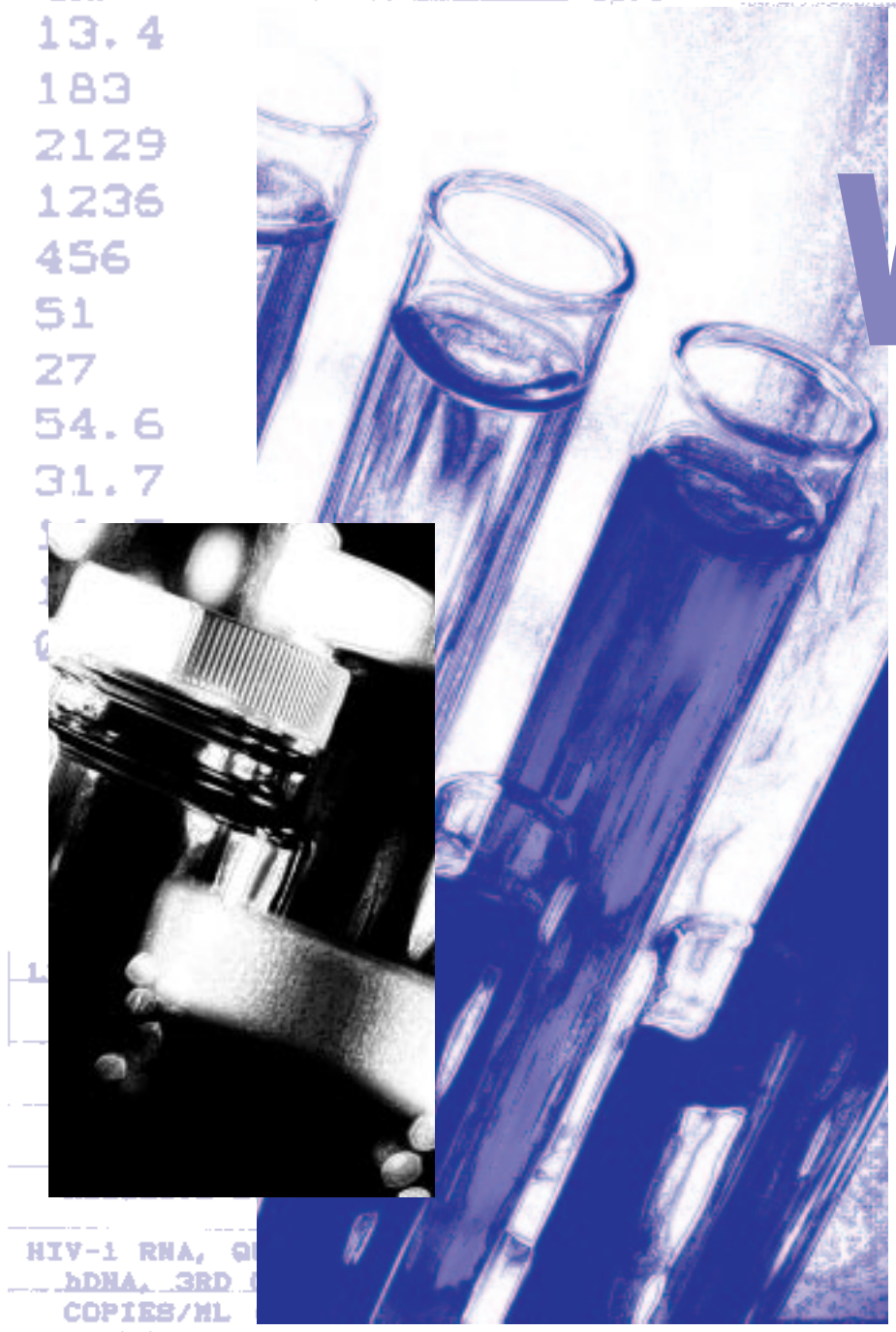
A Guide to Clinical Trials

PART I: UNDERSTANDING CLINICAL STUDIES



SAN FRANCISCO AIDS FOUNDATION

When a new drug, assay, device, procedure, or other potential medical innovation is developed, it must be thoroughly tested to ensure that it is safe and does what it purports to do.

Medical studies of new interventions involving human subjects are called clinical trials. Such studies test new or improved therapies in volunteer participants, first determining whether they are generally safe, then whether they are effective. Although clinical trials are governed by extensive regulations to ensure that they are ethical and as safe as possible, individuals considering clinical trials should carefully weigh the possible risks of participation against the potential benefits.

This article provides an overview of the clinical trial process. Part II will discuss interpretation of clinical study results, and will appear in the next issue of *BETA*.

Accelerated Approval, TIND, and Expanded Access

In the early years of the AIDS epidemic, HIV positive people and their advocates pushed for new mechanisms to make experimental drugs available more quickly. The FDA may grant **accelerated approval** for agents that treat serious illnesses for which there are few or no other therapeutic options. However, the agency still requires pharmaceutical companies to complete the clinical trial process and provide longer-term data before drugs are granted final traditional approval.

Some people who would like to try not-yet-approved but potentially beneficial therapies do not meet inclusion criteria, are too ill, live too far away, or are otherwise unable to participate in clinical trials. In 1987 the FDA instituted the **Treatment Investigational New Drug (TIND)** category to provide early access to promising medications for individuals with serious or life-threatening conditions and no good treatment options. For an agent to qualify as a TIND, there must already be some evidence that it is safe and effective. In addition to enabling more people to access experimental drugs, TINDs also provide information on safety and efficacy under "real world" conditions. Participants' regular physicians dispense the drug and provide such data to the manufacturer.

While experimental agents are actively under study in clinical trials—or when trials have been completed and drugs are awaiting approval—pharmaceutical companies may institute **expanded access programs (EAPs).** In effect, TINDs and EAPs act as open-label studies that do not involve blinding, randomization, or matched control arms.

The Drug Development Process

The process of developing a new drug is complex, lengthy, and expensive. It may take ten years or more for a candidate to make its way from the laboratory to pharmacy shelves. (However, there are various mechanisms in place to speed things up for experimental agents for HIV/AIDS and other life-threatening illnesses; see sidebar above.) According to the U.S. Food and Drug Administration (FDA) only one of every 1,000 candidate compounds makes it from the laboratory to clinical trials, and just one in five of these is ever approved and marketed.

Most experimental agents originate in university, government, or pharmaceutical company laboratories. Increasingly, they are designed by computers to meet certain structural or functional specifications. Promising compounds are then subjected to extensive testing. The first step involves *in vitro* (Latin for "in glass") testing in a laboratory. For example, a potential antiretroviral compound may be added to a culture in a petri dish containing human cells and HIV to see whether the agent slows viral replication.

But activity in a test tube does not mean an agent will work in the body (*in vivo*). Laboratory testing also cannot conclusively show that an agent is safe, although it can provide important information about its effects on cells. The next step in testing usually involves animal studies. Typically, drug candidates are first tested in mice or rats, then often in dogs, then sometimes in primates. Animals are not people, however, and many agents have been shown to be more or less safe or effective in different species.

Finally, if a candidate still looks promising after laboratory and animal studies, it may advance to testing in humans. Researchers must submit an application to the FDA, the federal agency that regulates drugs and medical devices. If approved, the experimental agent is designated an investigational new drug (IND) and may enter clinical trials.

Phases of Clinical Trials

Although the ultimate goal of the drug development process is to come up with treatments that work, researchers must first determine whether they are safe. The clinical trial process is divided into four phases, each of which includes a larger number of participants.

Phase I: The earliest safety trials of an experimental agent involve a small number of subjects (typically 10–100); these trials often use healthy volunteers without the disease under study. The aim is to detect any obvious toxicities (side effects or adverse events) before many subjects are put at risk. Usually subjects are exposed to the new agent for a short period, perhaps only a few days. These studies evaluate a compound's **pharmacokinetics**—how it is absorbed, metabolized, processed, distributed, and eliminated by the body. At this stage researchers also try to determine an optimal amount of the agent that will offer the most benefit without unacceptable toxicity, a process

known as **dose-ranging.** While there may be some early indications that a compound works, determining efficacy is not the goal of Phase I trials.

Phase II: Once it is established that there are no major safety concerns, an agent is further tested to see whether it still appears safe in a larger cohort of people (typically 50–500) with the disease under study. These studies also provide preliminary data on a candidate's efficacy (activity, or how well it works). Sometimes these trials are divided into Phase IIa (pilot studies) and Phase IIb (small controlled trials). The study period is longer than for Phase I trials, usually several months to two years. In an effort to speed the development process, trial stages are sometimes combined (Phase I/II or Phase II/III). This stage is where most drug candidates are weeded out; only about one-third of experimental agents successfully make it through Phase II studies.

Phase III: The goal of the third stage of human testing is to determine whether the experimental agent is effective in a still larger population, typically several hundred to several thousand. These trials usually last at least a couple of years, and often considerably longer. The most rigorous type of study is the prospective, double-blind, randomized, controlled trial (described in detail below), which compares a candidate drug against either a **placebo** (dummy drug) or a currently available therapy. During this stage, researchers continue to monitor the agent's safety, since some toxicities may become apparent only after a drug is used in larger groups or over longer periods. Data from the final Phase III studies—called pivotal trials—may be submitted to the FDA as part of a New Drug Application (NDA) to be considered as evidence for approval.

Phase IV: After a drug has been approved and is on the market, additional studies are done to see how well it works under "real world" conditions and to determine whether its efficacy is durable, or long-lasting. Importantly, postmarketing studies also look for uncommon or long-term toxicities that did not show up in earlier trials (as was the case for metabolic side effects associated with the first protease inhibitors). Over time, more information may be revealed about interactions with other drugs and use in different populations, such as people with coexisting conditions. Patient advocates have charged that pharmaceutical companies too often neglect postmarketing research, a problem exemplified by the recent controversy over COX-2 inhibitors (a widely used class of pain relievers) and their association with heart problems. Legislation is being considered to address this issue.

Trial Design

A good design is crucial to ensuring that a clinical trial is able to provide the answers the investigators are seeking. Each trial begins with a protocol, a written description of what hypothesis the researchers wish to test and what methods they plan to use. This includes details such as drug dosages, administration routes, schedule of clinic visits, and what monitoring tests will be performed. Often in the case of new HIV/AIDS therapies, a **Community Advisory Board (CAB)** made up of HIV positive people and their advocates may offer advice about how a trial should be conducted. All aspects of a trial should be set forth in the protocol; many of these will determine how useful the trial is and whether its results will be regarded as credible.

Who Are the Subjects?

Enrollment criteria specify who may participate in a clinical trial. Characteristics and qualifications that a prospective subject must have are known as **inclusion criteria,** while those that disqualify a subject are called **exclusion criteria.** Enrollment criteria may include demographic characteristics (e.g., sex, age), behavioral factors (e.g., injection drug use), disease status (e.g., CD4 cell count, HIV viral load), and current or past medical history (e.g., kidney dysfunction, use of cancer chemotherapy).

Researchers may be tempted to select trial subjects who are most likely to do well on an experimental therapy. In addition, trials are regarded as "cleaner" if they eliminate any potentially confounding factors that could affect the study's outcome. For example, many trials exclude subjects who have coexisting conditions such as active opportunistic illnesses (OIs) or chronic hepatitis C. Concurrent use of other medications is also often excluded because they might interact with the experimental agent, potentially impairing its activity or causing unforeseen side effects. Another common exclusion criterion is active substance use, since many researchers assume that alcohol and illicit drug users have chaotic lives and are less likely to achieve optimal adherence.

It is important, however, that trials include a range of participants similar to those who will ultimately use the drug in practice. Otherwise, treatments may appear much more promising when tested in an "ideal" subject population than when used under real world conditions.

Many early trials of HIV therapies were conducted mostly in gay white men, a population that was initially heavily impacted by AIDS and had a propensity to volunteer for clinical research. Since then women, people of color, injection drug users, and other marginalized populations and their advocates have pressed for broader inclusion in clinical trials, and competent researchers recognize the importance of including a representative cross-section of people affected by a disease. Recent research has shown, for example, that people of African descent as a group metabolize efavirenz (Sustiva) more slowly than white individuals, and thus achieve higher blood levels of the drug.

In the not too distant past, women "of childbearing age" were

routinely excluded from clinical trials because many experimental agents have the potential to harm fetuses or cause birth defects. More recently, a consensus has emerged that drugs should be studied in both sexes. However, pregnant and breast-feeding women are still typically excluded, unless the trial is for an immediately life-threatening condition or for a pregnancy-specific intervention. In addition, women "of childbearing potential" (meaning there is a chance they could become pregnant), as well as male partners of such women, may be required to use at least one form of effective contraception during and for some time after a trial.

Most drugs are tested in adults first, and only later—if ever—in children. A majority of HIV trials specify that subjects must be at least 13 or 18 years of age. In the meantime, many physicians use drugs approved for adults "off label" to treat pediatric patients, making educated guesses about pharmacokinetics and optimal dosing. To encourage more pediatric drug research, the federal government in 1997 passed a law granting extended patent protection for drugs tested in children. In 2000 the FDA imposed a regulation requiring that trials for certain drugs must include children. The rule was overturned in court, but some lawmakers continue to push for such legislation.

Who Else Is Involved?

The researcher in charge of a clinical trial at a specific study site is called the principal investigator. The lead researcher typically works with a team of health professionals, social workers, and others. There is often a study coordinator who oversees the administration of a trial. In many cases a study nurse will be the main person with whom trial participants interact on a regular basis.

While clinical trials typically provide excellent care and monitoring, it is important that participants continue to see their regular physicians if their providers are not part of the study team. This can help ensure that nothing done during the study will unexpectedly interfere with ongoing treatment, and vice versa. If possible, laboratory results obtained during the trial (e.g., CD4 cell count, HIV viral load) should be available to subjects' regular health-care providers.

> "All the progress we've made over the past two decades—even the past five years—has been made possible by the people who have decided to flip the coin and take the chance. Every time we're successful, it's because somebody went first."
>
> —Cal Cohen, MD (research director for the Community Research Initiative of New England)

How Many Subjects?

The number of subjects in a trial is a critical factor in determining a drug's efficacy, as well as influencing the study's perceived credibility. While it may take only a few subjects to uncover major toxicities, many more participants are needed to determine conclusively that an agent works. With a small number of subjects, there is always the possibility that an outcome could be the result of chance rather than being a true effect of an experimental therapy. Researchers, therefore, try to include enough subjects in their trials so that the results will be considered statistically significant, or very unlikely to be due to chance alone. The ability of a study to produce statistically significant data is known as its **power.**

How Long Will It Last?

Along with the number of participants, the length of a trial is an important factor when thinking about a study's credibility. Longer trials, not surprisingly, provide more data than shorter ones. In addition, as noted above, some adverse events show up only with prolonged use of a drug (e.g., type 2 diabetes mellitus, heart attacks). Conversely, some side effects may improve over time (e.g., gastrointestinal symptoms). In some cases, an agent may look promising at first, but then stop working (as happened with nucleoside reverse transcriptase inhibitor [NRTI] monotherapy). On the other hand, it may take time for a drug to become effective (as is the case with some antidepressants), so it should not be rejected too soon.

As a clinical trial progresses, the investigators may report preliminary or interim results at scientific conferences or in medical journals. If preliminary data indicate that an agent is either quite harmful or very beneficial, the trial may be halted prematurely. For example, in 1986 Phase II testing of the first approved anti-HIV drug—AZT (zidovudine, Retrovir)—was halted six months after it began when 19 subjects in the placebo arm had died compared with just one in the AZT arm.

Regardless of what is specified in the study protocol, any participant in a clinical trial may withdraw at any time for any reason.

Characteristics of Clinical Trials

There are a few major types of trials for people with HIV/AIDS. **Interventional** trials test new drugs or other types of therapies, or determine whether already approved therapies can be used in new ways. **Observational** trials look at certain factors or outcomes (e.g., disease progression) over time. Other studies examine what risk factors are associated with the development of a condition.

Several characteristics influence the usefulness of a trial and the credibility of its results. As noted above, the "gold standard" for clinical trials is the prospective, double-blind,

randomized, controlled trial with clinically meaningful endpoints. Often, however, one or more of these criteria cannot be fulfilled.

Time Course

A **prospective** study is one that looks forward in time. Typically, a study cohort is selected and followed for a predefined period, sometimes several years. A **retrospective** study is one that looks backward at events that happened in the past. Such a study might, for example, analyze medical records or stored blood samples.

Control

To determine whether a new therapy is truly effective, it is important to compare it against something else. In a **controlled** trial, one group of subjects receives the agent under study (the experimental arm), while another arm does not (the control arm). Some trials have complex designs with multiple experimental arms.

Traditionally, new therapies have been tested against a placebo, an inactive mock treatment that looks or feels like the experimental agent (e.g., sugar pill, saline injection). This is done to minimize the influence of a phenomenon known as the **placebo effect,** whereby the treatment process itself—receiving a pill, injection, or other intervention—can make a person feel better or experience side effects (including changes in biological markers), even if he or she receives an agent that has no therapeutic value or toxicity.

In modern HIV/AIDS trials, it is considered unethical to give subjects a placebo when effective therapies exist. Thus, experimental agents are now usually compared with either the standard-of-care or the best available known treatment. Often subjects in the experimental and control arms will receive multidrug regimens that are the same except for a single component (for example, AZT/3TC/nelfinavir vs AZT/3TC/efavirenz). Sometimes experimental agents are compared with a null control (for example, AZT/3TC/abacavir/efavirenz vs just AZT/3TC/abacavir).

Randomization

Another tool for assessing whether a new therapy is truly effective is to ensure that the experimental and control arms are similar in every way except for the fact that one is receiving the investigational agent and the other is not. If the experimental arm contains all women and the control group all men, for example, it would be impossible to say whether any differences in outcome were solely due to the treatment or were influenced by the sex of the participants.

Investigators ensure that trial arms are similar by employing a process called **randomization.** This means that any prospective participant has an equal chance of ending up in either arm (or in any one of multiple arms). In a two-arm trial, this would be like flipping a coin for each subject and assigning "heads" to one group and "tails" to the other. This is done to minimize **selection bias.** If it were up to investigators to choose which participants were placed in which study arm, they might, for example, tend to assign sicker subjects to receive the therapy they think will work best; conversely, they might favor healthier participants who are likely to respond better and make the experimental agent look good. If the study population is large enough, randomization should achieve a roughly equal distribution of potentially confounding characteristics (e.g., sex, age, race/ethnicity, HIV transmission route, disease status) in all arms.

Blinding

Blinding refers to whether the researchers and the study participants know which arm the subjects are part of. In a single-blind (or simply, blind) study, the subjects do not know whether they are receiving the experimental agent, an existing standard therapy, or a placebo. In a double-blind study, the investigators do not know either.

Blinding is also done to minimize bias, which could occur—consciously or unconsciously—due to participant or researcher expectations. For example, in an unblinded study, if an investigator believes the experimental agent is superior to an existing drug, she might have a tendency to emphasize positive outcomes associated with the new therapy while minimizing negative ones. Likewise, if a subject thinks the experimental agent is more risky than standard therapy, he might tend to overreport side effects associated with the new drug or underreport those linked to the old one.

Infrequently, differences in safety or efficacy between study arms are so dramatic that the trial code is broken early and the study is unblinded, allowing researchers to determine as soon as possible which subjects received which agents.

Endpoints

Endpoints are milestones, ideally specified before a study begins, that an experimental agent must achieve or bring about in order to be considered a success. Traditionally, trials have employed clinically meaningful endpoints, for example, disease

> "If it weren't for clinical trials, we would not have any of the new, more potent therapies we have today. Treatments of the future are totally dependent on the successful conduct of clinical studies today."
>
> —Michael Saag, MD (director of the Center for AIDS Research at the University of Alabama at Birmingham)

resolution, progression to an AIDS-defining illness, or death.

In the case of diseases like HIV/AIDS that typically progress slowly (especially when effective therapy is used), it could take very large studies with very long follow-up periods—perhaps a decade or more—before an appreciable number of participants experience clinically apparent disease progression or death. For that reason, contemporary trials often use **surrogate markers,** which are usually laboratory findings that are assumed to predict clinical outcome.

In the case of experimental anti-HIV drugs, for example, trials typically measure whether CD4 cell counts go up and viral loads go down, although the true outcomes of interest are OIs and death. Likewise, elevated cholesterol and blood pressure are considered surrogate markers for cardiovascular disease risk, although the true outcomes of interest are heart attacks, need for cardiac surgery, and death. The FDA may approve drugs based on surrogate marker data alone.

Ethical Research

All U.S. clinical trials must include mechanisms to ensure the ethical treatment of human subjects. Before a clinical trial gets underway, its protocol must be extensively reviewed to see that its benefits outweigh its risks. Reviewers include FDA officials and **Institutional Review Boards (IRBs),** committees at each research institution comprised of physicians, other health-care professionals, statisticians, ethicists, local community members, patient advocates, and people with the disease under study. IRBs not only approve studies before they begin, but also monitor their progress until completion. In addition to federal requirements, some states also have their own regulations governing human research. Finally, international agreements such as the Nuremberg Code, the Declaration of Helsinki, and the International Code of Medical Ethics put forth principles for conducting ethical research.

Ten Questions to Ask When Considering a Trial

- What experimental intervention is being tested?
- What is already known from earlier studies?
- Are there any known toxicities or side effects?
- What (if any) treatment will control subjects receive?
- How often are study visits and what do they involve?
- What monitoring tests will be performed and how often?
- What other treatment options are available?
- Can subjects still receive the study drug after the trial ends?
- What (if any) long-term follow-up will be done?
- Whom should subjects contact in case of problems?

Informed Consent

Before agreeing to take part in a clinical trial, prospective participants must be given information about all aspects of the study, including its risks and benefits, in language they can understand. All prospective subjects (or their parent or guardian, if the participant is a minor) must sign an **informed consent** document that describes the nature of the study, the therapy being tested, known or potential risks, the subject's rights, and who to contact in case of problems. Prospective subjects should also be informed of other options that exist if they decide not to enroll in a trial.

The document is only part of the informed consent process. The study should also be verbally explained to the subject, who should be encouraged to ask questions (see sidebar above). The prospective subject may take the document home to discuss with family and friends.

Informed consent does not end when the document is signed and the participant enters a trial. Researchers must inform subjects of any important changes in the study design or new information about the experimental agent that becomes available during the course of the study. Importantly, an informed consent document does not waive the participants' legal or medical rights, and researchers remain liable for damages due to negligence. The informed consent document is also not a contract; participants may discontinue a study at any time for any reason.

Financial Considerations—on Both Sides

Funding for a trial may come from various sources, including the federal government (e.g., studies conducted by the National Institutes of Health or the Department of Veterans Affairs), private grants, charitable organizations, and pharmaceutical or biotechnology companies. A trial's informed consent document should disclose all funding sources. In addition, all investigators must file financial disclosure statements explaining their financial relationship with the sponsor. The federal government and some states have various laws and policies concerning conflicts of interest, for example, when a researcher leads a trial of a drug produced by a company in which he owns stock.

Traditionally, drugs used in clinical research have been provided free of charge. Many studies also cover monitoring tests and other types of medical care. However, some observational trials—including studies comparing various new dosing schedules or combinations of approved agents—do not provide free drugs. Health insurance regulations differ widely, but many insurers do not cover treatments or monitoring tests that are considered experimental.

In some cases, trials may provide a stipend to participants. These can be used to reimburse participants for expenses such as transportation or childcare, or to compensate subjects for their time and inconvenience. Some researchers provide other forms of compensation, such as bus tokens or meals, especially if they are trying to include study participants from low-income and otherwise marginalized populations. However, it is illegal and unethical to pay people to join a trial, or to use stipends to persuade unwilling subjects to enroll.

Considering a Trial

Individuals considering whether to take part in a clinical trial have many factors to weigh. How do a trial's advantages and benefits stack up against its inconveniences, discomforts, and potential risks? Trials of new drugs—and especially novel drug classes—can offer few guarantees. Researchers cannot be sure how effective a treatment will be, nor can they rule out unforeseen toxicities and side effects.

Why Do It?

There are several reasons why clinical trials may be attractive. First, they provide early and usually free access to the newest therapies. Sometimes subjects are given continued access to experimental medications even after the study period ends. Early in the epidemic, before many antiretroviral medications were approved, trial participation was often the only way to obtain drugs. This is no longer the case, but clinical studies remain at the forefront. For individuals who have developed resistance to the three major classes of antiretroviral drugs, trials can provide the first access to agents that work by entirely different mechanisms.

Clinical trials also offer excellent medical care provided by expert physicians at leading hospitals and medical centers. In particular, trial participants typically receive frequent, intensive health monitoring using the latest testing methods (usually at minimum regular CD4 cell counts and viral load assays). Despite the institution of the AIDS Drug Assistance Program (ADAP) and other programs to help people with HIV/AIDS, too many people are still unable to access top-notch treatment and care for financial reasons, and trials may help fill this gap.

Last, but certainly not least, trial participants may get personal satisfaction from helping others and contributing to medical science. Even if a particular experimental agent does not provide much benefit for a specific subject, the data gathered during the trial will advance the overall state of knowledge about HIV/AIDS and its treatment, to the benefit of other people with the disease.

Drawbacks and Risks

There is no denying that participating in a clinical trial can be time-consuming and inconvenient, especially for subjects who do not live close to a study site. This may be especially problematic for individuals who continue or have returned to work, and for those who must arrange for childcare. Trials may also involve a certain amount of discomfort, for example, frequent blood draws.

Of greater concern are the potential adverse effects of a new therapy. These may range from temporary

Trial Pros and Cons

PROS	CONS
Early access to new therapies	Inconvenience
Free drugs and testing	Time-intensive study visits
High-quality medical care	Possible discomfort or pain
Expert doctors and leading medical centers	May not receive experimental agent
Frequent, intensive health monitoring	Experimental agent may not be effective
Satisfaction of helping others	Possible adverse side effects
Advancement of medical knowledge	Small risk of life-threatening toxicities

Find out about currently enrolling clinical trials from physicians, nurses, and other providers; from hospitals, universities, and medical schools; and from support groups, patient advocacy organizations, and activist groups. For online clinical trial listings and databases, see the introduction to "Open Clinical Trials" on page 50.

gastrointestinal distress to elevated blood cholesterol to life-threatening Stevens-Johnson syndrome (a type of serious hypersensitivity reaction characterized by severe rash). No matter how promising an agent looks in laboratory and animal studies, it may still cause unacceptable toxicities in humans. Some side effects may not appear right away, but only after prolonged use, and some may not diminish immediately (or ever) after a drug is discontinued. Participants in a trial should always be given information about what to do and whom to contact if they experience unexpected or serious reactions.

Another potential risk is being randomly assigned to the control arm rather than an experimental arm; often neither the subject nor the investigator will know whether this is the case. (Some study designs allow for a "cross-over" from experimental to control arms, and vice versa, or permit all participants to receive the experimental agent at the end of the study period, so even participants initially assigned to the control arm may benefit.)

Even if one is assigned to an experimental arm, it is possible that the new agent will not be effective. With the growing awareness of the importance of choosing optimal individualized regimens, avoiding resistance, and sequencing successive regimens in order to extend effective treatment, prospective subjects may be less willing to leave their therapy to chance, and more inclined to rely on the expertise of experienced physicians and the latest treatment guidelines.

Making the Decision

When the first anti-HIV drugs were being developed, there was no shortage of eager trial volunteers. In many cases, participating in a clinical study was the only way to obtain treatment, and doing so was a matter of life and death.

But today, with some 20 antiretroviral drugs on the market, many HIV positive people are doing well on treatment and may see little reason to put up with the inconvenience of a trial or risk unknown side effects to obtain the minimal improvement an experimental drug might provide. Also, many HIV positive people have returned to work and fuller lives since the advent of HAART, and no longer have time for extra clinic visits and meetings.

Yet the importance of clinical trials cannot be overstated. Trials still provide access to innovative treatments, including new classes of drugs for individuals who require salvage therapy. Clinical studies also provide the information needed to make adjustments to treatment strategies—such as the shift away from the "hit early, hit hard" approach and the increasing preference for protease-sparing first-line regimens to minimize metabolic complications—that may ultimately benefit all people with HIV. Finally, clinical trials are the only way to discover better immune-based therapies and effective HIV vaccines, not to mention the ultimate achievement: a cure for AIDS.

This article was prepared for the San Francisco AIDS Foundation by Liz Highleyman.

For More Information

An Introduction to Clinical Trials
National Library of Medicine
www.clinicaltrials.gov/ct/info/whatis

What Is an AIDS Clinical Trial?
Department of Health and Human Services
www.aidsinfo.nih.gov/other/clinicaltrial.asp

Should I Join a Clinical Trial?
AidsMeds.com
www.aidsmeds.com/lessons/ClinicalTrials.htm

The Food and Drug Administration: The Process of Approval
ACRIA Update
www.acria.org/treatment/treatment_edu_fallupdate2004_fda.html

For a partial listing of currently enrolling studies, see

"Open Clinical Trials"

on pages 50–54