, these trials take a long time and are very expensive. A faster, cheaper way to test new drugs is by using indirect measures of patient health. These surrogate markers are laboratory values such as [viral load](#) or [CD4 cell counts](#). The FDA approves the use of surrogate markers for full approval of new HIV drugs.

Clinical trials should include people like those who will use the drug. But manufacturers sometimes prefer to test their products in people who are as healthy as possible. For example, sometimes they exclude people living with [hepatitis B virus \(HBV\)](#) or [hepatitis C virus \(HCV\)](#) because of their liver problems, although many people with HIV also have hepatitis.

### **USING UNAPPROVED DRUGS**

There are three legal ways to use drugs that the FDA has not approved to treat a specific health problem:

1. **Expanded Access** is a program where manufacturers provide unapproved drugs to people who cannot take part in a clinical trial. Patients must meet conditions set by the drug manufacturer. The drugs are usually offered at no charge, but participating healthcare providers have to collect information on how patients respond to the drug.
2. **Treatment IND Protocol or Compassionate Use.** The FDA allows drug companies to provide new drugs to people who are very ill and who have no other treatment options. A related type of access is called **Parallel Track**. This policy was developed to provide investigational drugs to people with HIV/AIDS who are unable to participate in clinical trials of those drugs.
3. **Off-label use.** Health care providers can write a prescription for any FDA-approved drug, even to use it for some medical condition it was not approved for. This is called off-label use. There may be no information about how often medications are used off-label or how well they work.

### **THE BOTTOM LINE**

Developing a new drug can take 10 years or more. When a promising drug is identified, it goes through pre-clinical testing, which involves test-tube and animal studies. These show whether the drug works against HIV and how it works. They also show how it can be manufactured and make sure it is not too toxic (poisonous).

There are four phases of human clinical trials. These apply to all drugs, not just drugs for HIV/AIDS. If the

results from any phase of testing are not good enough, the company will stop developing the drug.

The FDA approves the use of surrogate markers, such as viral load and CD4 cell counts, for full approval of new HIV drugs.

There are several legal ways that healthcare providers and drug manufacturers may provide drugs that the FDA has not approved to treat a specific health problem.

#### ***MORE INFORMATION***

US FDA: [How Drugs are Developed and Approved](#)

ClinicalTrials.gov: [Find a Study](#)

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