Sustaining Support for Domestic HIV Vaccine Research: Social Issues Over the Long Haul of Human Trials

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By the time Kevin Shancady walked into the Denver Department of Public Health to enroll in an HIV vaccine trial, he'd managed to put most of his fears behind him: fears of a government hostile to gay men, fears that researchers might inject volunteers with a dangerous vaccine. "So many people have died," he said, "and I feel an obligation to advance prevention research. I'm willing to take some risk. And if the vaccine works, then I'll have protection."

It's that mix of optimism, altruism and hope for personal benefit that has made it possible for the National Institute of Allergy and Infectious Diseases (NIAID) to recruit over 4800 Americans into a cohort being readied for HIV vaccine trials. But what Kevin heard when he sat down with a study counselor shows why recruiting volunteers is just the first step on the long and difficult road of HIV vaccine testing. In the best tradition of public health, the study counselor warned him of the possible risks of trial participation. "He told me participants in this trial might not be able to join other vaccine trials," Kevin said, "and if a different vaccine is eventually developed later, it might not work as well in me as in people who had not been in one of these early vaccine studies. I felt blindsided, actually."

Kevin's dilemma is faced by thousands of other potential vaccine trial volunteers, and by whole communities directly affected by the HIV epidemic. The enormous potential benefits of vaccines are accompanied by difficult questions and significant risks. And beyond the physiological unknowns are social complexities. The lengthy, trial-and-error progress of HIV vaccine trials may create unique social dynamics in which media scrutiny, ethics, equity, and the perceived likelihood of success, and factors such as the ability to recruit and retain volunteers and overall public support are all intertwined as they never have been before.

So, given all these conundrums, what made Kevin Shancady decide to become an outspoken advocate for HIV vaccine research? In the history of public health, vaccines have proven to be among the most effective disease prevention tools. Diseases such as smallpox, polio, measles, and others have been eradicated or brought under control through mass vaccination programs. And in the fight against HIV, it's clear that new and powerful prevention technology such as a vaccine is badly needed. Without it, communities will continue to be devastated.

Well into the second decade of the epidemic, 40,000 people are infected annually in the United States. Internationally, over 8,000 people are infected every day. If current seroconversion rates remain unchanged, nearly half of twenty-year old gay men in the US who are now uninfected can expect to eventually seroconvert.1 Injection drug users and women will continue to account for a growing percentage of the domestic epidemic. And HIV is making deep inroads in a new generation: one in four new infections in the US occurs in people under 22.2

Behavioral interventions have proven effective at reducing risky behaviors and they will remain essential even if a vaccine becomes available. But for many reasons, including cost, political obstacles, and the difficulty of maintaining long-term behavior change, it is
unlikely behavioral interventions alone will stop the spread of HIV. To do that our best hope is a combination of approaches: a widely available vaccine, quality behavioral interventions, and access to condoms, microbicides, and clean needles.

But inherent in the promise of vaccines are very real risks. The potential for behavior change is just one example. When a vaccine is eventually licensed for widespread use, it is very unlikely to be 100% effective. What if recipients of a vaccine which is only partially effective feel newly invulnerable to infection, and greatly increase their risky behavior? Will the number of infections actually increase?

The benefits of HIV vaccine research seem far off and the risks far more tangible. In communities responding to the health care needs of thousands with HIV, the urgent need for a cure is ubiquitous, while the need for expanded prevention technology can be less immediately evident. And it is these same communities which have historical and present-day reasons to be distrustful of government-sponsored biomedical research and the motivations of pharmaceutical companies which will produce a vaccine.

Relative inattention to vaccines has had its costs: pharmaceutical industry investment has lagged, government research efforts have lacked coordination, and affected communities have only begun to address the myriad issues involved in vaccine trials.

The stakes could not be much higher. The great promise and potential perils of HIV vaccines add up to a clear reason for affected communities to adopt a more aggressive attitude regarding vaccine development: pushing for increased public and private investment in research, tackling the equity, safety and social issues involved, demanding protections from government, and debating what level of risk is justified given the potential benefits of particular clinical trials of vaccines. The principal question is not whether a vaccine would be beneficial, but under what conditions are vaccine research and dissemination ethical and effective?

The massive research effort and series of human trials necessary to produce an effective HIV vaccine is only sustainable if it has the support of individual trial participants, affected communities and the general public. This paper outlines concerns and potential remedies at each of those levels. It begins with a review of some of the factors which make HIV vaccine research unique, and concludes that specific action by communities, government, private industry and others will be needed in order to ensure ethical trials capable of sustaining support over the long haul of HIV vaccine research and testing, including:

- **the general public**
  - education regarding the timeline of HIV vaccine research and introduction of a new definition of "success" in clinical research

- **affected communities**
  - addressing equity issues which may cause tensions within communities
  - monitoring research efforts, particularly the safety of products and efforts to protect participants
- providing education and focused efforts at building trust with particular affected communities
- determining and fostering appropriate models for structured community debate
- placing value on HIV vaccine research efforts
- continued emphasis on non-vaccine intervention efforts

- **individuals considering participation in trials**
  - expanding the Participant's Bill of Rights
  - contracting with community-based organizations to provide information which will facilitate individual decision making about trial participation
  - providing the highest quality behavioral interventions to members of vaccine trial cohorts
  - reforming and expanding government HIV vaccine research efforts
  - expanding pharmaceutical industry investment in HIV vaccine research and product development

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**NEW CHALLENGES OF HIV VACCINE RESEARCH**

The search for a vaccine for HIV promises to require decades of work by researchers and sustained optimism on the part of trial volunteers and the public. The virus presents daunting scientific obstacles: no perfect animal model of HIV disease exists; recovery from HIV infection has not been documented; the "correlates of protection" (immune responses which would protect people from infection) are not known; the virus is highly variable so a vaccine for one "clade" (or type of HIV) may not protect against a different HIV-1 clade; and the virus mutates rapidly and may be able to elude a vaccine.

Traditional approaches to vaccine development, such as "whole killed" or attenuated virus methods raise special safety concerns with HIV, since a faulty vaccine which actually infects a recipient could have lethal consequences. Finally, it may be impossible to find a vaccine which prevents actual infection (also called "sterilizing immunity"). Instead, research goals may focus on a product which can inhibit progression to disease, or lower viral load in infected persons. Assessing a vaccine's ability to meet these post-infection goals may add years to human trials.

These obstacles may translate into a product development and human trial timeline measured in decades. When many people think of a vaccine trial, they picture one large trial that proves efficacy in a few years. Progress will probably be more incremental in the case of HIV vaccines. It is likely that a series of human trials will continue for many years and require tens of thousands of volunteers in several countries.

Vaccines for HIV are not the first to require multiple human trials over many years. The vaccine for haemophilus influenzae type B (HIB) was developed over a 17-year period and involved hundreds of thousands of individuals in human trials. The HIB vaccine may have limited application as a model of the social dynamics of HIV vaccine research,
however. Like HIB, HIV has a relatively low annual infection rate in the United States, meaning that efficacy trials will likely be lengthy, expensive, and generate results which are sometimes difficult to interpret. Unlike HIB, human trials for HIV will take place under intense media scrutiny and political activity, and involve adults in stigmatized risk groups, rather than children in the general population.

During the extended testing timeline for HIV vaccines, results from efficacy trials may create controversy even as they advance research. NIAID is now developing the concept of "Intermediate Sized Trials" to test early vaccine candidates. Unlike standard large-scale ("Phase III") human trials, intermediate trials would involve fewer volunteers and be less expensive, allowing researchers to test several different products and pursue only the most promising with full-scale efficacy trials. The drawback of intermediate trials is that their results have lower "statistical power" and may provide ambiguous results. For each intermediate sized trial, public health officials and researchers will need to decide whether the results justify expanding to a full-scale Phase III trial.

The three "phases" of human (clinical) trials

**Phase I:** Involves small numbers of low risk volunteers and is designed to test the safety, acceptability and appropriate dosage of a product.

**Phase II:** Involves larger numbers of volunteers (usually several hundred) and is designed to test safety and immunogenicity (the ability of the product to induce responses from the immune system).

**Phase III:** Large scale trials, usually involving several thousand volunteers designed to test the safety and efficacy (effectiveness) of a product.

**Intermediate Sized Trials** are intended to give an indication of whether or not product may be efficacious. These trials involve smaller numbers of volunteers than Phase III trials and can be expanded to full-scale efficacy trials if the product being tested shows promise.

If, in the early 21st century, trials have not succeeded in identifying a broadly licensable vaccine, thousands of new volunteers will be needed to sustain HIV vaccine research.
Scientists will still be making difficult decisions about the threshold for advancing to full scale trials, and each of these decisions may be an occasion for renewed public debate. Recent history suggests that the public perception of this process - its ethical conduct, its use of resources, its hope for success - will have a powerful impact on the successful development and distribution of vaccines for HIV.

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**THE NEED FOR SUPPORT FROM THE GENERAL PUBLIC**

Vaccine development has historically been influenced by many social forces, including media attention, the interests of pharmaceutical companies, and the hopes and fears of the general public. In the past, the interplay of these forces has had a critical impact on the ultimate public health outcomes of vaccine research.

Public enthusiasm was an essential ingredient in the race to find a vaccine for polio. Most of the funding for research came from the National Foundation for Infantile Paralysis (better known as the March of Dimes) which depended on individual contributions. Public support was needed to maintain financial contributions, but also played an important role in pushing the scientific establishment towards endorsement for a massive human trial. The press gave extensive coverage to polio vaccine research. In his analysis of the politics and public relations of polio vaccine development, Harvard medical school historian Allan M. Brandt observed that, "...where public demands and expectations are great, sound scientific judgment may be jeopardized. The Salk vaccine was sold to the public before its safety and efficacy were proven."5

Three decades later, it was fear of public reaction which prompted medical professionals to take the opposite approach and minimize the general public's knowledge of an epidemic in their midst. High rates of hepatitis B infection had been identified in some sectors of the population, including health care workers, gay men, Asian immigrants, and others. What followed was a series of decisions designed to quiet public concern about the problem: the medical community played down the potential threat of patient infection by health care workers, and physician organizations resisted large-scale testing of their members. hepatitis B was portrayed as primarily a problem of particular groups and not a major concern for the general population.

In 1982, a hepatitis B vaccine was developed with the assistance of the pharmaceutical company Merck, but because of previous efforts to keep the epidemic quiet, the public remained largely ignorant of the danger of the disease or the new potential to prevent it. William Muraskin, a professor at City University of New York, has observed that, "since there was no public concern, there was not public outrage at the high cost of the vaccine or the quasi-monopoly that Merck had obtained for itself."6 The result was a costly vaccine which failed to stem the epidemic for years after it was licensed.
In both these examples, leaders in the medical establishment and the media made choices about what should become general knowledge because it was assumed the public's expectations would play a pivotal role. A similar dynamic with HIV is likely.

Redefining "Success"

Researchers, the public, and trial volunteers will need to be willing to take reasonable risks and expect incremental successes on the road to an HIV vaccine. Neither the polio nor hepatitis B examples of public relations will sufficiently prepare people for this incrementalism. Media coverage or statements by researchers which fails to convey the complexity of the issues or which enthusiastically promotes early trials without acknowledging the incremental nature of progress, could damage public confidence if trials do not quickly produce a "magic bullet."

In May 1994, the Chicago Tribune ran a front page story reporting that an experimental HIV vaccine had failed to protect several people from becoming infected with HIV. The story itself was not startling news. No vaccine in history is 100% effective, and some number of "breakthrough" infections (infections of vaccinated trial participants) are expected in any vaccine trial.

As Dr. June Osborn (Chair of the former National Commission on AIDS) has written, "the brief excitement generated by any failure to protect served as a reminder that public expectations were exorbitant." Osborn pointed out that those expectations "will be of central importance to the capacity to conduct any HIV vaccine trials." But if collective hopes are dashed every time a vaccine candidate fails to prove highly efficacious, the search for an HIV vaccine may not be able to sustain long-term support from the public and affected communities. Community activist Mark Harrington has warned, "The potential consequences of an early failure, broadcast widely through a hysterical, fearmongering media, are grave. The vaccine trials will be subjected to unprecedented worldwide scrutiny." In order to avoid the sensationalizing of research findings it is incumbent upon researchers to provide the media and the public with enough information and education to put research findings in context.

There is also the danger that, like hepatitis B, HIV will increasingly come to be seen as a disease of isolated groups and of limited concern to the general American public. In the United States, HIV has always affected primarily stigmatized groups and is increasingly a disease of the poor, people of color, and drug users. Ninety percent of all new infections are now occurring in the developing world. As these trends accelerate, the general public may not continue to see HIV as a public health priority and support and funding for research and broad access may wane.

Sustaining public support for vaccine research while communicating the complexity of the research task will require a delicate balance of honesty and optimism. As Barney Graham and Peter Wright of the NIAID Phase I/II AIDS Vaccine Evaluation Group have written, "There is a need for a measured approach to communicating information, so that the public can be adequately informed. The sense of urgency the epidemic demands must
Researchers must redefine for the public the meaning of "success" in HIV vaccine research so that a human trial is not considered a failure if it contributes to knowledge which can eventually lead to an effective vaccine. Such a redefinition will require the public and potential trial volunteers to re-orient their expectations to gradual progress and to participation in trials which may not immediately produce a licensable product. The new understanding may make trial recruitment more challenging, but it will also likely make it more sustainable.

This re-orientation will be complicated by the fact that for each proposed trial there will need to be a reasonable expectation of ultimate success - of identifying a licensable vaccine. A trial which has little or no chance of demonstrating the efficacy of the candidate vaccine would be unethical and be unlikely to receive public, trial volunteer, and scientific community support. Faith in each separate trial will be required, as will ongoing support for vaccine research if a trial fails to prove the efficacy of a product.

However realistic it is, this "delayed gratification" definition of success can only become widely accepted by the public and affected communities if they have faith in the integrity of researchers and research efforts. While researchers tackle the difficult science, they also need to build a product development and testing infrastructure which can withstand scrutiny and maintain the faith of volunteers over time. Mistrust of government and cynicism about the medical establishment and pharmaceutical industry contrast with the relative faith of the Salk polio vaccine era. Today, building trust in researchers is more important than generating blind enthusiasm.

URGENCY AND DISTRUST IN AFFECTED COMMUNITIES

The concept of "community," will play a central role in HIV vaccine research. Individuals' perception of community membership is a prime motivator for individual trial participation, and community-based institutions (including media, service, and civil rights organizations) will help determine the level of support for vaccine research among trial participants and the public. At least two areas will require closer attention: the implications of community identity, and community involvement in decision making.

Community Identity

Trial participants are of interest to researchers primarily because of a specific HIV-risk behavior they practice, and not because of the community, or communities, with which they identify. Yet ties to one or more communities may help determine a person's desire to volunteer for vaccine trials, how they receive information, whom they trust, how they interpret the motivations of government and industry, and how they gauge their level
of risk for HIV. Some volunteers in trials will have a sense of belonging to more than one "at-risk" community; some will not identify with any of these communities. Though the importance of community will vary with each individual, we can anticipate that tensions within communities and trust-building efforts in particular communities will be important factors in vaccine testing.

### Populations being recruited for domestic HIV vaccine trials

- Men Who Have Sex with Men (Gay and Bisexual Men)
- Injection Drug Users
- Women at High Risk
- Populations within populations

It's important to note that investigators seek to recruit "higher risk" individuals within each of these populations. For example, younger gay men and gay men from communities of color are generally at higher risk for HIV, and this is one reason investigators at trial sites recruiting gay men seek to include members of these populations in trials.

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**Tensions within communities.** Concerns about the equitable sharing of risks and benefits of trials within communities have the potential to undermine volunteer enthusiasm. For example, researchers will need to recruit higher risk members of the gay community for trials. These volunteers will likely be younger, have lower incomes and educational levels, and have lower rates of health insurance coverage, than much of the gay community. Without a method to assure access to licensed vaccines by all people at high risk, only gay men with health insurance or financial resources to purchase a vaccine will benefit from this research. Many HIV vaccine trial volunteers might find that other gay men "like them" have limited access to a vaccine.

Injection drug users, people of color, young men who have sex with men and others enrolled in vaccine trials may face stigma within their own networks or communities, because they are seen as having been "co-opted" by researchers. The potential for being labeled a "guinea pig" may be particularly strong in communities which have experienced unethical biomedical research or which perceive themselves to be less likely to receive the benefits of research. The prospect of this stigma argues for offering participants as many protections and benefits as is appropriate without being coercive.
Vaccine trials may also spark tensions between infected and uninfected people within communities if it is perceived that vaccine funding is draining resources for therapeutics or other prevention approaches, or that significant effort is being expended to fight discrimination based on false positive (vaccine induced) HIV seropositivity, while discrimination against HIV-infected persons is allowed to continue in insurance and other areas. Equity issues such as these have the potential to undermine support for trials in the communities in which HIV vaccines must be tested.

The result of a community dialogue on these issues might be: setting guidelines for advocacy that vaccine funding will not come from resources for therapeutics or other prevention research; demanding a plan to secure subsidized access to vaccines to low-income, at-risk individuals; and, requesting personal statements and action on the part of vaccine researchers to support an end to discrimination against people with HIV infection.

### Why do individuals at increased risk for HIV need to be recruited for trials?

In order to determine the effectiveness of a candidate vaccine, investigators randomly divide volunteers into two groups: those who receive the vaccine, and those who receive a placebo. Investigators then keep track of how many infections occur in each group after the vaccine and placebo has been administered. If there are a significantly smaller number of infections in the "vaccine group" this probably means the vaccine is effective.

Volunteers at higher risk are needed because they are more likely to be exposed to HIV, allowing researchers to see if the vaccine was effective. If vaccine efficacy studies were done in low-risk populations, there would such a small number of HIV exposures, and such a small difference in the number of infections between the vaccine and placebo groups that investigators would not be able to tell for sure if the vaccine was having any effect.

### Communication and trust building

The goal of building trust between researchers and communities will involve more than simply educating affected community members
about the mechanics of vaccine research and testing. Also necessary is an open dialogue about community concerns regarding biomedical research and specific, concrete ways in which researchers can address or alleviate those concerns. For example, African-Americans may have less trust and willingness to participate in trials given historical incidents of abuse in biomedical research. Infamous examples - such as the Tuskegee Syphilis experiment during which penicillin treatment was withheld from the African-American study participants up through the early 1970's - remain powerful indictments of biomedical research which resonate with prospective research participants. In this case and others, community-specific dialogue and trust building which addresses unique historical concerns and establishes appropriate assurances and safeguards is necessary.

Involvement in Decision Making

When a single trial quickly identifies an effective vaccine (as in the case of polio or hepatitis B) the structure of the decision making process is unlikely to become an immediate, burning issue. When progress is incremental and extended over years, confidence in the quality of decision making may prove to be an important factor in sustaining volunteer willingness. Vaccine trials will require a series of complex and difficult decisions, including which candidate vaccines to test, when to begin large-scale human trials, whether or not to expand intermediate sized trials, and how to use the cohorts and Phase III infrastructure when vaccine products are not available for testing. As it becomes clear to the media, the public and volunteers that these decisions require judgment calls and engender controversy within the scientific establishment, there may be increased attention to how those decisions are made.

Representatives of communities enrolled in trials and community-based organizations must be involved in every stage of trial design and decision making. And their perception of whether the potential benefits of a trial justify the risks should inform research decisions and help fuel community debate on trials. NIAID and individual researchers have already shown commitment to involving representatives of trial volunteers in trial planning and implementation. Yet the complexity of scientific and social issues involved in HIV vaccine testing requires additional attention to the details of community discussion, debate, and decision making.

In The Search for an AIDS Vaccine, Christine Grady argues that since individual trial volunteers cannot expect personal benefit from the vaccine they are testing, it is the affected community which should be considered the beneficiary of vaccine research. She concludes that the community as a group should be empowered to decide for itself whether the potential risks and benefits justify a large-scale human trial of a particular vaccine candidate - a kind of "community informed consent" in addition to individual informed consent.

Grady proposes a multi-stage process of decision making for Phase III trials, starting with research priority setting, national level review of ethical and scientific issues, review by targeted communities, and finally individual participant "informed consent." Community review would include, "meetings with official community leaders and scientists,"
followed by a series of "town meetings" and discussions in the press, and concluding
with a community vote at an open meeting.14

Grady's community consent design is a laudable contribution to the debate on how to
fully involve affected communities in research decisions. Yet embedded with this
proposal are major assumptions about communities: that their membership is definable
and relatively cohesive; that divisions within communities do not prohibit reaching
credible decisions for all members; that self-perceived membership by trial volunteers in
multiple communities will not render decisions by one community illegitimate; and,
finally, that communities are comfortable choosing representatives or will be satisfied
with a majority vote at a meeting as a valid decision making process for the whole group.

What of injection drug users, who may feel membership in a network of people, but not a
cohesive "IDU community"? And what of the gay community - highly politically
organized, but uncomfortable designating leaders empowered to make decisions for
others? Derek Hodel of Gay Men's Health Crisis has written that, "The sad reality is that
while community involvement is critically important, community unity is unlikely - and
it is precisely that reality that the HIV vaccine research agenda must take into
account."15

Though communities may be the ultimate beneficiaries of vaccine research, individual
trial volunteers remain the ultimate arbiters of the merits of a trial. Whomever benefits, it
is individuals who must choose whether or not to bear personal risk for the benefit of the
group. Given the diversity and natural conflicts within any community, it is far from clear
that a community assembly could legitimately make final decisions on biomedical
research on behalf of the whole (however that is defined).

Affected communities are unlikely to reach consensus on the merits of an HIV vaccine
trial - what they can achieve is a thorough discussion, and a clear articulation of different
viewpoints which individuals can then choose to accept or reject. Grady's community
town hall design would be more useful if its stated goal was to provide an open and
structured debate covering the relevant issues. Individual trial volunteers at each trial site
could draw upon this discussion (perhaps after viewing it on video tape if they were not
present) in making their own personal decisions about whether or not to participate in the
trial. The only vote taken would be trial volunteers "voting with their feet" - using this
debate and other information to decide for themselves whether or not to participate in the
trial.

ALTRUISM AND AMBIVALENCE AMONG TRIAL PARTICIPANTS

Controversy may be a way of life in HIV vaccine research. Given the history of HIV
vaccine product development, we can assume that the merits of future candidate vaccines
being considered for trial will be the topic of intense debate within the scientific
community, and that this debate will receive ample media attention. As a result,
prospective volunteers may be making decisions about trial participation in an atmosphere of intense scientific debate.

Volunteers will need to be prepared to negotiate this controversy; embrace altruism as one of the few defensible motivations for trial participation; accept the physiological risks of being injected with an experimental product; face possible discrimination based on trial participation; get accurate information if the media misinterprets breaking vaccine news; and, finally, accept these difficulties knowing their participation may make them less likely to benefit from a vaccine which is eventually licensed.

Researchers will be asking HIV vaccine trial volunteers to take part in a long-term and risky collaboration, and volunteers will assume numerous risks and inconveniences. The experimental vaccine may make them test positive on standard HIV antibody tests, leaving them vulnerable to discrimination in international travel, health and life insurance, and several forms of government employment. They may experience difficulties simply by being labeled members of a "high risk" group under study.

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**Social Harm**

Vaccine-induced seropositivity (testing positive on a standard HIV test due to the vaccine) may cause discrimination in:

- health and life insurance,
- international travel, and
- some forms of government employment (such as Job Corps or Peace Corps).

Being identified as someone participating in an HIV vaccine trial (or someone considered sufficiently "high risk" to be accepted into a trial) may lead to discrimination in employment, housing, other venues, or among the volunteer's peers, family or co-workers. Participants may also be perceived as "suckers" at the service of researchers with little chance for personal benefit.

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To date, candidate HIV vaccines have proven to be safe. But there is at least a theoretical risk that vaccines will cause physiological harm by accelerating progression of disease in those who become infected or cause autoimmunity disease. Second and later generation vaccines may pose additional risks.16 It is also possible that participants in early vaccine
trials may be excluded from future vaccine research and benefit less from more effective vaccine products developed in subsequent studies. These risks, compounded by potential social and personal pressures resulting from participation in a high profile (and perhaps controversial) experimental trial will demand commitment on the part of those who volunteer and resilience from those who are retained in vaccine studies over years.

Participant satisfaction with trials will be essential to sustain a base of trial volunteers. Staff involved in Phase I/II studies for HIV vaccines have observed that, "...the best recruiting tool in minority populations, as well as all groups, is the satisfied customer. Our current and former volunteers are still the best recruiters for new volunteers."17

It is already clear that more needs to be done to allay the fears and maintain the confidence of trail participants if the government wants to recruit and retain multiple cohorts over many years or decades. In a 1994 article, Douglas et al.18 reported a survey of 1660 participants in a preparatory study for HIV vaccine trials (the "Jumpstart" study). Among these recruits they found "high levels of altruism and optimism regarding HIV vaccine trials," but also "major areas of concern in the areas of trust, confidentiality, and insurability."

More than half the participants (58%) said they were not sure the federal government could be trusted. Two of the questions related to the participants' sense of optimism are particularly interesting: 58% agreed that an HIV vaccine is likely within 10 years, and 52% agreed that being in an HIV vaccine trial would be "exciting." The results suggest that many participants expect a licensed vaccine much sooner than most in the scientific community. And these responses prompt the question: if your vaccine trial is just one of many trials in an extended research and testing effort, for how long will it seem sufficiently "exciting"? To remain interested, these trial recruits need their specific concerns addressed, and they need to understand and be prepared for the realities of the trial timeline.

Another study on the Jumpstart cohort by MacQueen et al.19 looked at participants' willingness to participate in a vaccine trial. Of the 1386 surveyed, 36% were "definitely" willing, 57% were "equivocal" and 7% were "not at all" willing. Responders were asked questions about their motivations for participation in the trial. Of the "equivocal" group - the largest group in the cohort - a third (33.3%) said they were participating to reduce their risk.20

This report is troublesome, since even if a volunteer receives a vaccine rather than a placebo, any vaccine tested in the near future may have a very low efficacy rate, if it is effective at all. The danger is that volunteers will increase their risky behavior because of a false sense of protection, and there exists the frightening possibility that a vaccine trial will lead to more, rather than fewer, infections. (The converse is also possible, that behavioral interventions associated with the trial or the process of discussing risk behavior on a regular basis with a study counselor may lower risk taking among the cohort.21) When they fully understand that they cannot assume any personal protection from trial participation, will "equivocal" volunteers move over to the "not at all" column?
When affected communities hear of seroconversions in trial populations, will their support for HIV vaccine research waver?

Articles like these have been quoted to make the argument that it is feasible to recruit and retain a large enough cohort for vaccine trials. That is very likely true - for the first trial. But it is expected that the process will require multiple efficacy trials of various sizes, and it is possible that recruitment of thousands of new trial participants will become increasingly difficult. The implication is not that vaccine trials are unworkable, but that to reach and maintain "readiness," outstanding concerns must be addressed and motivations for participation enhanced.

Action in at least four areas may contribute to the ability of researchers to recruit and retain thousands of individuals in a series of vaccine trials: 1) expanded rights and protections; 2) development of adequate materials to assist individuals in making informed decisions; 3) high quality behavioral interventions; and, 4) establishing the integrity of the product development process.

**A New Generation of Rights**

If an HIV vaccine is to be found, thousands of individuals will need to take some amount of personal risk. What is needed is a compliment of rights and protections to make these risks acceptable to, and equitable for, many thousands of people over years of multiple vaccine research studies. People considering an altruistic contribution to society may expect concrete efforts to protect them from harm. In addition, trial volunteers will be asked to assume a series of responsibilities (i.e., periodic reporting of risk behavior, consent to regular HIV testing, agreement to refrain from attempting to learn whether they have received a vaccine or placebo, and other obligations of trial participation).

It is widely accepted that a Participants Bill of Rights should be developed for HIV vaccine trial volunteers. In accordance with standard clinical research practice, NIAID has already agreed to many basic rights for HIV vaccine trial participants, including access to one's medical file, free counseling and HIV testing, permission to leave the trial without penalty, and others. Given that participants will instructed not to assume physical protection and the potential for social harm which participants will experience, the prospect of prolonged trials for HIV vaccines is an occasion to consider a "new generation" of participant rights and protections. The rights currently agreed to by NIAID fail to fully address several areas which may be critical in HIV vaccine trials: compensation for injury, lifetime efforts to alleviate social harm, and guaranteed free access to any HIV vaccine which may be found efficacious by later studies.

At this early stage in HIV vaccine research, these concerns may appear theoretical and distant. When a series of trials, and the accompanying media coverage and community debate begins, guarantees in these areas may become more tangible and prove to be important to long-term recruitment and retention of volunteers. And if these concerns are
not adequately addressed now, they may be ignored when implementation of large-scale trials gains momentum. The fact that prospective volunteers have voiced concerns about their ability to trust the government and come from largely disenfranchised communities also argues for comprehensive protections and a guarantee they will have access to the eventual benefits of research.

**Compensation for trial-related injuries.** A wealth of medical ethics literature argues that participants in clinical trials should be compensated for injuries related to their participation. Guideline 13 of the International Ethical Guidelines for Biomedical Research Involving Human Subjects states that, "Research subjects who suffer physical injury as a result of their [trial] participation are entitled to such financial or other assistance as would compensate them equitably for any temporary or permanent impairment or disability." Other documents, including those prepared by an AIDS Action Foundation working group and a report from the Office of Technology Assessment, have provided arguments for such protection. And medical ethicist Robert Levine has pointed out the practical side of this issue: "One of the purposes of establishing a compensation system is to encourage individuals to volunteer to take certain sorts of risks of injury to serve the interests of society."

Absent a liability system, vaccine researchers and manufacturers might face a series of lawsuits which would damage public and volunteer confidence in trials. Lack of an established liability system may to some degree also impede pharmaceutical industry investment in vaccine research and development. A system which provides compensation for physical harm need not absolve pharmaceutical companies from liability for damages caused by their own negligence, a move which would very likely undermine public confidence. But as of today, trial volunteers are promised no extended medical care or compensation to balance the risks they will be taking in HIV vaccine trials.

**Ongoing efforts to alleviate social harm.** Early phase testing of HIV vaccines has demonstrated that trial volunteers are putting themselves at social, as well as physiological, risk. Because current vaccine candidates make some vaccines test positive on the Elisa HIV antibody test, some uninfected trial volunteers have experienced difficulty with international travel, government employment, and life and health insurance - all areas in which discrimination against people with true HIV infection is legal.

So far, NIAID has been effective in working with insurers, government agencies and others to restrain much of this discrimination against vaccine trial participants, though, as the AIDS Action Foundation document attests, this has been "quite a labor intensive effort." But in preparation for Phase III trials, the Institute has not made a guarantee these services will be provided as needed for the life of the participant, even though the false positive test and hence the risk of discrimination could continue indefinitely.

When many thousands of individuals become involved in trials, a dedicated staff may be needed to address social harm against trial volunteers - to distinguish between
government-sanctioned discrimination and discrimination from vaccine-induced seropositivity. The issue may be compounded as HIV vaccine candidates become more sophisticated and complex, and therefore more difficult to differentiate from actual infection.

One solution to this large and looming problem requires legislative action: outlawing discrimination against people with HIV in all government employment, travel into the United States, and health and life insurance. In the absence of that, NIAID could make a commitment in writing to provide intensive efforts to address social discrimination for HIV vaccine trial participants as long as such protection is needed. These efforts might include designating NIAID staff to handle specific discrimination issues, and agreements in advance with insurance companies, government employers, and countries which require foreign travelers to take HIV antibody tests.

**Free access by all trial participants to whatever HIV vaccine is eventually licensed.**
In the current draft of the Participants' Bill of Rights, NIAID has indicated its intention to guarantee trial participants they will receive any HIV vaccine licensed within five years of the conclusion of the trial in which they are enrolled, but this promise may be of limited worth given the expected timeline for HIV vaccine development. A guarantee without a time limit would provide a more meaningful benefit for many volunteers, since trials will draw from younger, lower-income populations which are less likely to have health insurance coverage for vaccines.

Free access is consistent with the principle of equal sharing of benefits and risks of research - in this case adjusted to reflect the potential timeline of vaccine trials. It is also consonant with the likely development path of vaccine research: knowledge gleaned from early trials (which may fail to prove a product efficacious) will aid future vaccine design and trials. It follows that all those who have assumed risk to aid the HIV vaccine enterprise receive the eventual product of those efforts.

**Helping Volunteers Make Informed Decisions about Trial Participation**

To facilitate truly informed decisions on the part of individual trial volunteers, it may be useful for the government to fund community-based organizations (CBOs) to provide information which helps prospective trial participants think through complex issues involved in the decision about whether to participate in trials. Many volunteers will be more comfortable receiving information when it originates from community-based organizations, rather than government agencies.

As noted above, altruism is one of the few defensible motives for entering an HIV vaccine trial, since volunteers should not expect personal protection from the vaccine candidate (or placebo) they receive. This fact is implied in discussions about trial participation, but it must become explicit. To safeguard trial participants, it must be clear that personal protection from HIV is not a well-founded reason to participate - receiving behavioral interventions and regular interaction with a study counselor and the desire to make a contribution to humanity are the primary benefits one can hope to receive.
Yet there is limited literature available to help people put a value on this contribution - to understand the potential benefits of an HIV vaccine at various efficacy levels - so that they can weigh this value against personal and communal risks. It is relatively easy to list the social and physiological risks of doing a trial. It is more difficult to list the long-term implications of never accepting the risks inherent in doing a clinical trial. Derek Hodel writes that, "Ambivalence toward vaccines runs high in general, let alone for AIDS vaccines." 37 Individuals and communities may need to wrestle with this ambivalence directly if they are to maintain support for trials over time.

This is also the potential for a skewed public debate concerning the merits of particular vaccine trials. Some may argue for a trial of a proposed vaccine product simply because new prevention technology such as a vaccine is desperately needed. But an informed decision about participation in a trial should be based on an assessment of the likelihood that that specific trail will meaningfully contribute to HIV vaccine research - not solely on the obvious urgency of the epidemic.

Materials produced by CBOs could help address these complex areas of trial participation, including weighing risks and benefits and assistance unraveling the issues in scientific controversy. These materials would help people put risks and benefits in the context of their communities and their own lives. They would help individuals understand both the personal risks of trial participation, and the reasons why some level of risk may be justified by the potential benefits. They would recognize the potential dangers of participation, be absolutely clear that participants could expect no personal benefit, and explain the potential communal benefits of a vaccine.38

It is an ethical essential that educational materials not be coercive in any way. What is needed is an objective discussion of risks and benefits, not materials which encourage individuals to take risks they would not otherwise take. Materials should be developed by credible community-based organizations and provide a variety of perspectives on the sensitive and complex issues involved in trial participation. By offering a variety of perspectives - rather than attempting to provide the one "right" answer - organizations can facilitate informed decisions and avoid appearing as the "hired gun," of trial sponsors.

Counselors at trial sites are often themselves members of affected groups and develop trusting relationships with trial participants over time. They should be acknowledged as important conveyers of information who will likely be influential in helping volunteers think through the pros and cons of trial participation. Counselors need adequate training both on the scientific issues involved in a trial and on how to engage in an open and objective discussion about trial issues with volunteers.

**Behavioral Interventions Beyond Reproach**

Reports of high seroconversion rates in vaccine trial cohorts - not an unlikely occurrence among "high risk" trial participants - also have the potential to weaken community support for trials. Other analyses of the ethical issues of HIV vaccine trials have warned of the inherent conflict of interest of trial researchers: needing to counsel participants that
they should not assume any protection from a candidate vaccine, while knowing that participants will need to practice high risk behavior in order for the efficacy of the vaccine to be tested.39

Built-in contradictions like this may raise legitimate issues of trust, particularly among individuals from communities mistreated in previous biomedical research. The only way to run an ethical trial and maintain community support in the face of this is to provide trial participants with prevention interventions which have been shown to work: sustained behavioral interventions of the highest quality. The perception that behavioral interventions are receiving only limited attention from trial researchers could severely undermine sustained community support for trials.

The Integrity of Product Development Efforts

The perception trial volunteers have of the integrity of vaccine research and development efforts may affect their willingness to participate in trials. For a series of large-scale human trials to be successful among potentially skeptical populations, it may be important for trial volunteers to have confidence that the candidate vaccine going into their arms is the most promising product science can currently produce for efficacy testing, rather than an experimental agent chosen for testing because lack of public or private investment left few other good options.

One of the differences between a trial for an HIV vaccine and a trial for an AIDS therapeutic is that HIV negative participants in a vaccine trial will have a lower risk threshold and less of a sense of urgency about receiving the experimental product. Vaccine participants can be expected to have greater concerns about the safety and potential usefulness of the candidate vaccine than they would for a therapeutic because most will feel a less immediate need for the product.

As a series of trials begins in largely stigmatized populations which have a high level of distrust of the government and industry, participants and community leaders will begin to scrutinize more closely government and pharmaceutical industry efforts on vaccine research. Over the long-term of HIV vaccine testing, volunteer willingness could be jeopardized if it is widely perceived that vaccines proposed for testing are of limited promise because, 1) private and public investment and coordination were lacking, or, 2) the goal of encouraging private investment in vaccines is coloring the decision to advance to trials.

In order to produce candidate vaccines in which volunteers can have confidence, public and private investment in HIV vaccine research should match the magnitude of the public health emergency and the scientific challenges. NIAID has funded an array of basic science research and Phase I/II trials and taken steps to encourage private investment, including setting "milestones" which provide industry with criteria to be used in deciding when to advance with human trials. But a decade and a half into the AIDS epidemic, private pharmaceutical industry interest in developing HIV vaccines has been disappointing. Companies are more likely to recoup their investment in therapeutic drugs
than in HIV vaccines. And scientific challenges, licensing uncertainties, questions about the size of the market, and liability concerns make investment in HIV vaccines comparatively unattractive.40

The media have already begun to report concerns being raised regarding HIV vaccine research and development efforts. A September 1994 article in Science quoted NIAID Director Tony Fauci as saying of HIV vaccine development efforts, "When all of the clothes are ripped away, what do we have?" He was reacting to discussions of two government panels which, he said, "laid naked what a paltry effort' is being made to develop AIDS vaccines."41 One year later, a Village Voice cover story reported disappointing levels of private industry investment and lack of coordination of federal government efforts in HIV vaccine research.42 An Office of AIDS Research report issued in March 1996 advised that, "The entire AIDS vaccine research effort of the NIH should be restructured."43

Perhaps more potentially damaging to confidence in trial efforts is the argument that efficacy trials should proceed with candidate vaccine products if only to encourage pharmaceutical companies to maintain interest in HIV vaccine development.44 To date, there is no indication such arguments are affecting decision making at NIAID. But if affected community members - perhaps reacting to controversy-driven media coverage - perceive that they are being injected with experimental vaccines in part to entice private industry to serve public health needs, support for trials is unlikely to be sustainable.

There are many ways in which government can harness private industry scientific expertise for HIV vaccine research, including offering tax and licensing incentives, direct government funding of industry to pursue research in promising areas, addressing liability concerns, establishing clearer licensing guidelines, guaranteeing purchase of a vaccine when licensed, and other options.45 Equity issues can be addressed by offering these incentives as part of a negotiated package which includes commitments on the part of industry to maximize the availability of a vaccine when licensed (e.g., offering a reduced rate for those unable to purchase the vaccine).

When media attention focuses on the first large-scale HIV vaccine trials, volunteers will more likely be able to make sense of their participation if they believe they are working in concert with researchers and industry scientists who show a similar level of dedication. Trials are less likely to be supported over an extended timeline if volunteers come to believe that they are taking risks to fill in the gaps left by public and private disinterest.

An effective and widely available vaccine for HIV is our best hope to bring an end to the epidemic which causes over 8,000 new infections every day. But in order for HIV vaccine research to ultimately be successful, sustained support will be needed at several levels, including the general public, affected communities, and many thousands of individual trial participants. Members of affected communities have a crucial role to play in pushing for increased private and public HIV vaccine research, addressing safety and equity concerns, ensuring informed decisions on the part of trial participants, and securing dissemination of a vaccine to all those at-risk.
Communities, government, researchers and the private sector will need to form a partnership on HIV vaccine efforts, a partnership which is most likely to be successful in an atmosphere of mutual trust. The areas outlined above could play an important role in establishing and maintaining that trust. In the shadow of the Tuskegee Syphilis experiments and more recent revelations about government-sponsored radiation research on unwitting individuals, attention to the issues involved in trust building is timely, practical and an ethical prerequisite to success.

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RECOMMENDATIONS WHICH FOLLOW FROM THIS REPORT

Affected Communities

1. Vaccine development should be added to the AIDS activist agenda. Community organizations based in HIV-affected communities should include vaccine development and testing issues on their list of important policy issues requiring ongoing attention. Policy organizations should advocate for expanded public and pharmaceutical industry vaccine research, in addition to ensuring ethical conduct of trials. AIDS organizations should consider establishing a policy that public funding for HIV vaccine research must not come from resources for therapeutics or other prevention approaches.

2. Community-based organizations and leaders should publicly discuss the potential benefits and risks of HIV vaccine research and dissemination.

3. Elected officials, the media, organizations and individuals based in HIV affected communities should begin a dialogue about the ethical, educational, decision making, and equity issues raised by the prospect of HIV vaccine testing and dissemination. A central question is: Under what conditions are vaccine research and dissemination advantageous to members of affected communities? The answers to that question should help guide community-based advocacy.

4. Community organizations should prepare educational information to inform community members about vaccine-related issues (research, product development, trials, etc.) and to assist individual trial volunteers in making informed decisions about participation.

Government

5. The National Institute of Allergy and Infectious Diseases should work with researchers, members of affected communities, and public relations professionals to develop a long-term, comprehensive public relations and education plan which balances the need for optimism about vaccine development with realistic estimates of the risks, resources and time required to identify an efficacious vaccine for HIV. Community education, dialogue between researchers and community members, and public relations strategy should be tailored to meet the specific concerns of particular affected communities.

6. The National Institute of Allergy and Infectious Diseases should work with ethicists, members of vaccine trial cohorts, researchers at trial sites, legal
professionals, elected officials, and pharmaceutical manufacturers to broaden the rights guaranteed to HIV vaccine trial participants. The following rights should be part of this expanded Participants' Bill of Rights: compensation for trial related injuries, ongoing protection from social harm, and free access to whatever HIV vaccine is licensed. In addition, an open dialogue about affected community concerns regarding biomedical research and specific, concrete ways in which researchers can address or alleviate those concerns is needed.

7. The National Institutes of Health should provide trial participants with sustained behavioral interventions of the highest quality.

8. The National Institute of Allergy and Infectious Diseases should work with community advisory board members and representatives of HIV-involved community-based organizations to assess the prospects and approaches to facilitate open and structured community-level debate regarding participation in HIV vaccine trials.

9. The National Institute of Allergy and Infectious Diseases should contract with community-based organizations to produce materials which help prospective trial volunteers consider the personal and communal risks and benefits of HIV vaccine trial participation. These materials should detail the potential dangers of participation, be clear that participants can expect no personal physical protection, explain the potential communal benefits of a vaccine, and provide a variety of perspectives on these sensitive issues. Government should strive to establish early, ongoing relationships with key community-based organizations and leaders.

10. Counselors at trial sites need adequate training both on the scientific issues involved in a trial and on how to engage in an open and objective discussion about trial participation issues with volunteers.

11. Consistent with guidance from the March 1996 Office of AIDS Research Report, The National Institute of Allergy and Infectious Diseases should restructure its vaccine research work, and produce an annual report which identifies progress and impediments in HIV vaccine development. NIAID should articulate a plan, updated annually, to address aggressively gaps in vaccine development efforts. If industry fails to pursue promising leads in vaccine research, NIAID should take responsibility to fund these efforts either through its own laboratories or by contracting directly with industry or academic institutions.

12. In consultation with the National Institutes of Health, Congress should consider providing incentives for pharmaceutical industry investment in HIV vaccine development. Incentive options include establishing a liability claims system, tax incentives or credits, and others. Equity issues can be addressed by offering these incentives as part of a negotiated package which includes commitments on the part of industry to maximize the availability of a vaccine when licensed.

13. The federal Department of Health and Human Services and the President's National AIDS Program Office should begin to lay the groundwork to secure broad public access to HIV vaccines, once available. This may involve opening conversations with industry representatives, commissioning research on past methods of extending access to vaccines and other biologicals, and assessing the extent to which the Children's Vaccine Initiative may serve as a model.
Pharmaceutical Industry

14. Private pharmaceuticals and biotech companies, particularly those which have benefited financially from production of AIDS therapeutics, should commit additional resources towards vaccine research and development efforts. Companies which have successfully marketed AIDS therapeutics but do not have expertise in vaccine research could demonstrate support for this research by funding academic-based vaccine research or private, non-profit efforts such as the International AIDS Vaccine Initiative sponsored by the Rockefeller Foundation.

CITATIONS


3. For example, an article in the *Chicago Tribune* reported that "Dr. John Killen [Director, Division of AIDS at the National Institutes of Health] believes 'it will be a minimum of five years before we have a vaccine,' and other researchers say an effective AIDS vaccine may be 15 to 25 years away, assuming one can be developed at all." *Chicago Tribune*, 11/12/95, p.12; A NIAID publication quotes Director Tony Fauci, "It is very likely that progress toward the ultimate goal of an "ideal" vaccine will occur in incremental steps in which important lessons are learned from less-than-perfect vaccines." *AIDS Agenda*, NIAID, p.19, March, 1996.


10. In the current Phase III HIV vaccine preparatory study, community membership is an element of the initial recruitment procedure, but prospective volunteers must confirm that they have practiced specific behaviors within a particular time frame in order to be accepted into the cohort. Individuals need not self-identify as "gay" to be accepted into a "men who have sex with men" cohort.

11. The Centers for Disease Control and Prevention is currently funding Project LinCS. This project will examine the dynamics of information dispersal between researchers, trial participants, and community members, and also look at the role of community leaders in communities at high risk for HIV.


13. Those involved in human subjects research continue to have an important role to play in ensuring the ethical conduct of this research. "Today's oversight of tens of thousands of HHS-funded research and FDA regulated drug studies appears to have reduced the likelihood that serious abuses of human subjects, comparable to past tragic events, will occur...Various time, resources, and other pressures, however, have reduced or threaten to reduce the effectiveness of local review board and federal agency oversight." General Accounting Office, *Scientific Research: Continued Vigilance Critical to Protecting Human Subjects*, March 8, 1996, p.2


20. More recent research presented by Amy Sheon at a February 1996 NIAID Vaccine Conference is consistent with these results. In an anonymous survey of 247 participants in Phase II HIV vaccine trials, Sheon found that among those with a motivation other than pure altruism, 20% of volunteers identified "hoping for protection" from a vaccine candidate as their main motivation for being in the trial.

21. The same research reported in the previous footnote also reported that "overall, more volunteers decreased their risk [behavior] than increased it." But those volunteers who said they thought they had received the candidate vaccine rather than a placebo were 2.3 times more likely to believe they had unsafe sex with an HIV positive person than those who thought they received the placebo or who were uncertain what they received.


24. NIAID continues to negotiate with community representatives on an expansion of this list, and all rights will need to be negotiated with individual trial sites. Trials may also be launched by private companies without the direct sponsorship of NIAID. The rights and responsibilities of participants should apply equally to non-governmental trials.


28. The obligation to compensate for harm in non-therapeutic research is echoed by many other medical ethicists, and is particularly clear with HIV vaccines: as Christine Grady has pointed out, no good animal model exists to test HIV vaccines, and scientists cannot be absolutely sure of the safety of any vaccine product, so the physiological risks for participants are to some degree unknown. (Grady, Christine, p. 96) Other writers, such as Robert J. Levine and Wendy K. Mariner have questioned the fairness of the "informed consent" contract when the risks are unknown and compensation or necessary medical care not provided. (Levine, Robert J., *Ethics and Regulation of Clinical Research*, 2nd edition, Yale University Press, 1986, p. 157; Mariner, Wendy; Office of Technology Assessment 1995, p.82). Also see the earlier referenced paper by The New York City Community Vaccine Working Group.


33. Office of Technology Assessment, *Adverse Reactions to HIV Vaccines: Medical, Ethical and Legal Issues*, Congress of the United States, September 1995, p. 11. Research on more sophisticated tests which can differentiate HIV infection from vaccine-induced seropositivity is ongoing. An Elisa test which can distinguish between infection and vaccination with the ALVAC/gp120 vaccine candidate is now under development.

34. As a cost control measure, this might be limited by guaranteeing protection only as long as the participant continues to test positive for HIV on standard antibody tests.
35. This guarantee is consistent with recommendations from numerous sources, including: AIDS Action Foundation, *HIV Preventive Vaccines: Social, Ethical, and Political Considerations for Domestic Efficacy Trials*, July 1994, p.27; Christine Grady, *The Search for an AIDS Vaccine*, Indiana University Press, 1995, p. 120; and The New York City Community Vaccine Working Group paper, October 1993, though only the third document explicitly calls for participant access to licensed vaccines from subsequent trials.

36. San Francisco's Project Inform is one example of a community-based organization with an established track record for leadership and independence which may be able to deliver sensitive, complex information more effectively than a government agency. It is essential that contracts issued by government allow a wide degree of autonomy and editorial freedom to community organizations providing information on vaccines. To retain their legitimacy with members of affected communities, these organizations need to be candid about risks and benefits of trials from the perspective of communities which may be disenfranchised and distrustful of government-sponsored research or pharmaceutical industry motives. These organizations may provide reasons why an individual might choose to participate in a trial, but CBOs will lose credibility if they attempt to play the role of recruiter.


38. A similar recommendation is made by other writers, "...to facilitate vaccine trial recruitment, the community-based campaign should provide clear messages about the need for the trial and about the importance of the individuals in the community in meeting that need. Such an approach could help create a community norm supportive of participation." Chesney, Margaret A.; Lurie, Peter; Coates, Thomas J., "Strategies for Addressing the Social and Behavioral Challenges of Prophylactic HIV Vaccine Trials," *Journal of Acquired Immune Deficiency Syndromes and Human Retrovirology*, 9(1):31, 1995.


45. For a partial list of incentives to increase private investment in vaccines, see Office of Technology Assessment, *Adverse Reactions to HIV Vaccines: Medical, Ethical and Legal Issues,* Congress of the United States, September 1995, pgs. 145-146.

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