

HIV VACCINE TRIALS: LEGAL AND ETHICAL ISSUES, SOCIAL CONSEQUENCES

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INTRODUCTION

This paper looks at legal and ethical issues, and possible social consequences, associated with conducting trials of prophylactic HIV vaccines in human subjects. It is an edited version of a paper written by David Buchanan, Board member of ACON and one of AFAO's representatives on the Vaccines Working Group at the National Centre in HIV Epidemiology and Clinical Research.

WHY ARE VACCINE TRIALS DIFFERENT?

Clinical trials have always involved an element of risk for those participating - primarily risk of morbidity/mortality. Trials of preventive HIV vaccines may well be the first clinical trials to entail a risk to participants of significant discrimination by reason either of their mere participation, or by reason of the medical status which they assume through inoculation. The novelty of the consequences of participating in efficacy trials of preventive HIV vaccines derives mainly from the stigma which attaches to HIV infection, and the relatively large scale on which such trials need to be conducted.

In a population such as Australia's, where a history of homosexuality or injecting drug use is taken as indicating a least a predisposition to infection, if not actual infection, a person's positive antibody test is universally read as a marker of HIV infection, and is also read by many people as a indicating a high risk for any who come into contact with that person.

WILL DISCRIMINATION LAWS PROTECT TRIAL PARTICIPANTS?

Australian discrimination law defines disease as a physical impairment or disability. This now includes "the presence in the body of organisms causing or capable of causing disease", and thus provides remedies for discrimination because a person is HIV or hepatitis C positive, regardless of whether any other physical impairment or disability is present.¹ However it is clear that this definition would not include discrimination based on a positive antibody test when HIV is not present in the body.

Furthermore, developments in discrimination law have established that it is not unlawful to discriminate on the grounds of medical status, which includes the status of being at risk for HIV infection. This was decided in a case before the NSW Equal opportunity Tribunal, which found that it was lawful to refuse elective surgery to a sexually active gay man until he underwent a test for HIV. The Tribunal found that the area health service was entitled to treat the complainant less favourably, because the less favourable treatment was based not on his homosexuality but on his risk of HIV infection. His risk for HIV infection was determined by taking into account his sexual orientation, sexual behaviour and the fact that he lived in Sydney.

¹ The exception is South Australian law, which only covers disability discrimination where some impairment is present.



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The consequences of this decision are that it is lawful to discriminate against a person on the ground that they have been inoculated with an HIV vaccine, or that they are participating in a clinical trial of anything at all.²

The extent of HIV-related discrimination in health care settings³, and the vigour with which some health care professionals justify such discrimination, suggest that participants in vaccine trials, whether inoculated or not, may be unsuccessful in challenging discriminatory conduct. As a class, most medical practitioners will be astute enough to ensure that their HIV-related discrimination is on a ground other than perceived infection.

INSURANCE, SUPERANNUATION AND OVERSEAS TRAVEL

Legal protections against discrimination in the areas of superannuation and insurance, based on a presumed risk of HIV infection, is at best partial. The law exempts discrimination in these areas where it is based on "actuarial or statistical data" or is otherwise reasonable. In practice, discrimination against homosexually active men is rife, and HIV negative gay men are sometimes refused cover simply because they are gay. A person's participation in a vaccine trial, not to mention the likelihood that they will be HIV antibody positive as a result, will be a further marker for discrimination in insurance.

A number of countries, including the United States, prohibit entry to people with HIV. In many cases (for example applications for long-term or permanent residence in Australia) the onus is on the applicant to prove that they do not have HIV.

One suggestion has been that vaccine trial participants could be issued with a letter explaining that if the person tests HIV positive, it is because they are participating in a vaccine trial. However there is no guarantee that this would be acceptable to, or deter, would-be discriminators. Consider the usefulness of such a letter at the border post between Costa Rica and the Dominican Republic, or between India and China, or between the USA and Australia. How to address the issue that such a letter is valid only at the time that it is written, and cannot take account of the possibility of subsequent exposure to or infection with HIV by other means?

Because of the terms in which anti-discrimination laws are drafted, people who have been inoculated with an HIV vaccine will find it more difficult even than people with HIV to obtain recourse against discrimination. Trial participants will have little protection at all from discrimination on the grounds of their anti-body status.

PROSPECTS FOR LAW REFORM

Most jurisdictions in Australia overhauled their transmissible diseases and general public health laws as a result of the advent of HIV/AIDS. Whether motivated by populism or rational social and public health concerns, the impetus for these reforms was a perception of the needs of and the risks posed to not only the at risk populations, but through them the whole of the Australian population, culture and economy.

What then is a realistic assessment of the chances of achieving the complex reforms needed to address adequately, and throughout Australia, the needs of a far smaller population - those involved in preventive vaccine efficacy trials? Plainly chances of appropriate reforms within a short time frame are slim.

A solution might be to get the Commonwealth to conduct an intensive reform research project, of the kind conducted in 1989-92 for the production of the discussion papers for the Intergovernmental Committee on AIDS Legal Working Party. If the Commonwealth can pass a law to protect the

² See CO Tacket & R Edelman "Ethical issues involving volunteers in AIDS vaccine trials" *Journal of Infectious Diseases* 1990 (1 Feb); 161(2):356.

³ See, eg, NSW Anti-Discrimination Board *Discrimination - The Other Epidemic* Sydney, April, 1992, pp 30-45.

confidentiality of participants in epidemiological studies conducted for the National Health and Medical Research Council, then it would be interesting to explore whether it could make a law to protect participants in clinical trials from discrimination by reason of that participation and any medical status they assume as a consequence.

THE SIGNIFICANCE OF TRIAL PARTICIPANTS BEING YOUNG

There is little doubt that the discrimination as a result of vaccine inoculation will continue way beyond the life of the trial. Positive antibody status is forever. While designers of vaccine trials might see the operative factor determining the outcome of a trial as being the inadvertent exposure of trial participants to HIV, it is difficult for those in affected communities not to see the very essence of the trial as being reliance on significant numbers of participants engaging in risk behaviours. Thus, for preference in designing these trials, we are not talking about educated, white, middle aged doctors or community activists. We are talking about people who are young, not so well educated, and mainly male. Let there be no doubt about it: the rest of the lives of those who test antibody positive will be affected by participation in the trial and that effect will be universally negative.

A fair reply would be that the negative effect on the lives of trial participants will not be comparable to the negative effect on the lives of those whose infection or at least HIV morbidity and mortality could have been avoided had a vaccine against HIV infection or disease been developed earlier as a result of successful trials. The value to be placed upon the need for a vaccine is enhanced, obviously, if it turns out that vaccines need to be developed for the strain of HIV peculiar or largely endemic to Australia. That is a judgement that needs to be made. But what needs to be acknowledged or weighed in the balance is the negative outcomes for participants in prophylactic vaccine trials.

INFORMED CONSENT

Those who conduct the trials will have to be scrupulous to ensure that potential participants fully understand the consequences of participation. When combined with the number and complexity of the issues involved, the age and levels of education of preferred trial participants is such as to militate against achieving the full comprehension and attitudinal adjustment necessary for people to avoid negative outcomes of participation. One previous attempt in Australia to draft a vaccine trial consent form⁴ involved over four pages of detailed and complex information. These were followed by the written assertion that participants had explained to them the nature, objects and possible risks of participation in the trial and that they had had the opportunity ask questions about possible harm which might flow from participation. This was wholly inadequate and, in the circumstances of the preferred profile of participants, arguably unethical. Any responsibly designed procedure of obtaining appropriate informed consent for preventive vaccines efficacy trials will entail communication in culturally appropriate language both all negative outcomes, and the limits on any positive outcomes for the individual to ensure that the participant accepts those outcomes or their risk. It is difficult to understand why the process would not also communicate how the trial would operate - that is, by hoping that participants will expose themselves to HIV yet not contract HIV, or if they do, not succumb to HIV-related illness. On the other hand, the process must make it abundantly clear that participants must not put themselves at risk by unsafe sex or needle use.

A PARTICIPANTS' BILL OF RIGHTS?

If an HIV vaccine is to be developed, thousands of individuals will need to take some amount of personal risk. The AIDS Vaccine Advisory Coalition, an American community-based group has suggested that a compliment of rights and protections is needed to make these risks acceptable to, and equitable for, many thousands of people over years of multiple vaccine research studies.

⁴ Royal Prince Alfred Hospital Consent Form for a Double Blind, Placebo-Controlled Trial to Evaluate the Safety and Immunogenicity of United Biomedical Inc (UBI) HIV-1MN Octameic V3 Peptide Vaccine in HIV-1 Negative Human Subjects ("UBI consent form"), July 1993.

People considering an altruistic contribution to society are entitled to expect concrete efforts to protect them from harm. In addition, trial volunteers will be asked to assume a series of responsibilities (for example period reporting of risk behaviour, 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.

The AIDS Vaccine Advisory Coalition advocates for the development of a Participants' Bill of Rights for HIV vaccine trial volunteers. While some basic participants' rights are generally recognised by standard clinical research practice - access to one's medical file, free counselling and HIV testing, permission to leave a trial without penalty - the prospect of prolonged trials for HIV vaccines is an occasion to consider a "new generation" of participant rights and protections. These should include:

Compensation for trial-related injuries: Guideline 13 of the international Ethical guidelines for Biomedical Research Involving Human Subjects states "research subjects who suffer physical injury as a result of their participation are entitled to such financial or other assistance as would compensate them equitably for any temporary or permanent impairment or disability."

Ongoing efforts to alleviate social harm: One solution would be to prohibit by law discrimination against people with HIV in employment, travel and insurance.

Free access by all trial participants to HIV vaccines which are eventually licensed: In the US, the National Institute of Allergy and Infectious Diseases indicated an intention to guarantee participants any HIV vaccine licensed within five years of the conclusion of the trial in which they were enrolled. Community groups in that country say that a guarantee without a time limit would provide a more meaningful benefit for many volunteers, since trials will draw participants from younger, lower-income populations. Free access is consistent with the principle of equal sharing of benefits and risks of research, in this case adjusted to reflect the potential time line of vaccine trials. It is also appropriate given the likely development path of vaccine research: knowledge gleaned from early trials (which may fail to produce an efficacious product) will aid future vaccine design and trials. It follows that those people who have assumed risk to aid the eventual production of an efficacious vaccine receive the eventual product of those efforts.

WHO WILL LOOK AFTER THE RAMIFICATIONS OF VACCINES TRIALS

AIDS councils and HIV/AIDS legal advocacy groups have seen overwhelming demand for advice, advocacy and assistance on the very issues it is anticipated will affect and concern vaccine trial participants: discrimination, superannuation, insurance and travel. To this could be added compensation for the morbidity and mortality which is bound to some degree to flow from the conduct of the proposed trials - consent forms notwithstanding.

Who will finance the services necessary to meet these increased levels of demand? In the current environment, the answer is unlikely to be governments. From the perspective of communities affected by HIV/AIDS, the diversion of already stretched resources to deal with an artificially increased level of demand for services is not an attractive prospect. Why should people already with or at risk of HIV suffer a reduction in services? Why should the efficacy of education campaigns, and the level of peer support for both positive and negative be reduced? Why should the work to combat this epidemic be adversely affected, in order for Australia to be involved in the development of an effective preventive vaccine?

TASKS FOR COMMUNITY ORGANISATIONS

The AIDS Vaccine Advisory Coalition suggests the following components of an effective community response to the challenges posed by trials of prophylactic vaccines in human subjects:

- Community organisations based in HIV-affected communities should include vaccine development and testing issues on their list of important policy issues requiring ongoing attention. Policy organisations should advocate for expanded public and pharmaceutical industry vaccine research, in addition to ensuring ethical conduct of trials. AIDS organisations should consider establishing a

policy that public funding for HIV vaccine research must not come from resources for therapeutics or other prevention approaches.

- Organisations should publicly discuss the potential benefits and risks of HIV vaccine research and dissemination.
- Elected officials, the media, organisations 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.
- Community organisations 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.

This briefing paper should be read in association with the following briefing papers from AFAO:

Briefing # 70 Therapeutic and Prophylactic Vaccines.

Briefing # 71 HIV Vaccines: What do they mean to HIV education?

These briefing papers have informed AFAO's draft position paper "Draft position paper on prophylactic HIV Vaccine research & Development."