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The Applied Ethics of Community Involvement in HIV Vaccine Development

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Philosophy

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Abstract

Since the emergence of HIV/AIDS as a global pandemic in the 1980's, the focus of the scientific community has been to firstly identify, then treat and ultimately find a cure for, this disease. This has proven to be challenging and far from realistically achievable by the scientific community or the communities affected by this disease.

A funding allocation from the National Institutes of Health in the United States came to a consortium in Australia seeking to develop a prime-boost preventative HIV vaccine. The consortium included members of the Australian HIV/AIDS Partnership. This partnership emerged from a particular set of historical contexts and included affected community. The Australian Federation of AIDS Organisations was the affected community representative on the consortium. This thesis sets out the contextual and ethical reasons for this arrangement, and explores how this unusual partnership worked in practice, with a view to identifying its broader implications.

HIV vaccine development, and AFAO's role in that development, is complex and multifaceted. The consortium existed within a particular social context which I explore by describing the social history of HIV in Australia. The search for an HIV vaccine is difficult and complex work requiring significant effort and I describe the challenges involved in such an enterprise. Biomedical research more generally exists in the context of international and national research documents which govern the way in which researchers may conduct human experimental trialling. I discuss these documents and highlight the underlying ethical principles.

This research involved 9 interviews with 7 key informants who were members of the consortium. The accounts were analysed following a grounded theory approach, utilising the sensitising concepts outlined in the discussion of the social history of HIV in Australia, the science of HIV vaccine development and the general and specific ethical principles. Following this methodological approach, I identify common themes in the data and discuss the results in greater detail, paying particular attention to the ways this particular social practice plays out in practice and the key ethical considerations arising from the accounts. I also explore the risks, costs and benefits to AFAO of its involvement in the consortium. The overall aim of this research is to understand how practicable, feasible and effective community involvement was in this consortium.

Finally, I come to three major conclusions. First, that the consortium is an emerging social practice, which is the intersection of three established social practices; biomedical research, the affected community and the Australian HIV/AIDS Partnership. Using Langford's criteria for a social practice, I demonstrate the social practice of the consortium was clearly made up of members who were aware of each other's intentions and beliefs. It was clear from the commencement of the consortium's project that the consortium was directed at the overall purpose of developing an efficacious preventative prime-boost HIV vaccine. The unique history and tradition of the social practice of the consortium is slightly less clear but what the accounts of the informants demonstrated is that the histories and traditions of the Australian HIV/AIDS Partnership approach and biomedical research, in particular, were a significant influence on most of the consortium members. So much so, that the consortium adopted that unique history and tradition and it was this factor, perhaps above all others, that facilitated AFAO becoming a full partner in the vaccine development enterprise in the first place. Importantly, my research theoretically extends the notion of shared ways of seeing and doing within a social practice. The socialisation aspects are highlighted very strongly within the accounts.

Second, AFAO's involvement was highly concordant with the core principles of the *Good Participatory Practice Guidelines for biomedical HIV prevention trials* document, and it influenced important protocols within the consortium, but there were also conflict of interest issues for AFAO to manage. Third, the different approaches for community involvement in biomedical HIV prevention trialling (the partnership approach and the Community Advisory Board approach) each has strengths and weaknesses and should be carefully considered in light of the context of the trialling to be conducted.

This thesis concludes with a series of recommendations for future biomedical HIV prevention trials.

Declaration

This is to certify that

- i. *the thesis comprises only my original work towards the PhD except where indicated in the Preface*,*
- ii. *due acknowledgement has been made in the text to all other material used,*
- iii. *the thesis is less than 100,000 words in length, exclusive of tables, maps, bibliographies and appendices.*

GRANT DAVIES

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In a project of this size and duration, many people deserve thanks and acknowledgement. It has certainly been a journey and at times I thought it unachievable. My friends and family deserve some recognition for their encouragement and support during the time it has taken for me to complete this task.

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Special thanks also should go to Mr Michael Kennedy who started me on this path in the first place. The ethics of preventative HIV vaccine development when I started this project was the breaking wave of HIV ethics enquiry. It is broader now but Mike's wisdom in seeing this area as important beyond vaccines has enabled this research to be as relevant today as it was then. He was always willing to discuss aspects of my work with me and I thank him for his sage advice.

Finally, my parents, Tom and Trish Davies must be particularly mentioned. They never doubted I could do this. They encouraged me down this academic path at the start of my professional career. I suspect they have a view they have some genetic claim to this work which I am happy to attribute to them. It is a matter between them how much they can each claim as their own but any errors are mine.

Table of Contents

THE APPLIED ETHICS OF COMMUNITY INVOLVEMENT IN HIV VACCINE DEVELOPMENT	I
Abstract	i
Declaration	iii
Acknowledgements	iv
Table of Contents	v
Introduction	1
1 - A Social History of HIV in Australia	6
Affected Community	7
The 1980's – a time of uncertainty	8
The first reported cases – the Medical response:	8
The Growth of AIDS hysteria	11
The Australian Government and Community responses- an initial divergence	14
Combined responses/partnership approaches to the epidemic - Development of the First National Strategy.	19
The 1990's	21
Changing of Government	25
Community involvement in HIV vaccine trials	27
Australia	27
United States	29
Conclusion	30
2 - Scientific Background	31
Pathophysiology of HIV	32
Approaches to Vaccine development	33
Table 1 Vaccine Approaches	35
Typical example	35
Advantages	35
Disadvantages	35
Status	35
Clinical Trialling	36
Phases	36
Table 2 AIDS Vaccines candidates in clinical trials (2008)	37

Table 3	Protocol No. HVDDT-N01-AI-05395 Synopsis	39
	Conclusion	41
3 - General Ethical Principles		42
	The Nuremberg Code 1947	44
	Declaration of Helsinki 1964	45
	International Ethical Guidelines for Biomedical Research Involving Human Subjects 1993	46
	National Statement on Ethical Conduct in Research Involving Humans 1999; National Statement on Ethical Conduct in Human Research 2007	49
	Integrity, Respect for Persons, Beneficence and Justice	49
	Consent	50
	Research Merit and Safety	51
	Ethical Review and Conduct of Research	51
	Values and Principles of Ethical Conduct	52
	Themes in Research Ethics: Risk and Benefit, Consent	53
	Fundamental ethical principles	54
	Respect for Persons	55
	Beneficence	60
	Justice	62
	Conclusion	64
4 - Current ethical issues in HIV research		66
	Introduction	67
	Guidance Document on Ethical Considerations in HIV Preventive Vaccine Research 2000	68
	Ethical considerations in biomedical HIV prevention trials 2007; Good participatory practice guidelines for biomedical HIV prevention trials 2007	72
	1. Scientific and ethical integrity	75
	2. Respect	75
	3. Clarity in roles and responsibilities	75
	4. Towards shared responsibility	75
	5. Participatory management	76
	6. Autonomy	76
	7. More transparency	76
	8. Standard of prevention	77
	9. Access to care	77
	10. Building research literacy	77
	Summary of this section	78
	Current relevant ethical issues in HIV biomedical research	78
	Research in resource poor countries	78
	Standard of care, placebo controlled trials and equipoise	81
	Consent	86

Community involvement in research	87
Social Practices	87
Social practice	91
Relationships of a social practice with others	92
Conclusion	95
5 - Research Methodology	97
Introduction	98
Aims of this research	98
Theoretical framework	99
Reflexivity	100
Methodology	101
Research Plan	104
Sample:	104
Recruitment	105
Data Collection	106
Data Analysis	108
Rigour	109
Conclusion	112
6 - How Community Involvement Works in the Consortium	113
How the consortium works on scientific and ethical integrity	114
Informed consent processes/education processes	115
Balancing competing principles/ethical analysis	119
Challenges of the work :Grappling with the scientific process	121
Data Safety and Monitoring Board	123
Level of efficacy	125
Long term effects of participation	128
Interim results	128
Negotiating roles and responsibilities	131
Governance structures	132
Disagreements/conflict within the consortium	133
How much is the community component worth? Participatory management and clarity of shared responsibilities	138
Tensions in AFAO's roles	140
Suspicion about community involvement and commercial-in-confidence information	142
Community Representation	142
Different social practices coming together in the consortium	145
Researcher's roles/perceptions/views	147
Learning to work with community	153
Conflict of interest	157

What is a conflict of interest?	166
Why does it matter?	168
Chapter Summary	168
7 - Maintaining Autonomy and the Covenant	169
AFAO's relationship with its members	170
Costs and Risks to AFAO	170
Transparency, roles and responsibilities and internal governance structures	170
Conflict within the community: about participation; about process	178
Waste of community resources/Educating communities prematurely	183
Benefits of AFAO's participation	184
Involvement as a partner changes affected community's views	184
Comparisons with the alternative Community Advisory Board model	192
Chapter Summary	199
8 - Conclusions and Recommendations	201
Consortium as a Social Practice	202
Evaluating the consortium using the core principles of good community participation in biomedical HIV prevention trials	204
Areas of success:	204
1. Scientific and ethical integrity	204
2. Respect	206
3. Clarity in roles and responsibilities	206
4. Towards shared responsibilities	207
5. Participatory management	207
7. More transparency	207
8. Standard of prevention; and 9. Access to care;	207
10. Building research literacy.	208
The problematic area of autonomy;	208
How conflict of interest can be successfully managed	208
Awareness	209
Disclosure	209
Review and Authorisation	209
Prohibition and avoidance	210
Application for AFAO	210
Benefits of participation and comparison with Community Advisory Boards	213
Recommendations	215
9 - Reference List	217

Introduction

Since the emergence of HIV/AIDS as a global pandemic in the 1980's, the focus of the scientific community has been to firstly identify, then treat and ultimately find a cure for, this disease. No country has been left untouched by its presence, with some populations, in particular sub-Saharan Africa and Asia, decimated through sickness and death.

The search for a cure to the highly mutable HIV organism started with the search for a preventative HIV vaccine with wild claims by some politicians that a vaccine would soon be found. This proved to be speculative and far from the reality faced by the scientific community or the communities affected by this disease.

Governments, in particular the United States of America, funded the search for a preventative HIV vaccine through the allocation of funds to the scientific community, administered by the National Institutes of Health (NIH). One such funding allocation came to an Australian consortium seeking to develop what is called a prime-boost approach to vaccine development. The consortium included members of what is known as the Australian HIV/AIDS Partnership. The Partnership emerged from a particular historical context in this country. One member of the Australian HIV/AIDS Partnership, through its peak national body, the Australian Federation of AIDS Organisations (AFAO), was the affected community and it participated as a full partner on the consortium. This made the Australian consortium unlike similar consortia elsewhere in the world. This thesis sets out the contextual and ethical reasons for this arrangement, and explores how this unusual partnership worked in practice, with a view to identifying its broader implications.

In chapter one, I describe the social history of HIV in Australia. I briefly describe the way the Australian Government responded to the emergence of HIV and how the socio-political context shaped the public policy response, through the leadership of Dr Neal Blewitt, to include affected community as partners in that response. What was to be known as the Australian HIV/AIDS Partnership prevailed despite a highly contentious and politicised environment within the general community, the medical profession and conservative governments throughout Australia. This tradition has continued in Australia to the present day and explains why affected community was, almost automatically, included as a full partner in the Australian HIV Vaccine Consortium. I conclude the chapter by briefly comparing the

partnership approach used in the vaccine consortium in Australia with the Community Advisory Board approach used for community involvement in the United States of America.

In chapter two, I explore the highly complex nature of HIV as an organism with many confounding characteristics. These effectively inhibit the development of an effective and simple HIV vaccine. I provide a brief description of the various types of vaccines currently under development and a brief overview of the various phases of the clinical trial process from safety trials through immunogenicity trials to efficacy trialling. I show how complex the science is in this challenging field, and give an indication of what affected community had to come to grips with. I conclude the chapter by providing an overview of the trial protocol for the Australian trial.

In chapter three, I describe the general ethical guidelines for biomedical research, both internationally and nationally, which apply to the conduct of research on humans starting from the *Nuremberg Code* to the present day. I suggest that, fundamental to all of these instruments, are three underlying ethical principles; respect for persons, beneficence and justice and explore these concepts in some detail. I suggest that, while I have highlighted each individually, they are interrelated concepts.

In chapter four, I describe the specific national and international documents relevant to HIV vaccine development. I pay particular attention to the UNAIDS documents which state there should be community involvement in such research. Because vaccine trialling often occurs in resource poor countries due to their often high incidence of HIV, I briefly discuss the ethical problems and challenges raised by those trials such as threats to justice, exploitation and threats to informed consent. In particular, I discuss the difficult issue of standard of care in such countries as it relates to knowing what counts as acceptable standard of care in terms of what should be provided to trial participants both on the active arm of the trial and on the placebo arm of the trial. Part of this discussion involves the notion of equipoise. I argue that community participation is a possible way of resolving and addressing some of these issues and that it is ethically required in principle as a matter of justice. This provides the ethical rationale for community involvement in partnership. This chapter, therefore, has three purposes. The first purpose is to explain the ethical complexities that the affected community had to deal with as a consortium member. The second purpose is to examine the ethical rationale (as opposed to the socio-political rationale)

for community involvement. The third purpose is to introduce the idea of a social practice and argue that this concept is useful for understanding community involvement in practice.

While these ethical concepts aid an understanding of the complex considerations affected community must take on board as part of the biomedical research endeavour, and the theoretical rationale for its involvement, it is only part of the story. My further argument within this chapter is that the consortium I am investigating can usefully be understood as a social practice. In Australia, community participation is already well established within the social practice of the Australian HIV/AIDS Partnership. Within that context, I argue that the best way to examine how community participation in the consortium worked in practice is to see it as a social practice.

In chapter five, I state the aims of this research into community involvement in the HIV vaccine consortium, and describe the theoretical, epistemological and methodological approaches used to achieve those aims. In brief, the research involved key informant interviews with consortium members. The way in which the data were analysed is clearly explained and the limitations to the research described.

In chapter six, I draw on the interview data given by the informants to provide a description of how this particular social practice works in terms of the way community involvement plays out in practice. In addition, I highlight the key ethical considerations arising from the accounts given by the informants. I describe the ways the representatives of the community participating in the consortium interact with other members of the consortium and highlight in-practice examples of the three distinct social practices coming together. This analysis shows how the intersection of those social practices affects the work of the consortium and the consortium members. Of the six characteristics of a social practice (described in chapter four) of particular relevance to the community members on the consortium are the institutional dimension inherent in a social practice, the unity of purpose and the reciprocal self-awareness of the practitioners of a social practice. A fourth characteristic also highlighted is the learning and socialisation aspects of a social practice.

I conclude that while the consortium operates as a social practice, it is one in its infancy with all the inherent tensions and positioning that comes with the emergence of new, shared ways of seeing and doing. This is not unexpected, and on the basis of the data I have been able to collect (noting that two members of the consortium, the

CSIRO and ANU, did not participate in this research), it appears to have come to a mutually beneficial outcome. However, conflict of interest issues inherent in this new social practice do need to be explicitly acknowledged and managed.

In chapter seven, I explore, using the accounts of the informants, the risks, costs and benefits to AFAO of its involvement as a full partner in the consortium. I describe some of the internal re-structures required by AFAO and the significant learning required to make meaningful contributions to the discussions around the consortium table. Such learning, I show, has enabled AFAO to affect positive changes within the consortium and, most importantly, with the trialling itself. Such a partnership approach is very different to the Community Advisory Board approach used in other parts of the world and the informants have a clear appreciation of the differences those different models entail. They believe that partnership is better. Importantly, there were risks for AFAO to its relationship with its members through its participation as a partner. However, the community informants felt those risks were manageable because of the established social practice of the Australian HIV/AIDS Partnership. They took the view that the benefits of partnership were important and for which it was worth accepting some level of risk.

In my final chapter I make three major points. First, I summarise the ways in which the consortium, as a convergence of three other social practices, is an emerging social practice and show how my work has furthered the theoretical understanding of social practices, by drawing attention to the dynamic nature of shared ways of seeing and doing. Second, I evaluate the ethical foundation of the partnership by retrospectively examining the consortium's concordance with the *Good Participatory Practice Guidelines for biomedical HIV prevention trials* developed by the Joint United Nations Programme on HIV/AIDS (UNAIDS) and the AIDS Vaccine Advocacy Coalition (AVAC). I conclude there was a high level of concordance with the core principles for the consortium. While there was a high level of concordance, there was also a conflict of interest for AFAO which threatened its autonomy, and which AFAO needed to manage which threatened its autonomy.

Third, I compare and contrast the two different approaches for community involvement, the partnership approach and the Community Advisory Board approach. Each is a useful method with strengths and weaknesses and should be carefully considered in light of the context of the potential biomedical HIV prevention trial.

Finally, I make a series of recommendations for future biomedical HIV prevention trials in relation to community participation.

1

A Social History of HIV in Australia

Since the focus of this thesis is exploring the ways in which the affected community participates in HIV vaccine development as a partner in the Australian consortium, it would be useful to explore how affected community came to be part of the HIV response in Australia in the first place and how that has translated into its participation in preventative HIV vaccine development. Australia's policy response to the HIV/AIDS epidemic is frequently showcased as an enlightened and innovative model for addressing the HIV issue globally (Ballard in Dean and Hindess, 1998: 125). The affected community plays a central role in the response in Australia and has done so from the start.

I will draw on the key works already comprehensively undertaken by Ballard, Carr, Altman and others in this chapter to provide a context for the way in which the affected community has positioned itself, and been positioned, as a key player in Australia's response.

Affected Community

Throughout this thesis, the term 'affected community' will be used. I do not propose to explore the various meaning or contentious definitions of community here. For a comprehensive discussion of such matters, Altman (1994) and Grierson (1998) are two authors that have undertaken comprehensive research on the topic of community and its definitions. For the purposes of this thesis, I mean people living with HIV/AIDS, gay and bisexual men, sex workers, and injecting drug users. I use this definition because these are the groups most affected by HIV/AIDS in Australia and, as such, most affected by the development of a preventative HIV vaccine. This is a standard definition and is unremarkable. As I will describe later, apart from the early days of Australia's response to the HIV/AIDS epidemic, these are the groups which are of principal concern, targeted specifically in HIV prevention strategies and who have been enrolled as partners, in Australia's response. Therefore, I do not include general community in my definition of affected community. I also use the term affected community here because these groups are represented by the Australian Federation of AIDS Organisations whose genesis and whose role in preventative HIV vaccine development I describe later and, critically, is the key organisational community partner in the Australian Consortium.

As I describe later, affected community was enrolled as a partner in Australia's response largely because the then Federal Health Minister, The Honourable Dr Neal

Blewitt created that opportunity and, also in large part, because at the start of the epidemic, there was no medical treatment for HIV infection and the prevention focus was on behavioural strategies. This happened in a highly contentious and politicised environment where homophobia and bigotry was pronounced both within the general community and within conservative governments in power at the time. Indeed, some continued incidences of contention still appear in relation to affected community involvement.

The decision by Dr Blewitt has resulted in a unique outcome in HIV public policy by establishing, as nowhere else, affected community as partners in both the structures and advisory bodies and established a precedent called the Australian HIV/AIDS Partnership that continues to this day. This chapter describes that unique public policy approach from its infancy to the present day and demonstrates why affected community involvement in vaccine trialling is taken for granted and why it is a unique approach, particularly when compared with the way the United States engages affected community in vaccine trials.

So, while there is a well established tradition and policy of Australian affected community involvement in HIV prevention and treatment in general, little is known about how the affected community functions in the context of the HIV vaccine consortium which is why my research is important and novel.

The 1980's – a time of uncertainty

The first reported cases – the Medical response:

The emergence of HIV/AIDS in the 1980s came after a number of significant scientific and sociological innovations in the 1960s and 1970s. This progress, such as the development of molecular tools and the emergence of socio-behavioural frameworks promoting new understandings of human rights, social justice, disease prevention and community health coexisted with the biomedical sciences, providing notable impetus for forming the response to HIV/AIDS in Australia (Timewell, Minichiello and Plummer, 1992: xxiii).

In 1980, the Centers for Disease Control in Atlanta, Georgia recorded a number of cases of pneumocystic carinii pneumonia (PCP) and Kaposi's sarcoma which were hitherto rare diseases but later found to be common in immunocompromised individuals (ANCARD, 1998; Carr in Timewell, Minichiello and Plummer, 1992).

There are reports that the first evidence of the presence of HIV in Australia is in stored sera collected in 1980 from Sydney homosexual men (Crofts in Timewell, Minichiello and Plummer, 1992: 35).

It was not until 5 June 1981, however, when the Centers for Disease Control published the first scientific paper on HIV entitled *Pneumocystis Pneumonia in Homosexual Men – Los Angeles* in its *Morbidity and Mortality Weekly Report*. The *Sydney Star*, a paper distributed to gay venues, reports an account of this scientific paper, which is believed to be the first documented account of the HIV epidemic in Australia (ANCARD, 1998: 7).

Ballard (in Dean and Hindess, 1998: 127) suggests that medical epidemiologists at this early stage of the epidemic had a central role in the identification and definition of HIV, the medical response to it and that it existed within a cultural environment in which homosexuality was considered outside the boundaries of normal behaviour. The only shared feature of the young men presenting with otherwise rare diseases was their same sex sexual activity with multiple partners which led the epidemiologists to identify gay males as the ‘risk group’ and homosexual activity as the ‘risk behaviour’. Given the perception of gay men as ‘abnormal’ at the time, this marginalised an already stigmatised group, resulting in the stigma becoming a central component of the medical, social and policy response to AIDS.

As Carr (in Timewell, Minichiello and Plummer, 1992: 13) and Ballard (in Mitchell and Hindess, 1998: 127) suggest, it was inevitable that the early debate about AIDS would focus on the relationship between it and male homosexuality. Perhaps surprisingly, a great deal of this debate occurred in the gay community itself in addition to those who were hostile to the public acceptance of homosexuality. It is asserted by Carr that the more extreme views suggested by some gay men and by those who were hostile to public acceptance of homosexuality were mutually reinforcing, leading to self sustaining conspiracy theories which were both untrue and unhelpful. Such issues ranged from the Reagan administration in the United States concocting a plan to exterminate gay men, to the accidental release of a biological agent from a Central Intelligence Agency research facility.

Ballard (2003: 37) suggests that the existence of an active and well mobilised community immediately prior to the onset of AIDS was as a result of legislative battles over the decriminalisation of homosexuality which had yet to be won in some States. The vilification/stigmatisation of homosexual men may have hindered the

development of effective, early responses to the emerging epidemic as governments were withdrawing from actively policing acts of private consensual sex and, therefore, disinclined to engage with a disease primarily affecting homosexual men (Ballard, 1998: 127).

By the end of 1981, the number of AIDS cases in the United States (then known as 'GRID'-gay-related immune deficiency) had risen to 270 and by early 1982, international articles were published and reported in the *Sydney Morning Herald* relating to the link between PCP and Kaposi's sarcoma with immune system deficiency. On 11 June 1982, the Centers for Disease Control reported initial cases of PCP and Kaposi's sarcoma occurring in injecting drug users, on 16 July in the same year it reported these diseases among people with haemophilia and on 10 December reported similar cases among people receiving blood transfusions. On 24 September of that year, the Centers for Disease Control in Atlanta coined the term Acquired Immune Deficiency Syndrome or AIDS (ANCARD, 1998: 8-10).

In October 1982, Professor Ron Penny, the head of immunology at Sydney's St Vincent's Hospital, saw Australia's first suspected AIDS patient, an American visitor, although this remained publicly unreported until March 1993 (ANCARD, 1998; Ballard in Kirp and Bayer, 1992).

Altman (in Timewell, Minichiello and Plummer, 1992: 55-62) charts three fundamental issues that emerged from the establishment of AIDS as a serious epidemic between 1981 and 1982. The first issue was anxiety within the infected and affected communities, the issues surrounding talking about safe sex and the increasing visibility and presence of medical politics; second, the early medical definition and control of AIDS; and finally the indifferent response by government to the emerging epidemic.

For the next year or so, with the exception of the appointment of a working party under the National Health and Medical Research Council to plan AIDS surveillance and care and the formation of AIDS Action Committees in urban gay communities, the first of which was later known as the AIDS Council of New South Wales (ACON), there was little progress or attention paid to HIV/AIDS (ANCARD 1998; Ballard 1998). However, once it became clear that this was an epidemic which could affect other communities through blood transfusion and blood products, Australian governments became highly concerned (Ballard 1998; Blewitt 2003; Penny 2003).

There is an interesting underlying message in this response by government. While governments were prepared to accept and respond cautiously to an emerging fatal disease in a marginalised and minority group, once the likelihood of that disease spreading into the broader community via a medically administered treatment became clear, great interest and impetus was generated.

The Growth of AIDS hysteria

By mid 1983 the Australian Red Cross, a federation of State blood transfusion bodies, issued a statement recommending that centres not collect blood from “sexually active homosexual or bisexual men with multiple partners, from intravenous drug-users or from their partners” (Altman in Timewell, Minichiello and Plummer, 1992; Ballard in Kirp and Bayer, 1992). This prohibition was led by the Director of the Sydney Blood Transfusion Service, Dr Gordon Archer, after discussion with a visiting blood bank director from Oklahoma (ANCARD, 1998; Ballard in Kirp and Bayer, 1992).

Given the history of vilification and marginalisation experienced by gay men at this time, it is not surprising that a number of them protested outside the Sydney Blood Bank claiming Dr Archer’s statement was an overreaction and demonstrated a lack of consultation since he had refused to meet with activists to discuss alternative means of deterring donation. However, what this also provided was the impetus for the establishment of the AIDS Action Committee in Sydney (later known as the AIDS Action Council of New South Wales), the Victorian AIDS Action Committee (later the Victorian AIDS Council), the Western Australian AIDS Action Committee (later known as the Western Australian AIDS Council) and the AIDS Action Committee of the Australian Capital Territory (later known as the AIDS Action Council of the Australian Capital Territory) (Altman in Timewell, Minichiello and Plummer, 1992; ANCARD, 1998; Ballard in Kirp and Bayer, 1992; Ballard, 1998).

This period of the epidemic generated a variety of views, some of them strongly opposed to each other. For example, some anti-gay writers argued that AIDS was either deliberately or accidentally devised by gay men themselves, while others suggested that AIDS was the “inevitable” result of greater social and legal acceptance of male homosexuality and of “unnatural” gay lifestyles. Of particular note is that a similar theory found support in the gay community itself. Some gay writers argued that AIDS was the inevitable result of an excess of drugs and sex by a minority of gay

men. This “fast lane” lifestyle had led to “immune overload” and thus, led to AIDS (Carr in Timewell, Minichiello and Plummer, 1992: 13).

Perhaps the most significant example of this divergence of opinion occurred on the 29th June 1983. On that day the then Commonwealth Minister for Health, Dr Blewett, spoke out against what he termed the growing ‘AIDS hysteria’. On the same day the Reverend Fred Nile called for gay men to be quarantined (ANCARD, 1998: 16).

Also during this time Dr Luc Montagnier of the Institut Pasteur in Paris, published a paper in *Science* reporting that his team had isolated a virus, found in West Africa, that was the cause of AIDS. They named it LAV-lymphadenopathy-associated virus. Australia’s first AIDS death occurred at Prince Henry Hospital in Melbourne in 1982. At the same time the National Health and Medical Research Council formed a working party on AIDS, chaired by Professor David Pennington who quickly became the authoritative voice on AIDS to both the media and government. Later, this working party was absorbed into the National AIDS Task Force. Late in 1983, a Sydney dentist banned all gay clients from accessing his service, further adding to inflammatory nature of the epidemic (ANCARD, 1998; Ballard in Kirp and Bayer, 1992).

While the media and government focussed on other issues during this time, the infected and affected communities continued to address the issues presented by the epidemic. In June 1984, Bobby Goldsmith, a champion swimmer and well-known member of the Sydney gay community, died of AIDS at the age of 30. The friends who supported him during his illness and death formed a group that later became the Bobby Goldsmith Foundation, a leading AIDS charity (ANCARD, 1998: 17).

In San Francisco, city health authorities closed sex-on-premises venues and bathhouses and Dr Robert Gallo, a virologist with the US National Cancer Institute, announced the discovery of the virus that causes AIDS. The American team isolated the virus from the blood of healthy female prostitutes and called it HTLV-III-human T-cell leukaemia virus. It is the same virus French researchers announced discovering a year earlier. The French accused Gallo of scientific theft and commenced legal proceedings. The dispute was finally resolved out of court some years later when Montagnier and Gallo agreed to be named joint discoverers of HIV (ANCARD, 1998: 18-19).

It was at around this time that the various Australian Governments became very concerned about the epidemic as a result of the then Queensland Minister for Health announcing in November, on the eve of a Federal election campaign, that four babies had died after receiving “contaminated blood” from a homosexual donor (Altman in Timewell, Minichiello and Plummer, 1992; ANCARD, 1998; Ballard, 1998; Blewitt, 2003). The man donated blood without knowing he was infected and before the availability of an antibody test. Nevertheless, media headlines such as ‘die, deviant, die!’ appeared. The Reverend Fred Nile, the main anti-gay protagonist in Australia, condemned donors of infected blood as criminals. The Anglican Dean of Sydney, the Very Reverend Lance Shilton, accused gay men of ‘having blood on their hands’. There were reports of the Sydney gay community living in fear of reprisals because of the spreading of AIDS to ‘innocent’ victims (ANCARD, 1998; Ballard in Kirp and Bayer, 1992).

Dr Blewett, called an urgent emergency meeting of all Health Ministers in Melbourne in November 1984 in an attempt to limit the political advantage of some National Party politicians trying to turn the so called ‘gay plague’ into an issue for the election campaign. At that meeting it was decided that the NH&MRC Working Party be reconvened as the National AIDS Task Force. The National AIDS Task Force, as a result of its chair, Professor Pennington, agitating within the States and Territories, described reporting frameworks to the Federal and all State and Territory Health Ministers through the Australian Health Ministers Council. As there were no effective treatments for the disease, the Commonwealth decided to pursue community based peer education and Dr Blewett established his own advisory committee, the National Advisory Committee on AIDS (NACAIDS), recruiting Australia’s best-known woman journalist at the time, Ita Buttrose, to chair it. The Committee included representatives of various community groups, including representatives from ACON and VAC, which ensured its boycott by the highly conservative Queensland Government, and in future years the Committee would often appear to be at variance with the medically dominated Task Force. The Federal AIDS Coordinating Unit and the Federal Health Minister’s office were often strong defenders of NACAIDS in the conflicts that followed (Altman in Timewell, Minichiello and Plummer, 1992; ANCARD, 1998; Ballard in Kirp and Bayer, 1992; Ballard, 1998).

The two distinct approaches, medical containment and community education, thereby became institutionalised through the establishment of the two Commonwealth committees (Ballard in Kirp and Bayer, 1992; Ballard, 1998).

Despite these generally positive steps, vilification and hysteria continued as a feature of the political environment as was demonstrated by the Reverend Fred Nile on 28th November 1984, who called for ‘gay-free zones’ to be established around Australia and the Orange people, a religious sect, who announced a ban on kissing (ANCARD, 1998: 22).

The response in Australia during this period is characterised by increasing responses from the infected and affected communities, in large part due to the vilification and denigration of these communities by prominent public figures and the media. Dr Blewett’s contribution to the Australian response to AIDS cannot be overvalued. His contribution to establishing infrastructure and frameworks within government ought to be recognised as a significant contribution to the public policy development of the response to HIV/AIDS in Australia. Dr Blewett was awarded a Companion of the Order of Australia on 12 June 1995 in “... recognition of service to the Australian parliament, the development and implementation of public policy, particularly national AIDS policy and for scholarship” (http://www.itsanhonour.gov.au/honours/honour_roll/search.cfm?aus_award_id=884398&search_type=simple&showInd=true).

The Australian Government and Community responses- an initial divergence

In January 1985, after visiting the United States, Dr Blewett decided to adopt a policy approach involving affected communities, similar to the approach adopted in San Francisco at the time (Blewett, 2003: 9). Also at this time, the first HIV antibody test kits arrived in Australia. Professor David Pennington, the Head of the National AIDS Task Force, claimed the entire community, including heterosexuals, was at risk from HIV and AIDS (ANCARD, 1998: 23-24). Professor Pennington, after a proposal from the Commonwealth representative on the Task Force that its work be progressed within the Department of Health, mobilised support in the States on the basis that it was a Commonwealth takeover strategy. After the Commonwealth conceded to Professor Pennington’s demands, additional State representatives were included on the Task Force and the Commonwealth permitted AIDS research grant

recommendations to be made by the Task Force (Ballard in Dean and Hindress, 1998: 131).

On 5 February 1985, Australia's first safe-sex campaign, with the slogan '*Rubba Me*' was refused funding by the New South Wales Government. In addition, during February 1985, Professor David Cooper and colleagues from St Vincent's Hospital in Sydney were the first to describe seroconversion illness in *The Lancet*, which is associated with primary HIV infection. This finding has significantly influenced the early diagnosis and treatment of HIV infection throughout the world and remains a significant diagnostic marker (ANCARD, 1998: 24-25).

Despite calls for it to be abandoned and banned, including from Professor Pennington, the Sydney Gay Mardi Gras parade proceeded on the 23rd of February 1985. Consequently, a girls' school cancelled its swimming sports which were to be held in the same pool as the Mardi Gras swimming carnival. A report of the parade in the *Sydney Morning Herald* claimed HIV-positive spectators described themselves as 'elephant men' and was later the subject of a lengthy front page retraction and apology (ANCARD, 1998; Ballard in Kirp and Bayer, 1992). Despite the hysteria which still existed around this time, the public policy response continued with the establishment of the Albion Street Centre in Sydney as a major centre for HIV testing and counselling (ANCARD, 1998: 27).

Also as a result of Dr Blewett's visit to the United States and his determination that a similar epidemic should not occur in Australia, he directed resources to the HIV testing of blood and the heat treatment of Factor VIII and by April 1985, Australia was the first country in the world to secure its blood supply from HIV infection by screening all donors with questionnaires and antibody testing. There have been no reported cases of HIV transmission via blood or blood products since this time (ANCARD, 1998; Ballard, 1998).

Early 1985 saw an increase in the scientific interest in HIV with the publication of a study by John Ziegler and colleagues at the Prince of Wales Children's Hospital in Sydney documenting the first detection of transmission of HIV from mother to child via breast milk and a second study, enrolment of homosexually active men from sex on premises venues to document their sexual practices and to promote safe sexual activity by Petherbridge and Bennett (ANCARD, 1998: 28).

In April 1985 the first International Conference on AIDS opened in Atlanta, Georgia and in Australia, Dr Blewett made the first major parliamentary statement on

HIV/AIDS in the lead up to a meeting in May with his counterparts in the States and Territories. At this meeting, the Health Ministers endorsed a National Health Strategy for AIDS Control that placed a high emphasis on education, social and medical research. This Strategy remained in place for three years (ANCARD, 1998, Ballard in Kirp and Bayer, 1992). Also at this meeting, State Health Ministers agreed to match Commonwealth funding for the State and Territory programs, while the additional costs for AIDS care in hospitals would be incorporated into the Medicare Agreements. All jurisdictions, except Queensland, agreed to a shared funding arrangement of Community Based Organisations (CBO) which included AIDS Councils (Ballard in Dean and Hindress, 1998: 132-133). In Sydney, the *Ankali* project was established to provide emotional support for people with HIV/AIDS and their supporters (ANCARD, 1998: 30).

Australia also experienced a change in community hysteria. After being withdrawn from the school in response to protests from other parents, Eve van Grafhorst, an HIV-positive toddler living in Gosford on the New South Wales central coast, briefly returned to school on 4 September 1985. Eventually, she and her family left Australia to live in New Zealand after a long battle with parents and school authorities (ANCARD, 1998: 30).

On 17 November 1985, Australia's first National AIDS Conference began in Melbourne amid disputes between groups advocating the two response approaches, one for testing led primarily by the Albion Street Centre, and the second on peer education, led by the AIDS Councils. The State AIDS Councils, with funding assistance from the Commonwealth, formed a national peak body, the Australian Federation of AIDS Organisations (AFAO), which later included representatives of injecting drug users and sex workers, and elected Dr David Plummer as the inaugural President (ANCARD, 1998, Ballard in Kirp and Bayer, 1992).

In 1986 the Commonwealth established two new national centres. At the University of New South Wales, the NHMRC Special Unit in AIDS Epidemiology and Clinical Research was established. At the same time, the Commonwealth established the NHMRC Special Unit for AIDS Virology as a national centre for research linking facilities in five States. In 1990, following implementation of the first National HIV/AIDS Strategy, these centres were renamed as the National Centre for HIV Epidemiology and Clinical Research and the National Centre in HIV Virology Research respectively. The Centres have been subject to reviews in

subsequent years, all of which have resulted in recommendations for further funding (ANCARD, 1998: 34-35).

In February of the same year, the advocates for the divergent views of, on the one hand, a medically driven response, while on the other, the peer education model, developed a confrontational relationship when Professor Pennington criticised 'safe-sex' education as inadequate and instead proposed testing high-risk groups. AFAO responded by issuing its own guidelines emphasising confidentiality and peer education. This resulted in a number of public disagreements. To diffuse the increasingly political nature of the disagreement between the National Task Force and AFAO, Dr Blewett called a summit. This summit was not held until July, after the Second International Conference on AIDS in Paris which Professor Pennington attended. At the International Conference, it was agreed by the participants that a scientific response was not possible in the foreseeable future and that the only alternative available was for the resourcing of preventative education programs. Professor Pennington returned and urged Dr Blewett to develop campaigns warning the heterosexual population of the dangers of the epidemic. NACAIDS was tasked with the development of a National Education Program aimed beyond 'high risk' groups and into the general community (Altman in Timewell, Minichiello and Plummer, 1992; ANCARD, 1998; Ballard in Kirp and Bayer, 1992).

In October 1986, the tensions between the National AIDS Task Force and NACAIDS culminated at the second Australian National Conference in Sydney when disputes between Professor Pennington and Ms Buttrose over testing of the Indigenous population were publicly aired (Altman in Timewell, Minichiello and Plummer, 1992; ANCARD, 1998).

In February 1987, AZT, the drug that was first developed as a cancer treatment, began limited use in Australia for HIV (ANCARD, 1998: 37).

In response to the task assigned to them by Dr Blewett, NACAIDS released Australia's national AIDS education campaign in April 1987 with the controversial '*Grim Reaper*' television advertisement (ANCARD, 1998: 38).

One highly successful result of this media strategy was an increase in the funding available for HIV programs throughout the country which enabled a funding formula to be applied to each State and Territory's Financial Assistance Grants (FAG) based on population, number of AIDS cases and IV drug users. Additional funding was administered by a Commonwealth AIDS Research Grant Committee to education

programs through AFAO and the State and Territory AIDS Councils (Ballard in Dean and Hindress, 1998: 133-136).

While the Commonwealth had provided the initial leadership in policy development, the States and Territories by this time had developed programs of their own. To coordinate the public policy effort and financial arrangements throughout the nation, the Commonwealth, State and Territory governments established the Intergovernmental Committee on AIDS (IGCA) (Altman in Timewell, Minichiello and Plummer, 1992; ANCARD, 1998; Ballard in Kirp and Bayer, 1992).

Australia's innovative response to the AIDS epidemic was beginning to receive world-wide attention and in July 1987, Australia hosted a World Health Organisation (WHO) Inter-regional Ministerial Meeting on AIDS, attended by representatives of 29 countries from the Asia Pacific region. It issued the Sydney Declaration on AIDS (ANCARD, 1998: 40).

Also during 1987, the then Governor-General, Sir Ninian Stephen, established the AIDS Trust of Australia, the only national AIDS fund-raising charity and AZT was approved as a treatment for HIV with a cost sharing arrangement between the Commonwealth and States and Territories (ANCARD, 1998: 41). AZT was found, in 1987, not to be the only nucleoside analogue with potential against HIV. Two drugs in the same class and which work in the same way as AZT, dideoxycytidine (ddC) and dideoxyinosine (ddI), were trialled in 1988. By 1990, it appeared that both drugs would be as effective as AZT, possibly with a decrease in the side effects experienced by individuals. When using two of these drugs in combination, research discovered that it reduced the ability of the highly adaptive HIV developing resistance to either of the drugs (Carr in Timewell, Minichiello and Plummer, 1992: 9).

At the end of 1987, the Prisons Committee of the NACAIDS (chaired by Professor John Dwyer) issued the first comprehensive policy paper addressing HIV/AIDS in prisons. It advocated condom availability, voluntary testing and approved the segregation of prisoners with HIV/AIDS (ANCARD, 1998: 42).

Under the new international definition, officially adopted by Australia at the start of 1988, patients with HIV were considered as having AIDS if they contracted one of the typical opportunistic infections such as PCP, Kaposi's Sarcoma and others. These diseases are also known as 'AIDS-defining illnesses' (ANCARD, 1998: 43).

With the resignation of both Professor Pennington in 1987 and Ms Buttrose in 1988 from the National AIDS Task Force and the National Advisory Committee on

AIDS respectively, Dr Blewett seized the opportunity to restructure and rationalise the advisory system he had established. This he did, after seeking the approval of State and Territory Health Ministers, by consolidating both advisory bodies into the Australian National Council on AIDS (ANCA) which he announced on 28 March. The Council was chaired by Emeritus Professor Peter Karmel, a government advisor on education. The Council consisted of 15 members, seven medical and eight non-medical including some of the prominent participants from both the National AIDS Task Force and NACAIDS. ANCA became the principal Advisory body on all aspects of the HIV epidemic to the Commonwealth (Altman in Timewell, Minichiello and Plummer, 1992; ANCARD, 1998; Ballard in Kirp and Bayer, 1992).

In May 1988 despite the criticisms levelled at the '*Grim Reaper*' campaign, the Commonwealth began its second national awareness media strategy with the '*Beds and Feet*' media release, targeted primarily at young heterosexually active people. The first advertisement targeting Indigenous people appeared in conjunction with the '*Beds and Feet*' campaign and was called 'Condoman' (ANCARD, 1998: 45).

Combined responses/partnership approaches to the epidemic - Development of the First National Strategy.

On the 4th of August 1988 the third Australian National AIDS Conference was held in Hobart. The Federal Shadow Minister for Health, Mr Wilson Tuckey, delivered a paper in which he claimed 'AIDS isn't something you get; it's something you allow someone to give you' (ANCARD, 1998: 46). This represented a significant threat to the bipartisan political approach that the variety of stakeholders had sought to achieve over the preceding years. Mr Tuckey was removed from the Shadow portfolio of Health some weeks later (Altman in Timewell, Minichiello and Plummer, 1992; ANCARD, 1998; Ballard, 1998).

December in 1988 saw Australia participate in the first World AIDS Day, the formation of the Australasian Society for HIV Medicine and the policy discussion paper, *AIDS: a time to care, a time to act*, published. In order to facilitate discussion around the various aspects of the discussion document, Dr Blewett convened six panels to investigate their particular issues. The panels were: *Aboriginals, Torres Strait Islanders and HIV/AIDS* (chaired by Ms Bernadette Hudson); *Discrimination and Other Legal Issues-HIV/AIDS* (chaired by Professor Marcia Neave); *Education and Prevention-HIV/AIDS* (chaired by Professor Ron Penny); *Intravenous Drug Use*

and HIV/AIDS (chaired by Senator Peter Baume); *Testing for HIV/AIDS* (chaired by Senator Chris Puplick); and *Treatment, Services and Care-HIV/AIDS* (chaired by Ms Marilyn Beaumont). The panels held public discussions around the nation in early 1989 (ANCARD, 1998; Ballard in Kirp and Bayer, 1992).

In mid 1989, the six panels appointed to facilitate public discussion of the Green Paper *AIDS: A time to care, a time to act* published their reports (ANCARD, 1998: 47-49). The panel secretaries convened as a writing group to prepare the first draft of the strategy which was then reviewed by a steering committee comprised of the Secretary of the Commonwealth Department of Health, the Chairperson of ANCA, the Chairperson of IGCA and the Executive Director of AFAO. The penultimate draft of the Strategy was provided to State and Territories, and a National AIDS Forum convened at the same time as ANCA, for comment prior to its presentation to Cabinet (ANCARD, 1998; Ballard in Kirp and Bayer, 1992). Also during this period, a Melbourne hospital refused admission to HIV positive patients which sparked intense media interest on the risks of transmission of HIV to health care workers. This concern was aggressively taken up by Dr Bruce Shepherd, President of the NSW Australian Medical Association (Penny, 2003: 24).

Finally, after extensive consultations, the first National HIV/AIDS Strategy, *National HIV/AIDS Strategy – a policy information paper*, was released by Dr Blewett in August 1989. Some of the recommendations contained within the Strategy were perceived to be controversial including the decriminalisation of homosexuality and prostitution, condom provision in prisons and the mandatory testing of immigrants seeking permanent residence. What it also sought to do was to reaffirm the requirement for informed consent and confidentiality of testing, clearly at variance from popular medical opinion and, importantly, commit the Commonwealth to four years of funding, rising from \$42.5M in 1988/89 to \$93M in 1992/93. During the 1990's, the collaboration of government, researchers, clinicians and the infected and affected communities became known as the Australian HIV/AIDS Partnership (Altman in Timewell, Minichiello and Plummer, 1992; ANCARD, 1998; Ballard in Kirp and Bayer, 1992; Ballard, 1998).

The Strategy contained two goals: to eliminate transmission of HIV; and to minimise the personal and social impact of HIV infection. The Strategy also affirmed the principles of the *Ottawa Charter for Health Promotion, 1986* in the Australian

context and the government's social justice principles (Commonwealth of Australia, 1989; Feachem, 1995; WHO, 1986).

In September of 1989, the New South Wales Equal Opportunity Tribunal handed down a decision that in some cases medical treatment may be withheld if the HIV status of a patient is unknown. This decision differed significantly from the access and equity positions articulated by the Commonwealth at the time. The decision, however, was overturned by the same Tribunal in 1995 and in November of 1989, a Sydney doctor infected four women with HIV. A NSW Health Department inquiry found that this was a result of a failure to follow approved infection-control guidelines, resulting in the cross-infection of these women from an HIV-positive male patient who was treated by the doctor in the surgery on the same day. This was considered the first documented case of patient-to-patient HIV transmission (ANCARD, 1998: 50-52).

The 1990's

After the Labor Government was re-elected for a fourth term in 1990, a Cabinet reshuffle saw Dr Blewett appointed Minister for Trade Negotiations and Mr Brian Howe appointed as Minister for Health. Mr Howe set about reappointing the advisory bodies and restructuring ANCA with greater community representation, although it was agreed that the Committee would not be a representational one. One of the first decisions he made in the HIV area when assuming his portfolio responsibilities was to announce a review to examine delays in approval of new drugs and clinical trials (ANCARD, 1998: 53).

At the same time, IGCA started planning with the States and Territories around the issues of HIV in prisons and the development of school programs. Education among Australia's youth and indigenous communities also formed priorities for the Committee (Ballard, 1998: 12).

In August 1990, the delays in approval for drugs came to a head at the Fourth National AIDS Conference in Canberra, when people with AIDS and their supporters calling themselves ACT-UP, modelling themselves on the radical United States lobby group of the same name, demonstrated against Mr Howe. They demanded that the approval system be reformed to allow faster access to experimental drugs for people with AIDS. The Minister commissioned an enquiry by ANCA to examine the issue.

At the same time, AZT was approved for people with fewer than 500 T-cells in Australia (ANCARD, 1998; Timewell, Minichiello and Plummer, 1992).

Also in 1990, while traditional scientific interest in HIV continued to grow, so did the interest in social research. Consequently, the National Centre in HIV Social Research, based initially at the University of Queensland and with branches at the University of New South Wales and Macquarie University, was established. The Centre has been reviewed regularly since, resulting in recommendations for further funding. The same year saw the introduction of another Commonwealth education campaign targeted at intravenous drug users entitled '*Be Safe, Be Sure*' (ANCARD, 1998: 56).

In December 1990 ANCA, after completing the drug process evaluation, recommended sweeping changes to Australia's drug evaluation and import system, to speed affected community's access to new treatments. This report, *The Availability of HIV/AIDS Treatments* identified many matters raised in the subsequent Baume Report. During 1990, 1138 people were diagnosed with HIV infection, 801 were diagnosed with AIDS, and 515 died in Australia (ANCARD, 1998: 56).

The focus for 1991 was on the development of drug approval processes that better served the affected community, the development of effective peer education campaigns and the start of legislating to make unlawful discrimination on the basis of HIV/AIDS.

In March 1991, Professor Peter Baume, a former Liberal senator, was commissioned by the Commonwealth to undertake a review of Australia's system of pharmaceutical approvals and licensing following on from the recommendations made by ANCA and in July, the report, *A Question of Balance* was published recommending significant reform. The recommendations only provided for changes to the initial licensing process, not the Pharmaceutical Benefits Scheme (ANCARD, 1998: 58-59). In 1991 the AZT-ddC combination was the best available anti-HIV treatment option, being used by the majority of people with advanced HIV along with the release of results of promising anti-HIV treatments in the United States and Europe. ddC and ddL were approved for use in Australia in 1991 and 1992 respectively (ANCARD, 1998; Carr in Timewell, Minichiello and Plummer, 1992).

In the same year, the first comprehensive AIDS education policy entitled *AIDS Education: the next three years, 1991-1993* was released along with the first Commonwealth education campaign targeting gay and men who have sex with men

called '*That Feeling Doesn't Stop HIV-Safe Sex Does*'. This type of explicit targeted campaign was often opposed by conservatives but did not stop the discussion of sexual matters by the general public (ANCARD, 1998; Ballard, 1998).

In 1991, as a result of persistent lobbying by the Haemophilia Foundation and others, Western Australia was the first State to provide compensation to individuals with medically-acquired HIV. The other States and Territories eventually followed (Altman in Kirp and Bayer, 1992; ANCARD, 1998).

In August of 1991, the New South Wales Anti-Discrimination Board held an inquiry into HIV related discrimination. Its report entitled *Discrimination: the other epidemic*, clearly identified HIV related discrimination as a significant problem in Australia. As a result, a number of jurisdictions legislated against such discrimination. The ACT legislated to make it unlawful to discriminate on the grounds of HIV/AIDS in January 1992, Queensland in July of 1992, the Equal Opportunity Tribunal in South Australia in the case of a teacher found to have been illegally discriminated against because he was gay and HIV positive by the Department of Education in 1993, in March of 1993, the Commonwealth through its Disability Discrimination legislation, in August 1993 by the Northern Territory. Later in November 1993, Anti-gay vilification amendments to the New South Wales *Anti-Discrimination Act* were passed and came into effect on 1 March 1994 and *The Courage of our Convictions*, a report was published by the New South Wales Ministerial Review of HIV/AIDS Legal Working Party. This report examined all State and Territory laws in relation to the recommendations of the IGCA Legal Working Party report (ANCARD, 1998: 61-69).

In November 1992 the final report of the IGCA Legal Working Party was released calling for law reform in the areas of public health, civil liability, discrimination, homosexuality, prostitution, employment law, injecting drug use, therapeutic goods and broadcasting and censorship. Later that year, the evaluation report of the first National AIDS Strategy was released resulting in a fine tuning of the approaches and programs it used (ANCARD, 1998; Feachem, 1995).

In December of 1992, the University of Sydney notified students in the Faculties of Medicine, Nursing, Health Sciences and Dentistry that if they tested HIV positive they might not be permitted to complete their courses. This approach resulted in complaints to the New South Wales Anti-Discrimination Board which were resolved in 1996 with the publication of guidelines (ANCARD, 1998: 69).

In January 1993, The Commonwealth of Australia became the first government in the world to launch an HIV/AIDS-related discrimination campaign called '*HIV Doesn't Discriminate, People Do*'. This year also saw the release of a technical handbook for doctors called *Could it be AIDS?* which was distributed free to all general practitioners (ANCARD, 1998: 72-73).

In mid 1993, the NHMRC assumed responsibility for the Commonwealth AIDS Grants Research Program from ANCA and in October, the Commonwealth Minister for Health, Senator Graham Richardson, launched the second National HIV/AIDS Strategy, on which Australia's response was based until 1996 (ANCARD, 1998: 76). The Second Strategy helped the States and Territories in taking a more active role in planning and service delivery, thus lightening the burden of such activities on the Commonwealth. The Second National Strategy had four program areas on which implementation was guided. They were: the Education and Prevention Program, the Treatment and Care Program, the Research Program and the International Assistance and Cooperation Program (Commonwealth of Australia, 1993; Feachem, 1995). In December of 1994, Professor Richard Feachem was appointed as the evaluator of this National HIV/AIDS Strategy and in September 1995, delivered the report of the evaluation, *Valuing the Past... Investing in the Future*, to Prime Minister Keating. In all, he made 79 recommendations spanning the four Program areas and recommended the creation of one other, Legal and Ethical issues (ANCARD, 1998: 85-87).

Over the ensuing years, leading up to the review of the Second National Strategy by Feachem, the response to the epidemic consolidated. Of particular note was the growth in social research efforts in seeking to understand changes in behaviour and attitudes among high risk groups and in particular gay men who comprised 86% of those living with HIV (Ballard, 1998: 13).

In 1995 after conducting research on the less virulent strain of HIV-1 uncovered by Learmont, Nick Deacon and colleagues in the Macfarlane Burnet Centre for Medical Research in Melbourne demonstrated this was due to a deletion in the nef gene. This suggested the potential for a live attenuated vaccine and the possibility of targets for antiviral chemotherapy. The editorial board of the *Harvard Health Letter* voted this research as one of the top-10 medical research discoveries of the year (ANCARD, 1998: 88).

Changing of Government

In 1996, a major restructuring of the Commonwealth Department of Health occurred at the same time as a change of government. This was the first conservative coalition government in power since the start of the epidemic. The restructuring of the Department transferred many activities performed by the Commonwealth to the States and Territories in line with a Funder-Purchaser-Provider arrangement. This meant the diffusion of much of the work of the AIDS Branch within a National Centre for Disease Control which focussed, and continues to focus, on a wider range of public health issues (Ballard, in Dean and Hindress 1998: 137). Also a number of new anti-HIV drugs were licensed or subsidised for use in Australia such as 3TC (lamivudine) and Saquinavir (ANCARD, 1998: 91).

Between 7-12 July 1996, the eleventh International Conference on AIDS, perceived by many to be a pivotal turning point in the AIDS pandemic, was held in Vancouver, Canada (ANCARD, 1998: 92).

In October 1996, the Federal Court upheld a finding of the Human Rights and Equal Opportunity Tribunal on 29 June 1995 that it was unlawful for the Australian Defence Force to dismiss a soldier who tested HIV positive. This ruling was overturned by the Full Federal Court on appeal in January 1998 on the grounds that the 'inherent requirements' of employment in the Australian Defence Force includes a requirement to be available for combat-related deployment (ANCARD, 1998: 92).

In December 1996 the Commonwealth Minister for Health and Family Services in the new Liberal-National Coalition Government, Dr Michael Wooldridge, announced the National HIV/AIDS Strategy 1996-97 to 1998-99. Interestingly, since his resignation from the Federal Parliament, Dr Wooldridge was appointed as the Chair of the Ministerial Advisory Council. This strategy was an expanded one, taking into account diseases that intersected with HIV/AIDS such as hepatitis and sexually transmissible diseases. The new Australian National Council on AIDS and Related Diseases (ANCARD), the successor to ANCA, met for the first time with former Senator Chris Puplick as Chairperson. The membership reflected ANCARD's broadened responsibilities and included experts in Hepatitis C (ANCARD, 1998; Ballard, 1998).

Early in 1997 the Research Advisory Committee (successor to the Commonwealth AIDS Research Grants Committee) was absorbed back into

ANCARD from the National Health and Medical Research Council, in line with the recommendations made by Feachem (ANCARD, 1998: 95).

In recognition of its central role in treatment and care management and in particular with combination therapies, in February 1997, Dr Wooldridge announced interim funding arrangements that allowed free access to viral load testing for all Australians with HIV. Combination therapy usage had, by this time, already demonstrated a sharp correlative reduction in the AIDS death rate (ANCARD, 1998: 95).

In March 1997, *The National Indigenous Australians' Sexual Health Strategy 1996-97 to 1998-99* was endorsed by Dr Wooldridge, who agreed to fund its major, but not all, its recommendations (ANCARD, 1998: 97).

Of particular note for this thesis is that the first serious interest in vaccine research was heralded by the US President Bill Clinton in May, announcing that the development of a preventive vaccine for HIV will be a top national priority with similarities to the 1960s' space program (ANCARD, 1998: 97).

From 1 July 1997 the Public Health Partnership Memorandum of Understanding between the Commonwealth and States and Territories came into effect. These agreements outlined, broadly, the agreed performance measures and targets each jurisdiction was to report against for the duration of the Agreement. A separate Public Health Outcomes Partnership Agreement provided an overall allocation of funds to the jurisdictions to achieve these measures and targets without indicating a Specific Purpose Payment (SPP) for particular public health areas (Ballard, 1998; Commonwealth of Australia, 1999). It is the first time HIV/AIDS has no specific funding allocation.

In December 1997, Professor John Mills of the Macfarlane Burnet Centre for Medical Research in Melbourne was awarded one of only three major international grants (valued at A\$635,800) by the International AIDS Vaccine Initiative to continue his work on development of a DNA-based AIDS vaccine (ANCARD, 1998: 104). Currently, as I will outline in the next chapter, there are many international trials under way.

Since this time, the National strategy has been developed and reviewed twice more. The fifth National HIV/AIDS Strategy was launched by the then Minister for Health and Ageing, the Hon Tony Abbott on 17 June 2005 identifying five priority areas: the development of a targeted prevention education program for people at risk

of contracting HIV/AIDS; improving the health of people living with HIV/AIDS through treatments; better support services for people living with HIV/AIDS; and forming an annual research roundtable to direct research priorities (Australian Government, 2005: 1).

In late 2007, the Australian Labor Party, led by the Honourable Kevin Rudd, attained office. The Prime Minister, via the Council of Australian Governments (COAG) obtained agreement from the State and Territory Premiers and Chief Ministers to commence an ambitious rationalisation of the funding arrangements between the Commonwealth and the States and Territories which aims at a reduction in funding agreements from 92 Specific Purpose Payments (SPP) to just five or six (Australian Government, 2008: 3). This may result in the identified funding for the HIV response being absorbed into an overall health agreement which, in the absence of specific performance indicators, may significantly affect the response of the States and Territories to HIV.

The ways in which the affected community is involved in vaccine research both within Australia and in the United States is set out below.

Community involvement in HIV vaccine trials

Australia

The Australian HIV/AIDS Partnership, until June 2005, was a participant in HIV vaccine trialling with the successful acquisition by the University of New South Wales of a US National Institutes of Health (NIH) Grant in June 2000 to undertake research into a prime-boost vaccine model (NIH, 2000). The Australian consortium subcontracted with the University of New South Wales to undertake the work. The consortium, led by Professor David Cooper, Director of the National Centre for HIV Epidemiology and Clinical Research (NCHECR) at the University of New South Wales had as members several academic research centres (including the University of Melbourne and the Australian National University, Commonwealth Scientific and Industrial Research Organization (CSIRO)), social researchers (National Centre in HIV Social Research (NCHSR), community represented by the Australian Federation of AIDS Organisations (AFAO) and a biotechnology company (Virax Immunotherapeutics Inc.). These organisations were represented on a Program

Management Committee that acted as a Board of Directors to oversee the vaccine development program.

As I have indicated, AFAO is the peak national non-government organisation “representing Australia’s community-based response to HIV/AIDS”. AFAO’s membership is comprised of the State and Territory AIDS Councils, the Australian Injecting and Illicit Drug Users League Inc (AIVL), the National Association of People Living with HIV/AIDS (NAPWA), and Scarlet Alliance which is the national association for sex workers and, most recently, Anwernekenhe, a national indigenous HIV alliance. AFAO’s governance structures include the election, by the membership represented by two voting delegates, of a Board of Directors to govern the organisation and oversee its activities. The Board is comprised of a President, Vice President, Secretary, Treasurer, Ordinary Member, NAPWA representative, AIVL representative, Scarlet Alliance representative, the Executive Director (ex officio), and a Staff representative. AFAO is represented on the Program Management Committee by the Executive Director of AFAO and/or the Manager, Policy and International team. AFAO also has Policy Reference Groups (PRG) which assist the organisation to formulate policy positions and has members from constituent organisations with expertise/interest in a particular area, in this case HIV vaccines, to assist the Board in formulating a position (AFAO, 2004).

The two voting members who elect the AFAO Board are Board members themselves of their constituent organisations. The Annual General Meeting, like all such meetings, discusses and votes on resolutions and provides direction to the Board of AFAO (www.afao.org.au).

The Policy and International Team of AFAO has a key role in ensuring “informed volunteer participation and comprehensive community education about the program and vaccine development generally” (AFAO 2004: 14).

Therefore, the governance structures of AFAO facilitate the involvement of grass roots affected community in both the decision making process and the broad strategic issues of vaccine trialling. In addition, the PRG gives practical support and advice to the staff of the Policy and International Team in their development of informed consent processes and educational resources for the trial participants and the affected community more generally.

The ways in which AFAO participates on the consortium is poorly documented and largely confidential as both the representative on the consortium and the AFAO

Vaccines Policy Reference Group have been required to sign confidentiality agreements for commercial reasons.

Because commercial-in-confidence agreements exist and limit how I am able to observe the affected community's participation in the consortium, my research approach is to interview the consortium members and extract information about the affected community's involvement from the informants' perspective. This research is important because, as I have described, the Australian Consortium is unique in the way in which it has been constructed to incorporate affected community as a full partner and because affected community are not involved in the same way in the US, for example. It is worth noting here that similar commercial-in-confidence agreements exist in other trials which also prevent detailed analysis and examination of vaccine trial methods and practices.

United States

The HIV Vaccine Trials Network (HVTN) is an international collaboration of scientists, formed in 1999 by the US National Institute of Allergy and Infectious Diseases (NIAID) and the National Institutes of Health (NIH), whose goal is to accelerate the development and testing of HIV vaccine candidates and who views itself as a hybrid organisation with a structure resembling that of a commercial vaccine company (HVTN, 2001: 1).

The HVTN is organised in a 'hub and spoke' format whereby the investigators are at the 'hub' where protocols and vaccine design concepts are developed and HIV Vaccine Trial Units (HVTU), the sites at which vaccines are trialled, are the 'spokes'. In each of the sites, a Community Advisory Board exists to provide community input into study design and local procedures. This varies from the consensus Australian approach as the AFAO representatives are an equal partner in the consortium and are able to veto decisions on such matters. It is unclear from the documentation what impetus, apart from an ethical one, the Community Advisory Boards bring to the process. Theoretically, Community Advisory Boards may express serious concerns about a trial design but there is no capacity to influence the design directly. Rather, the Community Advisory Boards would need to rely on vocal community opposition that mobilises public support.

The Community Advisory Boards are a mix of local study participant representatives, professionals with training in clinical trialling, community activists and services delivering HIV services. The role of the Community Advisory Board is:

- *to assist in the planning, development, and implementation of the research;*
- *to assess community impact and make sure community concerns are considered;*
- *and to serve as a voice for the community and study participants.*

(<http://www.hvtn.org/community/cab.sht>)

Another role of the Community Advisory Board is to assist in the preparation and education of the community within which the trial will be conducted. This means that community educators are present at each site to help community members understand the science around HIV vaccine development in addition to the clinical trial processes. Conversely, these educators help researchers appreciate the historical, cultural, social and political issues associated with the community.

Conclusion

This chapter provides a brief overview of how the emergence of HIV/AIDS in Australia shaped the public policy response to include affected community as partners in that approach. My account would be widely accepted in Australia. There may be some room for difference of opinion over the details and personalities, but that is not relevant here. The key point of this chapter is to describe the social practices of the affected community and the evolution of the Australian HIV/AIDS Partnership.

What was to be known as the Australian HIV/AIDS Partnership prevailed despite a highly contentious and politicised environment both within the general community, the medical profession and conservative governments throughout Australia. This tradition has continued to the present and explains why affected community was, almost automatically, involved as a full partner in the Australian HIV Vaccine Consortium.

The next chapter explores the complexity of HIV itself, the approaches to vaccine development and the ways in which it is trialled.

2

Scientific Background

In order to understand the complexity of the task before preventative HIV vaccine researchers and the challenges they face in finding a cure for this disease, a brief explanation of the science of HIV will provide a context for those challenges will be useful.

An understanding of the science of HIV and HIV vaccine development is also important for affected community representatives to understand in order that they can effectively advocate on behalf of the community they represent. As I have outlined in chapter 1, because affected community in Australia has been a part of the public policy response to HIV from the beginning, their involvement in HIV vaccine development in Australia is, while unique, not surprising in that context. In order to be effective participants in the vaccine development and trialling process, however, affected community representatives have needed to learn and understand the complex science involved in this undertaking. This chapter gives an outline of what the community representatives needed to come to grips with as part of the consortium.

Pathophysiology of HIV

The Acquired Immune Deficiency Syndrome (AIDS) is defined as “an illness characterised by one or more indicator diseases...” and “if there is laboratory evidence of HIV infection...” (Adler, 2001:1226). The average time from HIV infection to the development of AIDS is eight to ten years but a small number of people (around 5 – 10%) have been characterised as long-term nonprogressors (Hogan and Hammer, 2001: 761).

HIV is a double-stranded ribonucleic acid (RNA) virus. Retroviruses tend to undergo rapid genetic mutation, referred to as the mutability of a virus. When the virus replicates, this mutability causes mistakes in the copying of the base-pairs within the virus. These mistakes accumulate at each replication which results in mutation of the virus. The virus is not only highly mutable, but replicates rapidly which results in a greater mutation rate. These changes predominantly manifest themselves in changes to the surface proteins on the viral surface. There are several distinct proteins found in HIV. Of significance to the development of HIV vaccines is the gp 160 protein which consists of two other proteins, gp 120 and gp 41. Slight variations to these proteins will prevent human antibodies from recognising them. The mutation has resulted in distinct subtypes or clades which may differ from each other by as much as 25%. Clades appear to predominate in particular geographic

locations. This means that a vaccine developed for one clade may not be effective against other clades. In addition, viral DNA becomes a part of the hosts DNA which makes it virtually undetectable to the immune system (Klein and Ho, 2000: 299-303).

The immune system in humans works in two ways to prevent infection from viral agents. These two methods are called humoral and cellular immunity. Humoral immunity involves the immune system making antibodies which is a protein in the blood that is produced to neutralise infectious agents or antigens (like viruses) that exist in the plasma of the blood. Humoral immunity refers to the production by B cells of highly specific antibodies for unique antigens and is designed to prevent the infection of host cells by circulating virus (Klein and Ho, 2000; ICASO, 2003). Cellular immunity or cell-mediated immunity involves the body mobilising lymphocytes (white blood cells) to kill other infected cells (Snow, 1999, ICASO, 2003). Cell-mediated immunity occurs with two types of lymphocyte, CD4+ and CD8+. CD4+ cells, often referred to as T-helper cells, regulate the immune function of the body by mobilising nonspecific immune cells to the infection site, stimulate antibody production by B cells and augment the response of CD8+ cells. CD8+ cells, often referred to as cytotoxic T cells, destroy infected cells and release antiviral cytokines, an immunity enabling chemical. HIV targets the human immune system so for an HIV vaccine to be effective, it is hypothesised that it must activate both humoral and cell-mediated immunity (Klein and Ho, 2000: 298-299).

Approaches to Vaccine development

In May 2000, the United States National Institute of Allergy and Infectious Diseases (NIAID) published a status report on the development of HIV vaccines. The report stated that “over 60 phase I/II trials of 30 candidate vaccines have been conducted worldwide” (www.niaid.nih.gov/daids/vaccine/whsummarystatus.htm:01). Current vaccine trials in various phases are contained in Table 2. Grady (1995:12) suggests that there are essentially two types of vaccines; live vaccines or inactivated vaccines. This broad approach can be further refined into six categories; recombinant subunit protein vaccines, whole inactivated HIV vaccines, live attenuated vaccines, live vector vaccines, DNA vaccines and combination vaccines (Dale and Kent, 2000; ICASO, 2003).

After HIV was isolated in the mid 1980's, the first vaccine types to be studied were the subunit protein and whole inactivated HIV vaccines (Dale and Kent, 2000;

NIAID, 2000). This approach was seen as the most logical one since it is that envelope or surface protein which is the target for antibodies in HIV infected individuals and the approach was used with great success in Hepatitis B surface protein vaccines (Dale and Kent, 2000; NIAID, 2000). Most of this attention focussed on the so called gp120 envelope rather than the gp140/160 envelope since the gp140/160 forms were more difficult to produce and had no clear advantage over the gp120 form. These subunit protein envelopes were also specific to clade B isolates of HIV. There are two main genetic variants of HIV, HIV-1 and HIV-II. HIV-I is the variant responsible for the majority of HIV infection throughout the world. As I have stated, clades are different sub-types of HIV-I and are often characteristic to particular geographical regions. For example, clade B is mainly found in Australia, Western Europe and the USA, clades A and C are found mainly in Africa, and E and C are found mainly in Asia (AFAO, 2000; NIH, 2000). Phase III trials of this type of vaccine are underway in the United States and Thailand (Dale and Kent, 2000: 2).

Whole inactivated viruses were among the first to be reported to prevent Simian Immunodeficiency Virus (SIV) infection in macaque monkeys. This type of vaccine uses the whole virus but with the disease causing agent killed with chemicals or heat. Ultimately, these simian models were found not to be effective. One of the first pioneers of this type of method in HIV vaccine research was Dr Jonas Salk, the polio vaccine pioneer. In 1990, Dr Salk's team proposed injecting people with killed HIV, stripped of its outer protein coat. Recently, alternative methods of deactivation of HIV while preserving the external proteins have produced immune responses (Altman, 1990; Dale and Kent, 2000; ICASO, 2003).

Live attenuated (weakened) vaccines have been highly successful in other infectious diseases. Currently, however, no candidate HIV vaccines using this method have been shown to be completely safe in animal modelling. Exploration of this type of vaccine was further encouraged by the discovery of a 'non-pathogenic' strain of HIV-1 in a Sydney blood bank cohort. This strain was found to contain deletions in the *nef* gene and U3 region of the HIV molecule. Other types of deletions are being developed. This approach continues to show promise for HIV protective immunity (Corey, 1999; Dale and Kent, 2000).

Live vector vaccines (a vaccine that utilises another mechanism like a non-harming virus to insert a foreign gene or DNA fragment into a host) and DNA

vaccines are believed to be among the most promising approaches in preventing HIV. The live vector approach enables the inserted gene or DNA fragment to express HIV-I antigens, thus producing an antibody response from the host. Among the first of these types of vectors described was in 1988 of the smallpox virus. This approach has been modified since to attenuated poxviruses such as canarypoxvirus, fowlpoxviruses and modified vaccinia Ankara since smallpox virus may have undesirable consequences for individuals with impaired immune systems (Corey, 1999; Dale and Kent, 2000).

DNA vaccines were first raised as an alternative in the early 1990's and have been suggested as a cheap and effective vaccine approach. They are "generally relatively simple to design, construct and manufacture" (Dale and Kent, 2000: 5). Early DNA vaccine models were poorly immunogenic, that is, evoked a poor immune response. DNA vaccines work by injecting 'naked' plasmids of DNA into a host which elicits a cell mediated immune response. A plasmid is "any extrachromosomal self-replicating genetic element of a cell" (Miller and Keane, 1983: 882).

Attention most recently has turned toward developing a combination 'prime-boost' vaccine. The host's cytotoxic lymphocytes are initially 'primed' into a cell mediated immune response by a DNA vaccine and 'boosted' by introduction of an attenuated poxvirus-HIV vaccine. This approach, while initially highly promising, has failed to yield the expected results (Corey, 1999; Dale and Kent, 2000; NIAID, 2000; AFAO, 2004). Australia was a participant in this type of research and successfully competed for highly contested research funding through the US National Institutes of Health (AFAO, 2000: 1). A summary of the vaccine approach, advantages, disadvantages and the status of development of these types of vaccines is seen at Table 1.

Table 1 Vaccine Approaches

Vaccine Examples	Typical example	Advantages	Disadvantages	Status
Protein vaccine	Subunit envelope protein	Safe	Limited efficacy in animal models	Phase III trials started
Whole inactivated viruses	Inactivated HIV	Commonly successful for other pathogens	Inactivation must be complete. Limited efficacy to date	Novel interaction methods being assessed in animal models

Live attenuated vaccines	Nef-deleted HIV-I strains	Good efficacy in animal models	Unsafe to date	Safer versions being constructed and assessed in animal models
Live vector vaccines	Attenuated poxviruses	Safe; some induction of cellular immunity	Immunity to the vector may be limiting	Extensively assessed in Phase I/II trials
DNA vaccines	HIV-I <i>env-rev</i> HIV-I <i>gag-pol</i>	Safe to date Simple to engineer	Early versions have limited immunogenicity alone	Phase I/II trials underway

(Dale and Kent, 2000: 2)

The way the different approaches will be tested is through a three phase clinical trial protocol which is the universal means of testing such products internationally.

Clinical Trialling

Phases

Prior to clinical trialling in humans, experimental products are tested extensively in the laboratory and on animals to minimise the risk of serious toxicity and to establish a degree of efficacy in a living being. In other words, the potential vaccine must be relatively safe and there must be a demonstrated immune response against HIV in animal studies (Kerns, 1997; Haire and Murphy, 2001).

Phase I trials involve small numbers of people, normally 50-80 participants, who are healthy. In HIV vaccine trials, there is some debate about whether these participants should come from high risk groups or not. The primary purpose of phase I trialling is to determine the safety of the vaccine in a human population, so there is no scientific reason to include participants from high risk groups at this stage of the trialling process (Kerns, 1997; Haire, 2001; Haire and Murphy, 2001).

Sometimes phase I and phase II are joined together. Phase II trialling is concerned with the immunogenicity of the potential vaccine. In other words, this phase considers proper dosage regimes and the level of immune response of the potential vaccine anticipated from pre-clinical studies. This phase normally involves a larger population and may last for approximately two years before the promising

vaccine candidate progresses to phase III trialling (Haire and Murphy, 2001; Kerns, 1997).

An ‘intermediate’ step has emerged in the HIV vaccine field in the recent years. It is called a Phase IIb or ‘proof of concept’ trial. Phase IIb trials have a larger number of participants than standard Phase II trials but significantly fewer participants than Phase III trials. These trials are designed to gather information on the efficacy of a potential vaccine candidate without the costs associated with larger Phase III trials. Of course, with fewer participants, the range of uncertainty, or confidence intervals, around the estimate of a vaccines efficacy will be much greater. For example, most Phase III trials have confidence intervals of + or – 15% which means that the actual efficacy value of the potential candidate falls across a span of 30%. In a Phase IIb trial, the confidence interval is + or – 30% generating a 60% span. Cost in both human and financial terms in conducting large Phase III trials is a significant factor in the use of IIb trials. The financial costs alone, running into the millions of dollars is prohibitive, however, the costs in human terms (identifying a sufficiently large pool of people to test the product on and the risks of infection associated with trial participation) are also real (Bass, 2004: 1-5).

Phase III trialling, often called efficacy trials, are large scale trials involving thousands of people from high risk populations to determine whether or not a vaccine prevents the incidence of HIV or not. It is likely that this phase of trialling will last approximately 4 years. This depends, to some extent, on what criteria are used to measure the success of the potential vaccine (Haire and Murphy, 2001; Kearns, 1997).

A summary of current preventative HIV vaccine clinical trials is at table 2 below.

Table 2 AIDS Vaccines candidates in clinical trials (2008)

Protein Prime + Vector Boost	Phase III
Canarypox Clades B, E, gp120 prime	US Department of Defense, Ministry of Public Health Thailand, National Institute of Allergy and Infectious Diseases, Thai AIDS Vaccine Evaluation Group, sanofi pasteur, VaxGen

DNA Vectors +/- Vector Boost	Phase I/II
Clade B'C + Electroporation	International AIDS Vaccine Initiative, Ichor, Aaron Diamond AIDS Research Center
DNA polyepitopic, MVA boost	Epimmune Pharmexa, Bavarian Nordic
Clade B, MVA boost	GeoVax, US Military HIV Research Program
Multiclade A, B, C, Ad-5 boost	National Institute of Allergy and Infectious Diseases
Multiclade A, B, C, MVA boost	Karolinska Institute
Clade B'C, MVA boost	Johns Hopkins University, Guangxi, Changchun Baike
Clade C, NYVAC boost	EuroVacc, Agence national de recherches sur le sida et le hépatites virales
Clade B + IL-12, IL-15, peptide boost	Wyeth
DNA Clade C, MVA boost	South African AIDS Vaccine Initiative
DNA Clade A, E, FPV boost	The HIV Netherlands Australia Thailand Research Collaboration
Pennvax-B	University of Pennsylvania, VGX Pharmaceuticals
Viral Vectors	Phase I/II
<i>Adenovirus</i>	
Ad-6 Clade B	Merck
Ad-35 Clade A, +/- Ad-5 (prime or boost)	National Institute of Allergy and Infectious Diseases, Vaccine Research Center
Ad-26 Clade A	National Institute of Allergy and Infectious Diseases, Harvard University
<i>Pox</i>	
ALVAC-HIV	National Institute of Allergy and Infectious Diseases, sanofi pasteur
MVA Clade A, E	Walter Reed Army Institute of Research

MVA multiantigen	Bavarian Nordic
MVA Clade C	International AIDS Vaccine Initiative
Vaccinia multiclade (DNA & protein cocktail)	St. Jude Children's Research Hospital
Proteins	Phase I/II
Gp140 Clade C <i>mucosal</i>	St. George's, University of London
C-terminal p17, full p24, fragment of gp41 with polyoxidoonium adjuvant	Institute of Immunology, Moscow
Adjuvanted Gag, Pol and Nef	GlaxoSmithKline

(IAVI, 2008: 7)

The protocol for the Australian Consortium is below at Table 3.

Table 3 Protocol No. HVDDT-N01-AI-05395 Synopsis

Title	A Randomised, Placebo-Controlled, Double-Blind I/IIa Clinical Trial to Evaluate the Safety and Immunogenicity of a Candidate Prophylactic DNA Prime-rFPV Boost HIV Vaccine Strategy
Objective	To assess the safety and immunogenicity of a candidate prophylactic human immunodeficiency virus (HIV) vaccine strategy in non HIV-infected individuals
Design	A randomised, double-blind, placebo-controlled 52-week study <ul style="list-style-type: none"> • Arm A - prime with 1.0mg DNA IM at week 0 and 4 <ul style="list-style-type: none"> - boost with 5×10^7 pfu/mL rFPV IM at week 8 • Arm B - prime with diluent only (placebo) IM at week 0 and 4 <ul style="list-style-type: none"> - boost with diluent only (placebo) IM at week 8
Summary of Patients	Adult volunteers will be included who are at low risk of HIV infection of either sex aged between 18 and 55 years. Women

	<p>of reproductive potential must have a negative pregnancy test. Volunteers must have normal laboratory values and provide written informed consent.</p>
Study Numbers	<p>24 volunteers with 18 randomised to receive the candidate vaccine (arm A) and 6 randomised to the placebo vaccines (arm B).</p> <p>After the first 8 volunteers have been enrolled, vaccination of volunteers will be suspended until after the first 8 volunteers have received their rFPV vaccination. The DSMB will then carry out an assessment of major unanticipated safety events. If this assessment is satisfactory, randomisation will recommence.</p>
Study Agent	<p>Naked DNA and non-replicating, recombinant fowlpox virus each encoding HIV antigens. Both vaccines will be delivered by intramuscular injection.</p>
Study Procedure	<p>Eligible patient will be randomised to one of two study arms:</p> <p>Arm A - prime with DNA encoding HIV-1 gag-pol administered intramuscularly on day 1 and at week 4, followed by a boost with rFPV encoding HIV-1 gag-pol administered intramuscularly at week 8.</p> <p>Arm B - prime with diluent only (placebo) administered intramuscularly at week 0 and 4, followed by a boost with diluent only (placebo) administered intramuscularly at week 8</p> <p>Participants will be assessed for safety at 8 assessment points during the study duration of 52 weeks: at weeks -8/-4 (screening), 0 (baseline), 4, 8, 9, 12, 24 and 52. Assessments will include a clinical evaluation (including medical history/recording of adverse events, physical examination, haematology, clinical chemistry, HIV virology, and T-cell enumeration), as well as urine dipstick for protein excretion, urine pregnancy testing and HIV pre and post-test counselling.</p>

	Immunogenicity assessments will be carried out at weeks 0 (baseline), 8, 9, 12 and 24 and will include, lymphoproliferative assays (LPA), enzyme linked immunospot (ELISpot) assays for interferon-gamma (IFN- γ) producing cells, intracellular cytokine staining of IFN- γ /CD69 (ICCS) + flow-cytometric analysis, ⁵¹ Cr release cytotoxic T-lymphocyte (CTL) assays and human leukocyte antigen (HLA) class 1 matched tetramer analyses.
Statistical analysis	The primary safety analysis will be made between active group and the control

(University of New South Wales, 2000)

Conclusion

What I have demonstrated in this chapter is that HIV is a highly complex organism with many confounding characteristic that effectively inhibits the development of an effective and simple HIV vaccine. I have provided a brief description of the various types of vaccines currently under development and a brief overview of the various phases of the clinical trial process from safety through immunogenicity to efficacy testing. The affected community representatives needed to understand all of this in order to participate effectively in the consortium. Knowledge of the scientific background all has influence on the way in which affected community representatives can advocate on behalf of the community they represent, in particular in relation to the consent processes of a trial. Now that I have set out the scientific context, I move on to describe the ethical context in the next chapter. I describe the ethical issues and ethical guidelines the community representatives had to familiarise themselves with in order to participate effectively on the consortium and in order to advocate effectively for the affected community.

3

General Ethical Principles

The affected community also needed to familiarise themselves with relevant ethical issues and guidelines so that they might participate effectively on the consortium as a full partner, and so that they might advocate effectively for the affected community on the consortium.

Since the end of World War II, increasing attention has focused on the rights of participants in biomedical clinical trials (Commonwealth of Australia 1999: 1). From 1947 with the introduction of *The Nuremberg Code* (Kerns, 1997:218) through to the review of the *Declaration of Helsinki 1964*, a variety of international ethical instruments have been developed to provide guidance to researchers about their obligations toward research participants enrolled in research trials. I use the term instruments because they are more than voluntary guidelines to be given cursory acknowledgement. They have some sanctions attached to their breaches. These instruments, apart from some notable exceptions which I will discuss in the next chapter, do not raise the notion of community involvement in research. What they do clearly indicate are the key ethical principles that the community representatives had to be aware of and understand.

In addition to the international ethical instruments, Australia has also developed guidelines governing the conduct of research involving humans. The *National Health and Medical Research Council Act 1992* provides for the development of a *Statement on Human Experimentation* for “the protection of the welfare and the rights of participants in research” by the National Health and Medical Research Council (NHMRC). The NHMRC has the statutory authority under its Act to demand the establishment of Human Research Ethics Committees (HREC) to undertake a review of all health related research by the organisation proposing the research (Commonwealth of Australia 1999: 3). The NHMRC in conjunction with the Australian Research Council (ARC) and the Australian Vice-Chancellors’ Committee (AVCC) recently reviewed the statement in 2007 (Australian Government, 2007).

Both the international instruments and, because the type of research that is the subject of my thesis is being conducted in Australia, the Australian National Statement on ethical conduct in human research, were important documents for members of the consortium to understand. These instruments, in addition to the general ethical principles of autonomy, beneficence and justice, provided the

framework around which the consortium members sought to reach mutual agreement in relation to the conduct of the trial. The affected community representatives also had to be aware that the guidance documents are constantly being reviewed and modified which shows that the ethical issues they attempt to articulate are not fully resolved. The representatives had to be prepared for some ambiguity and difference of opinion about how to interpret and apply these guidelines in their particular context. The instruments may be case in fairly black and white terms, but cannot always be used that way.

I will briefly set out the contents of the main international and national instruments, then discuss the fundamental ethical principles of respect for persons, beneficence and justice.

The Nuremberg Code 1947

The Nuremberg War Crimes Tribunal uncovered a number of human experimentation issues arising from the experimental treatment of concentration camp prisoners by Nazi doctors during World War II. This led to the development of the *Nuremberg Code* in 1947 to govern medical research involving human subjects and has significantly influenced the subsequent development of codes of ethics (Commonwealth of Australia, 1999; Grady, 1995; Kerns, 1997).

There are ten fundamental principles dealt with by the Code. A summary of those principles is that:

- consent must be voluntary;
- the research should be for the good of society but not random or unnecessary and the knowledge must be unable to be obtained by other means;
- a knowledge of the ‘natural history’ should be obtained through animal experimentation so that anticipated results will justify the experiment;
- there should be an avoidance of all unnecessary physical or mental suffering and injury;
- experiments should not be conducted if there is reason to believe that death or disability will occur except where investigating physicians are also research participants;
- the level of risk should not exceed the humanitarian importance of the problem;

- adequate attempts should be made to ensure injury, disability or death do not result from the experiment;
- research should only be conducted by scientifically qualified persons;
- there must be the capacity for the participant to terminate the experiment; and
- the scientist must terminate the experiment if injury, disability or death is a likely outcome if it is continued

(Kerns 1997: 218-219).

This foundation document helped form the basis for subsequent guidelines on the obligations of researchers in human clinical trials. The Code did not explicitly address the issue of subject or community participation in research and, indeed, Seidelman states there remains an unanswered moral question around the exercise of professional power and its impact on vulnerable people seeking medical care during research (1996: 1463). Some of the issues either not addressed or rejected in the Nuremberg Code were taken up by the Helsinki Declaration. Those issues include the inclusion of therapeutic research into the guidelines and the issue of participation of people who otherwise may be ethically problematic to include such as prisoners, members of vulnerable populations and “all those who feel that they might bear a cost by refusing” to participate in research (Leaning, 1996: 1413-1415). Prisoners may be problematic in terms of being unable to extract themselves from their environment and feeling compelled to participate to avoid retribution. Vulnerable populations may be problematic as some participants may believe services provided to them will be withdrawn if they do not participate or they do not have the capacity to provide fully informed consent. I will address the issue of informed consent later in this chapter.

The next iteration developed, with the *Nuremberg Code 1947* as its foundation, was the *Declaration of Helsinki 1964*. Over the course of its existence, the Declaration has undergone a number of revisions and ratifications.

Declaration of Helsinki 1964

The World Medical Association (WMA) drafted *the Declaration of Helsinki* in 1964. This document was subsequently amended in 1975, 1983, 1989, 1996, 2000, 2002 and 2004 by the WMA and most recently in 2008. The fundamental principles of the Declaration are similar to those of the foundation document for all such research ethics codes, the *Nuremberg Code 1947*. However, there are some significant differences between the two documents, which warrant further discussion.

Key aspects of the current Declaration include:

- the right to informed consent for participants;
- that the benefits of the research must outweigh the risks involved in the research;
- the provision of best current prophylactic, diagnostic and therapeutic methods to research participants;

'Best' proven diagnostic and therapeutic method refers to the current best practice standard of medical diagnosis and treatment, commonly encountered in resource rich countries. It is also referred to as the 'standard of care'. The debate around this issue will be discussed in greater detail in the next chapter. The other significant difference between the Code and the Declaration is the following aspect:

- that the interest of science and society never takes precedence over considerations relating to the well-being of the participant, including stopping the research if it may be harmful to the individual.

Another set of guidelines which have not been exclusively developed by researchers, are the *International Ethical Guidelines for Biomedical Research Involving Human Subjects 1993* developed by the Council for International Organizations of Medical Science (CIOMS) of which I will now provide some brief focus.

International Ethical Guidelines for Biomedical Research Involving Human Subjects 1993

In 1949, CIOMS was established as an international, not-for-profit, non-government organisation by the World Health Organization (WHO) and the United Nations Educational, Scientific and Cultural Organization (UNESCO) and in 2001, CIOMS had 51 international member organisations and 16 national members which represented a large proportion of the biomedical scientific community. Its main objectives are to:

- *facilitate and promote international activities in the field of biomedical sciences, especially when the participation of several international associations and national institutions is deemed necessary;*

- *maintain collaborative relations with the United Nations and its specialized agencies, in particular with WHO and UNESCO;*
- *serve the scientific interests of the international biomedical community in general.*

(http://www.cioms.ch/what_is_cioms.htm)

The following 15 guidelines were developed and ratified in 1993 and covered:

1. Individual informed consent;
2. Essential information for prospective research subjects;
3. Obligations of investigators regarding informed consent;
4. Inducement to participate;
5. Research involving children;
6. Research involving persons with mental or behavioural disorders;
7. Research involving prisoners;
8. Research involving subjects in underdeveloped communities;
9. Informed consent in epidemiological studies;
10. Equitable distribution of burdens and benefits;
11. Selection of pregnant or nursing (breastfeeding) women as research subjects;
12. Safeguarding confidentiality;
13. Right of subjects to compensation;
14. Constitution and responsibilities of ethical review committees; and
15. Obligations of sponsoring and host countries.

(Kerns, 1997: 220-224)

The current guidelines are outlined below; however, I do not intend to discuss these guidelines in great detail since they are provided as background to the issue of community participation/partnership in research. Novel additions that relate to the issue of participation by individuals and community in biomedical research will be explored later in the section on community involvement in trials. The guidelines fall into the following categories:

1. Ethical justification and scientific validity of biomedical research involving human beings
2. Ethical review committees

3. Ethical review of externally sponsored research
4. Individual informed consent
5. Obtaining informed consent: Essential information for prospective research subjects
6. Obtaining informed consent: Obligations of sponsors and investigators
7. Inducement to participate
8. Benefits and risks of study participation
9. Special limitations on risk when research involves individuals who are not capable of giving informed consent
10. Research in populations and communities with limited resources
11. Choice of control in clinical trials
12. Equitable distribution of burdens and benefits in the selection of groups of subjects in research
13. Research involving vulnerable persons
14. Research involving children
15. Research involving individuals who by reason of mental or behavioural disorders are not capable of giving adequately informed consent
16. Women as research subjects
17. Pregnant women as research participants
18. Safeguarding confidentiality
19. Right of injured subjects to treatment and compensation
20. Strengthening capacity for ethical and scientific review and biomedical research
21. Ethical obligation of external sponsors to provide health-care services
(http://www.cioms.ch/frame_guidelines_nov_2002.htm)

What I have discussed this far is the three primary but general international research ethics guidance documents that provide some direction to researchers in all fields of the biomedical research endeavour. Of particular relevance to Australian researchers is the National Statement published by the Commonwealth of Australia. This will be the focus of the next section of my discussion.

National Statement on Ethical Conduct in Research Involving Humans 1999; National Statement on Ethical Conduct in Human Research 2007

As I have stated above, in the Australian context, the Commonwealth of Australia has published its own set of guidelines for the conduct of research on human participants.

In 2007, the joint NHMRC, ARC and AVCC review of the *National Statement on Ethical Conduct in Research Involving Humans* resulted in the publication of the *National Statement on Ethical Conduct in Human Research*. The original statement, the *National Statement on Ethical Conduct in Research Involving Humans*, required that the protocols espoused within the Statement conform to the Declaration of Helsinki, rather than the CIOMS guidelines. Unfortunately, like the Helsinki Declaration, the National Statement does not address the participation of communities in any meaningful sense.

I do not intend to outline, point by point, the issues involved with this document. Rather, I will provide a brief indication of the scope and basic principles of the National Statement document. I will briefly outline both the 1999 Statement that applied when the consortium was conducting its research and the revised 2007 Statement to reflect the current guidance from the NHMRC.

The *National Statement on Ethical Conduct in Research Involving Humans 1999* (Commonwealth of Australia, 1999) provided for a number of basic principles of ethical conduct during the research endeavour which it expressed as values underpinning it as a document. Those principles were: integrity, respect for persons, beneficence and justice; consent; research merit and safety; and ethical review and conduct of research (Commonwealth of Australia, 1999: 11-14). I will explore these foundation ethical principles in later sections of this chapter, however, in the next section, I will provide a brief overview of the Australian documents.

Integrity, Respect for Persons, Beneficence and Justice

According to the Commonwealth of Australia (1999: 11) the integrity of researchers is expressed in a commitment to the search for knowledge, in the way in which they conduct their research and through the dissemination and communication of the results of the research in an honest and ethical way.

Respect for persons is defined as regard by the researcher for the “welfare, rights, beliefs, perceptions, customs and cultural heritage, both individual and collective, of persons involved in research” (Commonwealth of Australia, 1999: 11). There is no mention of individual/community participation in the design and conduct of trials.

Beneficence and non-maleficence, as interpreted in this document, requires that researchers ensure that the benefits/goods of the research are maximised (beneficence) and the harms and burdens minimised (non-maleficence) (Commonwealth of Australia, 1999; Kerns, 1997; Lewins, 1996).

The principle of justice requires that there is a fair distribution of benefits and burdens within populations and that for individuals, there is a balance of benefits and burdens with particular safeguards for vulnerable individuals (Beauchamp and Childress, 1994; Commonwealth of Australia, 1999; Kerns, 1997).

Consent

The National Statement maintained that consent be obtained from each participant of research and that this should involve:

- (a) provision to participants, at their level of comprehension, of information about the purpose, methods, demands, risks, inconveniences, discomforts, and possible outcomes of the research (including the likelihood and form of publication of research results); and*
- (b) the exercise of a voluntary choice to participate.*

(Commonwealth of Australia, 1999:
12)

The Statement asserted that for the participation of people who lack the competence to make decisions for themselves, researchers must obtain consent from the person with the legal authority to make such decisions for these individuals and must provide them, the surrogate decision maker, with the same level of information provided to competent participants. This consent must be clearly established by a signed form, tape recorded agreement or similar verifiable document. The 1999 Statement maintained that a person may freely refuse to participate in the research and must not be subjected to coercion or undue inducement or influence. Participants

must also be free to withdraw consent at any time (Commonwealth of Australia, 1999: 12-13).

Research Merit and Safety

The proposed research to be conducted must demonstrate that it is justifiable in terms of its potential to contribute to knowledge and is based on an adequate literature review and previous studies whether they are conducted in the laboratory or in animals. The potential harms for the participants in the study must be “balanced by the likely benefit to be gained” and the research must be conducted by research teams with adequate experience, qualifications and competence to perform that type of research (Commonwealth of Australia, 1999: 13).

Ethical Review and Conduct of Research

In my view, of principal concern for research that involves human participants, the research must be reviewed by a Human Research Ethics Committee (HREC) and must not proceed until that body has granted approval for the research. Additionally, the study must be stopped if the risks are found to outweigh the benefits to the participants. Agreements should be reached with participants about the way in which information obtained in the course of the research is utilised and the security of records must be maintained by the researcher and auspicing organisation. Interestingly, the 1999 Statement requires research conducted by an Australian institution or organisation overseas to comply with the requirements of the Statement in addition to the laws and guidelines of the host country (Commonwealth of Australia, 1999: 13).

A discussion point of significant interest in this section of the 1999 Statement is point 1.18 which suggested the process by which the results and methods utilised in the research “should normally be published in ways which permit scrutiny and contribute to the public knowledge” (Commonwealth of Australia, 1999: 13). A trend recently, and in particular in AIDS vaccine research, is to announce significant findings of research in press conferences without having previously submitted those findings to publication in peer reviewed journals. The reasons for this practice vary. However, of fundamental importance to the researchers (and the pharmaceutical organisation supplying the funding for the project) is their capacity to protect the discovery in order to generate profit from its marketing and to generate additional

venture capital to continue the research and undertake clinical trialling of the experimental product (Hirsch and Guess, 2001: 1423).

As I will discuss in a later chapter, biomedical research is a social practice. Social practices, ultimately, receive authorisation to pursue their overall objectives from the community. Indeed, the community, however that is defined, provide priorities for research and funding. By announcing discoveries in popular press, researchers inhibit due scrutiny by the community of their, the researcher's, product and, in my view, violate the covenant they have with the community they serve. Such a covenant is a critical component for practitioners participating in the social practice of biomedical research. It is also unclear how announcing discoveries in popular media satisfies the requirement of point 1.18 of the National Statement.

As I have previously mentioned, a review of the 1999 Statement occurred in 2007 which resulted in some changes to its content and focus. As the 1999 Statement was the applicable instrument in force when the consortium conducted its research, I will not discuss the 2007 Statement in any great detail except to highlight the aspects of the Statement that have changed.

Values and Principles of Ethical Conduct

The 2007 Statement outlines the following as the core ethical principles underpinning research involving humans: respect for human beings, research merit and integrity, justice, and beneficence. The 2007 Statement also explicitly states that these principles “help to shape that relationship as one of trust, mutual responsibility and ethical equality. For this reason, the National Statement speaks of research ‘participants’ rather than ‘subjects’” (Australian Government, 2007: 11).

Research merit and integrity is addressed first in the 2007 Statement because “[u]nless proposed research has merit, and the researchers who are to carry out the research have integrity, the involvement of human participants in the research cannot be ethically justifiable” (Australian Government, 2007: 11).

The 2007 Statement suggests justice involves “a regard for the human sameness that each person shares with every other”. It goes on to state that in the research context, distributive justice will be expressed in the fair distribution of benefits and burdens of the research and procedural justice expressed in the “fair treatment” in the recruitment of research participants and the review of the research (Australian Government, 2007: 11). In our article in *Monash Bioethics Review*, Associate

Professor L Gillam and I argued for the provision of statements of reasons for Human Research Ethics Committee's decisions on both ethical and legal grounds to improve the transparency of decision making of such bodies and promote procedural fairness (Davies and Gillam, 2007).

Finally, the 2007 Statement touches on beneficence and suggests researchers exercise it in several ways: "in assessing and taking account of the risks of harm and the potential benefits of research to participants and to the wider community; in being sensitive to the welfare and interests of people involved in their research; and in reflecting on the social and cultural implications of their work" (Australian Government, 2007: 11).

Themes in Research Ethics: Risk and Benefit, Consent

Interestingly, a different approach adopted by the 2007 Statement is the suggestion that there are two ethical themes which must be considered in all human research endeavours, the risks and benefits of the research and participants' consent. The themes themselves were addressed in the 1999 Statement but not in the context of underlying ethical themes.

In relation to risks and benefits, the 2007 Statement links the principle of beneficence with assessing the harm likely to befall human participants, and others, in the research and that the research would be ethically acceptable only "if its potential benefits justify those risks" (Australian Government, 2007: 15).

The 2007 Statement usefully discusses how risks might be assessed, discusses what harm, discomfort and inconvenience are, how researchers might gauge risks, how researchers might minimise those risks, the benefits justifying the risks involved in the research and how the risks might be managed (Australian Government, 2007: 16-17).

The 2007 Statement suggests the requirement for consent has a number of conditions: "consent should be a voluntary choice, and should be based on sufficient information and adequate understanding of both the proposed research and the implications of participation in it". It says what is needed to satisfy these conditions depends on the research being conducted and the context (codes, laws, ethics and cultural sensitivities of the community) within which the research is being conducted. The 2007 Statement suggests variations on these conditions may be ethically justified

in some instances but that respect for human beings must be shown in any alternative arrangement (Australian Government, 2007: 19).

The 2007 Statement then goes on to discuss a number of related matters in consent. The discussions are brief but highlight some of the complexities in this area. The discussion in the document includes: renegotiating consent, coercion and pressure, reimbursing participants, where others need to be involved in participation decisions, consent to future use of data and tissue, declining to consent and withdrawing consent (Australian Government, 2007: 20-21).

An entire chapter in the new Statement is devoted to qualifying or waiving conditions for consent.

The 2007 Statement describes research involving limited disclosure as covering a spectrum from not fully disclosing the aims of the research to actively concealing information and deceiving participants and provides guidance on managing such research contexts (Australian Government, 2007: 23-24).

The remainder of the 2007 Statement addresses ethical considerations specific to research methods or fields, ethical considerations specific to participants, and processes of research governance and ethical review. It is not necessary to undertake an in-depth analysis of these sections here. What is worth stating, however, is that this revised document is a significant step forward by the NHMRC and its partners to more fully explore, and provide guidance around, the complex ethical context of research involving human participants.

What I have discussed thus far are documents both international and national, which address the guiding principles for all biomedical research. I will now discuss the fundamental ethical principles which underpin those documents because the consortium members needed to have an understanding of the underlying principles to determine how to apply the guidelines in practice. The guidelines are open to interpretation, so an understanding of the ethical principles was necessary to help interpret them. It was also important for consortium members to have such understandings so that they could engage in ethical debate and reasoning to reach a justifiable outcome.

Fundamental ethical principles

As discussed previously, there are three fundamental ethical principles pervading international research. The following discussion will briefly outline the

three principles of respect for persons (incorporating consent), beneficence (incorporating non-maleficence) and justice. Once outlined, I will describe how these principles might apply in the situation of community participation/partnership in HIV vaccine trialling.

While authors generally attempt to differentiate these principles (Department of Health, Education and Welfare, 1978; Levine in Reamer, 1991; Kerns, 1997; Wigjer, Dickens and Meslin, 1997), they interrelate with one another as the various guidance documents show.

Respect for Persons

A document that was one of the first attempting to outline the foundation principles was the *Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research* (Belmont Report), which was in part a response to the infamous Tuskegee study of the United States Public Health Service. The Tuskegee study stated its purpose was to study the natural history of untreated syphilis over a forty-year period. Initiated in 1932 among poor black men from Alabama in the United States, these men were not given the standard treatment at the time or when penicillin became available in the 1940s and many died (Levine in Reamer, 1991: 78-79).

The Belmont Report states that the principle of respect for persons incorporates at least two ethical convictions: that individuals should be treated as autonomous agents; and that people with diminished autonomy are entitled to protection.

Autonomy has a variety of meanings ranging from self-governance to being one's own person (Beauchamp and Childress, 1994: 120). Beauchamp and Childress suggest that theories of autonomy have two central conditions: liberty (meaning independence from controlling influences) and agency (meaning the capacity for intentional action) (1994: 121). Feinberg's (1989) account of autonomy identifies four essential aspects to a person's autonomy: the capacity to govern oneself, the actual condition of self-government, an ideal of character and the sovereign authority to govern oneself. I do not contend that the state of autonomy described by Feinberg is possible all of the time. I do contend, however, that in engaging in 'autonomous authorisation' and actively being engaged in making an autonomous decision, most or all of these states are employed. Autonomy, of both research participants and the affected community, is a critical aspect of the way in which affected community

works for the greatest respect for participants and community autonomy on the consortium. Feinberg's description is a useful context for understanding that participation.

Feinberg (1989: 27-29) considers that a person has the capacity for self-government if they have the necessary intelligence and rationality to make decisions. He argues that there is a "threshold conception" related to autonomy that must be attained for an individual to have the capacity to make a decision.

The condition of self-government explores the notion that individuals may be constrained in exercising their ability to self-government, a notion which has particular significance in a health care context, especially in large institutional settings such as hospitals. For example, a patient may have the capacity to make a self-determining decision but may be constrained because they have not been fully informed about their medical condition. In a research context, a participant may have the capacity to decide to participate in a clinical trial but because all of the relevant risks have not been provided or because they have been deceived, they are constrained.

Feinberg (1989: 30-43) explores the notion of an "ideal of character" by contemplating the ideal virtues an individual should possess to claim autonomy.

Highly applicable in the biomedical research arena is the notion of self-possession. Self-possession is described as the self-ownership of the individual, that is, the person is not another's property or possession. This is a particularly relevant consideration in biomedical research. By using the term 'subject', researchers objectify their dealings with research participants. As objects, there is a risk that they will not treat those who participate in their research with the respect and consideration they deserve and subordinate their welfare to the objects of the study (Angell, 1997; Chalmers, 1998). An individual must also have a distinct individuality or self-identity that is authentically theirs and not a composite of others. An individual must be authentic, that is, the person must form their own beliefs about the environment in which they live and not simply be a parody of another's beliefs. In this way individuals have the ability for self-creation or self-determination. A person must also possess the ability to self-legislate or be in charge of oneself. This also leads to the notion of moral authenticity. Moral authenticity is seen as those beliefs that are genuinely the person's. Moral independence described as the moral obligation to oneself and in pursuing such aims, requires that a person has the integrity or self-fidelity to remain true to those beliefs. Self-control or self-discipline is a concept eloquently stated by Feinberg (1989: 39-41) when he describes self-government

as a constitutional monarchy, “ruled by King Reason under the terms of a basic charter of values”. This combination forms, in Feinberg’s view, the basis of the person and are the terms by which that person exercises their autonomy. Were an individual devoid of such a symbiotic relationship, their ability to control desires and wants would impair their ability to make self-determining choice. Self-reliance is a virtue whereby an individual has the ability not to rely on the commitments of others to him or her. Initiative or self-generation describes that virtue where projects and enterprises are generated by the individual, and responsibility for self, the ability to accept the responsibility for all the foreseeable consequences to themselves that are generated from a choice, are all features of an authentic autonomous individual.

A person who is capable of determining what their “rights” and what their “duties” are, can be said to possess a degree of sovereignty over themselves. As such, a person who is a moral agent possesses rights that they may or may not exercise (Feinberg, 1989: 47-48).

Feinberg’s (1989) writings have extended the understanding surrounding the concept of autonomy. What this implies for health care research is that there is an obligation on the participant to maintain their autonomous being by being active agents in the way clinical research is conducted. Of importance to biomedical researchers and clinicians is the definition of respect for persons expressed in its negative form. Beauchamp and Childress (1994: 126) declaim “[a]utonomous actions should not be subjected to controlling constraints by others”. Those controlling constraints can take many forms in the biomedical sphere and it is important for researchers and clinicians, not only to understand the nature of autonomy for individuals, but that they have an obligation to respect and promote autonomy in the way that they conduct themselves with others, and in particular, with patients and research participants.

Beauchamp and Childress (1994: 123) suggest that autonomous actions have three aspects: that they are intentional, that the action occurs with understanding, and occur without controlling influences. They state that an autonomous act is either intentional or not but that there are no degrees of intentionality. In other words, you mean to act autonomously or you do not. They assert that an autonomous action “should only require a substantial degree of understanding and freedom from constraint, not a full understanding or a complete absence of influence”. The issue then becomes, who decides what a ‘substantial degree’ of understanding is? Research participants cannot make the judgements since they may be in ignorance and researchers, who have a vested

interest in the outcome of the proposed research, are hardly impartial participants. They would seem to ‘hedge their bets’ with such a statement. As demonstrated in my discussion of Feinberg’s autonomy, participants may be constrained in the way that they exercise their autonomy in the consent process if they do not have sufficient information to make such a choice.

What follows is that a critical aspect of respect for persons requires that participants in biomedical research “do so voluntarily and with adequate information, i.e., give their voluntary informed consent” (Grady, 1995: 42).

Informed consent is that process where researchers inform potential volunteers about the proposed research, what the researchers hope to find out from it, what will be expected of them and what they can expect to happen to them during and after the experiment. Potential participants should be informed of their rights and obligations during the experiment and informed that they can stop participating at any time without penalty or cost. This must occur freely and without constraint or coercion, with understanding and voluntariness (Kerns, 1997; Alderson and Goodey, 1998). In essence, “... [e]very participant must be fully informed and must give free consent” (Kerns, 1997: 154). Beauchamp and Childress (1994: 142-157) suggest that this particular concept should be regarded as two different conceptions. In the first conception, they suggest that informed consent should be interpreted as an ‘autonomous authorization’ by individuals of a medical intervention or participation in research. In other words, the individual concerned does more than passively agree to or comply with a proposed course of action. They must ‘authorise’ the proposal through an active informed and voluntary consent. This approach relies on the individual understanding the proposal being described to them. The second conception describes a ‘social rule of consent’ which relies on institutional rules or policies. For example, a minor may consent to be included in a vaccine trial, having fully understood the risks, but the institution may not give effect to that consent because the rules and policies of the institution explicitly forbid participation by a minor.

Building on the concept of autonomous authorisation, Beauchamp and Childress (1994: 145-146) suggest the following elements for informed consent:

- I. *Threshold Elements (Preconditions)*
 1. *Competence (to understand and decide)*
 2. *Voluntariness (in deciding)*

II. Information Elements

3. *Disclosure (of material information)*
4. *Recommendation (of a plan)*
5. *Understanding (of 3. and 4.)*

III. Consent Elements

6. *Decision (in favour of a plan)*
7. *Authorization (of the chosen plan).*

As an underlying concept, no discussion of informed consent can occur without exploring the notion of veracity or truth-telling. Much contemporary debate is occurring regarding the use of truth in society. Bok (1992: 105) has asserted that “deception, even for the most unselfish motive, corrupts and spreads”. Beauchamp and Childress (1994: 150-157) suggest as a corollary of truth telling in the context of research that as deception (such as the use of placebos) or substantial risk are added to a protocol, the more difficult it becomes to justify the research. They suggest that research cannot be justified if:

1. significant risk is involved; and
2. subjects are not informed that they are being placed at risk (with an adequate understanding of the deceptive practices).

This has particular significance in the context of randomised controlled trials (RCT) when control groups receive a placebo against which the prospective product will be tested. International guidance documents have suggested that the use of placebos is only permissible if a treatment does not exist for the disease for which the prospective product is being tested.

Within the vaccines arena, because they will be tested in resource poor countries, there are significant hurdles that must be overcome to satisfy both the international documents and the requirements set out by Beauchamp and Childress. One is that the participant communities must understand the nature of the trial they are volunteering for. This will require, not only an understanding of the ways they are being placed at risk and being told about it, but also having an understanding of the nature of HIV and vaccine approaches as a means of understanding that risk. Because HIV mutates readily, and because vaccine approaches are novel, community participants may not understand the level of risk being assumed unless they have

some understanding of both the general pathophysiology of HIV and the various proposed methods of vaccination against it. Without an adequate knowledge of these issues, participants are not fully informed, cannot fully appreciate the risks associated with the research, cannot exercise autonomous decision-making and, therefore, cannot freely consent to the research as truly autonomous agents.

As Doyal (1997: 1107) states:

Volunteers must have accurate and detailed information about potential risks in order to protect themselves. Equally, for them to weigh up their personal willingness to face such hazards... volunteers must also have adequate information about goals, methods, and possible benefits of research. To deny volunteers such information is a clear breach of their moral rights.

This statement highlights the interrelated nature of these foundation ethical principles, for without adequate respect for persons, researchers are unlikely to be promoting benefits and goods. Discussions of benefits and goods fall under the broad category of beneficence which is discussed next.

Beneficence

The principle of beneficence “refers to a moral obligation to act for the benefit of others” (Beauchamp and Childress, 1994: 260). The Belmont Report claims that those conducting research “are obliged to give forethought to the maximization of benefits and the reduction of risk that might occur from the research investigation” (Department of Health, Education and Welfare 1978: 5). It is important to point out the difference between beneficence and the principle of non-maleficence, the duty not to harm others. Beauchamp and Childress (1994: 262-263) make the distinction between the two by suggesting the rules of non-maleficence are a negative prohibition of an action, that they must be obeyed impartially, and that they provide reasons for legal prohibitions of certain forms of conduct.

Beauchamp and Childress (1994: 193) suggest the concept of harm often refers to the notion of injury in the physical sense but may also refer to “... injustice, violation, or wrong...” as well. Harm is “... thwarting, defeating, or setting back the interests of one party by causes that include self-harming conditions as well as the (intentional or unintentional) actions of another party” (Beauchamp and Childress,

1994: 193). Feinberg, expanding on his previous work in *Harm to Others* (1984), argues that "... to harm a person was to set back his interest and violate his right". He suggested that what was *in* a person's interests is what was good for them and that to *have* an interest is to have a stake in an outcome (1986: 26). He also provided a means of determining the relative importance when comparing opposing interests. He suggested determining how vital those interests are in the networks of the possessor, the degree to which those interests are reinforced by other public and private interests, the inherent moral quality of those interests and whether they are personal or external interests (Feinberg, 1986: 27-28). This notion of set-back to self interest is important in the HIV vaccine research context because a participant in such research could be harmed by being unable to receive a more efficacious vaccine in the future because they have been given a less efficacious one now. They may not even be aware that this could be a consequence of such participation and if a more efficacious vaccine is developed, they may never find out that it will not work for them. Even so, on Feinberg's account of harm, this participant would have been harmed. Stigma associated with HIV positivity, whether through seroconversion or through a vaccine is also a set-back to a person's interests.

The rules of beneficence, conversely, require positive action, do not always need to be obeyed impartially and rarely provide reasons for legal punishment when one fails to abide by them. They also make the distinction between *general* beneficence and *specific* beneficence. The former refers to beneficence toward all people whereas the latter refers to "specific parties, such as children, friends,... patients" and research participants. In the context of my research, I will mainly be concerned with notions of specific beneficence.

Van Ness makes the claim that in the context of biomedical research involving humans "benefits are intended and harms are not" and that if harm does befall a participant, it should be as a result of bad luck (2001: 366). He further supports the suggestion of 'intention' by Beauchamp and Childress that benefit "connotes the presence of agency and intentionality" (2001:367). But, he says, the level of uncertainty in terms of risk and benefit is desirable (2001: 365-369). The Belmont Report states that assessments of risk and benefit are concerned with probabilities and possibilities of harm and anticipated benefits (Department of Health, Education and Welfare, 1978: 9).

Yarborough and Sharp (2002: 9) state that the goals of biomedical research are: "the relief of suffering; the advancement of knowledge, the preservation of life, and

the promotion of human well-being”. The Belmont Report suggests the obligations of beneficence affect both individual researchers and particular projects and society at large and what it calls the ‘enterprise’ of research (Department of Health, Education and Welfare, 1978: 5). Yarborough and Sharp (2002: 9) maintain that the research institutions conducting the study share these goals with the supporting community in which the research is conducted and justify the resources committed to the enterprise. What these authors are describing is the social practice of biomedical research and its relationship with the community that authorises it.

As I have claimed, associated with ‘doing good’ or providing a benefit to participants is the notion of preventing harms to them as a concurrent process. How we balance these two sometimes competing notions often falls into the next category of discussion, justice.

Justice

Related to the distribution of risks and benefits is the concept of justice, and distributive justice in particular. Interpreting the Belmont Report, Grady (1995: 43) states this refers to “the distribution of benefits and burdens of research” and that the selection of research participants should not be simply on the basis that they are easily accessible, in a vulnerable position or are easily manipulated. Indeed, they should derive benefit from the research.

Interestingly, the assessment of risk and benefits appears to fall to the researchers to assess rather than the participants of the research. It is important to note that researchers do not come to such decisions from an unbiased position. As previously argued, in order for participants to understand the risk they are assuming and potential benefits they (or their community) are receiving, they must be fully informed and they, not researchers, are in the most compelling position to assess whether they wish to participate or not. This is consistent with Powers in Kahn, Mastroianni and Sugarman (1998: 149) statement of libertarianism in this context by saying “injustice is a matter of interference with the freedom of individuals to make their own choices according to their own values and their own assessments of the risks and potential benefits”. This view is based on “protecting individual liberty rights (to exercise autonomous decision making) and the welfare of subjects (to be free from imposition of unwarranted risk without offsetting personal benefit)” (Kahn, Mastroianni and Sugarman, 1998: 167). In other words, they see justice as a right. Oversight bodies too, such as research ethics

committees, have an obligation to ensure they understand, and are fully informed about, the potential risks and benefits associated with a particular trial. In doing so, they fulfil the regulatory covenant they have with the community as a whole.

There is no doubt that the development of an efficacious HIV vaccine would, provided there are no clade specific limitations, benefit both resource rich and resource poor countries. The concept of equity, however, requires that “no one group... receive disproportionate benefits or bear disproportionate burdens”. The concern about research in resource poor countries is that participants in these countries bear disproportionate burdens in terms of the risks without the collateral benefits flowing from the research (Macklin in Kahn, Mastroianni and Sugarman, 1998: 132). Macklin further makes the claim that to fulfil the requirements of distributive justice in international research, in particular in resource poor countries, two conditions must apply. Firstly, research design and assessment of risks and benefits must be undertaken using the same standards as research undertaken in the sponsoring country; and the beneficiaries of the research must include people in the host country where the research is being conducted.

Macklin in Kahn, Mastroianni and Sugarman (1998: 133) briefly explores different conceptions of justice, including the formal principle of justice which advocates to ‘treat like cases alike (and different cases differently), the principle of procedural justice which relates to the *process* by which decisions are made and procedures undertaken, and compensatory justice which is concerned with providing compensation for injured research participants or paying them for their time and inconvenience.

Helmann and Hellman (1991: 1586-1587) also outline the utilitarian or social utility arguments. Utilitarianism is a theory that the right action is the one that produces greatest good overall and that the morally correct act, in terms of health care, is the one that produces the greatest pleasure and the least pain overall. They suggest that physicians are significantly restricted in applying the utilitarian approach in research because they have an overriding covenant with the patients that they treat and assigning them to a placebo arm in a randomised control trial, if a therapy is available, breaches that covenant of fidelity and in large part depends on the physician – researcher’s state of equipoise (which I will discuss in the next chapter in more detail). They go on to suggest that trials designed to prevent physicians from accessing data during the trial that would indicate benefit or harm should not be

undertaken since this will limit the physician's ability to act in the patient's best interests. They claim that violation of physician – patient relationships through randomised controlled trials was brought to the attention of the academic medical community (and indeed the general community) by AIDS activists (1991: 1589).

Kahn, Mastroianni and Sugarman (1998: 168-170) maintain that considerations of justice pervade each step in the entire research process, from conception to outcome. Research ideas may be investigator driven but may also be driven by available funding, institutional priorities or advocacy group lobbying. This has implications for the populations and communities that will participate in the research and potentially benefit from its results. As the level of funding is finite, decisions about how that funding ought to be best utilised, what research priorities ought to be given precedence and what populations (gender, ethnicity etc) ought to have precedence will have implications for justice. Once these decisions have been made, participant selection and access to participation in the trial require decisions about how recruitment will occur, what conditions are imposed on participation and how participants will be retained which may all employ justice as a consideration. Finally, once results are known, how those results will be disseminated, promoted or employed will all have components of justice.

Conclusion

What I have described in this chapter are the general biomedical research instruments, both internationally and nationally, which apply to the conduct of research on humans. I have said that, fundamental to all these, are three underlying ethical principles; respect for persons, beneficence and justice. While I have highlighted each individually, they are interrelated concepts. I have discussed these principles at some length in order to show the complexity of the ideas, and the extent to which the interpretation is contestable. I have offered particular interpretations of these principles, but contestation in relation to those interpretations does not materially affect the conclusions or recommendations that flow from it. The key point is that these are complex concepts and an understanding of the complexity is needed by the affected community representatives in order to be effective members of the consortium.

In the next chapter, I will discuss those international instruments which are specific to HIV, and in particular, vaccine and biomedical HIV prevention research. I

will explore the key issues involved in research of this type and discuss the involvement of affected community in the whole vaccine trialling process.

4

Current ethical issues in HIV research

Introduction

The previous chapter addressed the general ethical instruments and the core ethical principles designed to provide guidance to researchers in relation to biomedical human experimentation. The Australian consortium began its work on the development of the vaccine and its trialling at a time of some volatility and controversy in international research ethics. For example, there was significant debate around changes to the Declaration of Helsinki and there was also the introduction of new UNAIDS documents. This chapter addresses the more specific ethical issues involved in HIV research, and vaccine trials in particular. Some of these issues are implicit in the general ethical guidelines outlined in the previous chapter. Others, especially involvement of affected community as a partner in research, are new developments.

The first document to raise community participation as an aspect of ethical conduct of human research is the UNAIDS *Guidance Document on Ethical Considerations in HIV Preventive Vaccine Research 2000*. This document is an attempt at incorporating community into the research process. The second suite of documents to raise community participation as an aspect of ethical conduct in human research trialling is the joint UNAIDS/AVAC document; *Good participatory practice guidelines for biomedical HIV prevention trials* and its companion document *Ethical considerations in biomedical HIV prevention trials* both published in 2007. The guidelines are broader than an examination of HIV vaccines and deal with biomedical prevention trials more generally which includes topical microbicide research, male circumcision and pre-exposure prophylaxis (PrEP).

The rationales espoused by these documents for community involvement suggest that it is, at least a partial solution to the problems raised by research in resource poor countries and attendant concerns regarding standard of care. They also suggest it is a mechanism for improving informed consent. These are, for the most part, universalist arguments which only examine part of the issue and do not acknowledge the particular history or practice of the involvement of the affected community in such enterprises. Such arguments assume a similar type of community in all contexts, which is clearly not so. While such arguments apply, it is a one size

fits all approach which does not take into account the diverse range of ways affected community can participate in biomedical research.

In this chapter, therefore, I will address the specific ethical issues involved with HIV vaccine research and describe the relevant UNAIDS documents that explicitly incorporate community participation. An exploration of standard of care, placebo controlled trials, equipoise, protection of participants during vaccine trialling and research in resource poor countries will follow, to explain in more detail the nature of these issues. Then I will discuss the involvement of affected community in the whole vaccine trialling process. Finally in this chapter, I introduce the Langfordian notion of a social practice as a means of exploring that community involvement in a way that is sensitive to the particularities of the community and the context. The social practice framework will be used as one of the key interpretive frameworks from this point onwards in this thesis.

Guidance Document on Ethical Considerations in HIV Preventive Vaccine Research 2000

UNAIDS has developed guidelines of its own, now in its third reprint, specifically to provide advice about how the conduct of HIV vaccine research should occur. Those guidelines are called a *Guidance Document on Ethical Considerations in HIV Preventive Vaccine Research*.

This guidance document was developed over two years and was based on a series of consultations with 33 countries and involved a broad range of people; from the affected community to scientists. The document sets out 18 guidance points that are paraphrased within this section.

Before I summarise the guidance points, it is important to keep in mind that this document outlines the *minimum* standards vaccine research should comply with, not the 'gold standard'. This is a key document, however, which the Australian consortium would have referred to and applied at the time of the trialling in Sydney.

The first guidance point indicates that sufficient capacity and incentives need to be developed to foster work in developing an effective vaccine. This point identifies the significant ethical imperative to support vaccine development given the high burden of disease that HIV causes, particularly in resource poor countries (UNAIDS, 2000: 6-7).

Linked with this point is the second guidance point that suggests there should be early availability of an effective vaccine to all trial participants and other populations at high risk of infection. A high level of planning should occur in the initial stages of research development to ensure availability occurs. This will require detailed discussions with relevant stakeholders before the trials begin (UNAIDS, 2000: 7).

Thirdly, there should be capacity building in host countries to enable participation in vaccine research as equal partners. Host countries and communities (those where the research will be conducted) have the right, and the responsibility, to take decisions about the nature of their participation in HIV vaccine research (UNAIDS, 2000: 7-8). I will explore the theoretical underpinnings of this argument in greater detail later in this chapter.

Fourthly, the research should also be scientifically appropriate and should potentially benefit the participant/host population. In other words, the population selected for trialling should be made on the basis of relevant characteristics for the research (UNAIDS, 2000: 8-9).

The guidelines, fifth, also suggest affected community representatives be involved in the design, development, implementation and distribution of the results of HIV vaccine research. The research development, therefore, should be undertaken as a partnership, not as a single encounter (so researchers can say they have consulted) or in one direction, but meaningful discourse between equals. This means that the affected community should be appropriately represented on committees charged with the review, approval and monitoring of HIV vaccine research (UNAIDS, 2000: 9). This guideline is closely related to the third mentioned above, the theoretical underpinnings of which will also be explored in greater detail later. This requirement for community involvement is the focus of this thesis.

Sixth, HIV preventive trials should only be carried out in countries and communities that have the capacity to conduct independent and competent scientific and ethical review. This ensures that the analysis of the trials is conducted by people familiar with the prevailing conditions in the potential research population. If this type of infrastructure is inadequate, the research sponsor should ensure adequate structural development prior to the commencement of the research (UNAIDS, 2000: 9-11).

Guidance point 7 suggests that the research protocol should identify and take steps to address conditions that create possibilities for exploitation and increase

vulnerability among the research participants. The identification of these conditions in each of the host countries and communities should be individually assessed rather than along developing/developed or resource poor/resource rich country lines. It is more appropriate to view countries as located along a *spectrum* of resource richness and resource poorness (UNAIDS, 2000: 10).

Guidance points 8 to 13 address issues of informed consent. In essence they state that the early clinical phases of testing of a potential HIV vaccine should be undertaken in communities that are less vulnerable to harm or exploitation, usually within the sponsor country. The potential harms related to the research should be explicit and the means by which these harms will be redressed also made explicit. The benefits to the person should be outlined in such a way as to fully inform but not induce participation in the trial. Where there is no known effective HIV vaccine, placebo-controlled arms may be considered ethically acceptable. Individuals should understand both before and during the trial all relevant information to enable freely informed participation. Special measures should also be taken by sponsor researchers to ensure that persons who are or may be limited in their ability to provide informed consent due to their social or legal status are protected during the trial, or if protection is not possible, excluded (UNAIDS, 2000: 10-15).

Point 14 relates to appropriate risk-reduction counselling and access to prevention methods which should be provided to all vaccine trial participants. This means that all participants should receive comprehensive counselling, independent from the research consortium, before, during and after the trial. Participants should also be provided with adequate access, provided it is legal, to condoms, sterile injection equipment and treatment for other sexually transmissible infections. There exists, however, a potential for a conflict of interest between the risk reduction goals of counselling and the vaccine trial's scientific goals in exposing participants to HIV in order to test the protective effects of the potential vaccine (Kirby, 2000; UNAIDS, 2000).

A plan for monitoring the adequacy of informed consent of participants and the risk reduction strategies should be agreed to before the trial commences is point 15. The appropriateness of such plans should be determined by the scientific and ethical review committees responsible for providing prior and continuing review of the trial (UNAIDS, 2000: 16).

Guidance point 16 states that “care and treatment for HIV/AIDS and its associated complications should be provided to participants in HIV preventive vaccine trials, with the ideal being to provide the best proven therapy, and the minimum to provide the highest level of care attainable in the host country... A comprehensive care package should be agreed upon through a host/community/sponsor dialogue which reaches consensus prior to initiation of a trial...”. In light of the debate around just this issue in the Declaration of Helsinki, this approach, of not taking a definitive stance on the standard of care issue, is a significant disappointment. There was an opportunity, largely squandered, to provide leadership on the ‘standard of care’ debate that was not taken by UNAIDS. UNAIDS suggests that a number of factors need to be taken into account when considering this issue including the level of care and treatment available in the sponsor country; the highest level of care available in the host country; the highest level of treatment available in the host country, including the availability of antiretroviral therapy outside the research context; the availability of infrastructure to provide care and treatment in the context of the research; and the potential duration and sustainability of care and treatment for trial participants. While there is no consensus around ensuring care and treatment for participants who become HIV infected during the course of the trial, there is a compelling ethical imperative that this occurs (Barry, 2001; UNAIDS, 2000).

The final two guidance points specifically identify both women and children as being potential research participants provided that adequate safeguards are in place to ensure informed consent and harms are minimised (UNAIDS, 2000: 18-19).

While this document was developed largely for vaccine trialling in resource poor countries, the consortium, nevertheless, needed to be aware and take into account all of these issues during the course of its work. They needed to be aware of these issues because many of the principles espoused by the document are relevant in all contexts, not just resource poor ones. Also, an arm of the trial was proposed in Thailand as a possibility early in the study which would have made this document of central importance to the consortium.

The next two HIV specific documents had not been developed and were not available to the consortium during the course of the trialling of the consortium’s prime-boost vaccine construct in Australia. As such, they did not guide or regulate the consortium’s approach per se, although the ideas and concepts these two

documents espouse may have influenced the functioning of the consortium during the course of its Australian trial, as the ideas were current within the affected community and HIV research community for quite some time before the guidelines were published. Indeed, they provide a useful analytical framework for assessing the Australian consortium's unique approach to affected community involvement in HIV vaccine trialling specifically and biomedical prevention trialling in general.

Ethical considerations in biomedical HIV prevention trials 2007; Good participatory practice guidelines for biomedical HIV prevention trials 2007

Since the development of the UNAIDS document in 2000, the biomedical HIV prevention approaches under development internationally have broadened beyond that of just preventative HIV vaccine development to include such approaches as vaginal (and rectal) microbicides, male circumcision and oral pre-exposure prophylaxis. To address this shifting biomedical prevention landscape, UNAIDS undertook another series of consultations in 2005 with investigators, ethicists, government representatives, advocates and community representatives to assist it in defining the key elements involved in creating effective partnerships in HIV prevention trials. It was also a response to the halted pre-exposure prophylaxis trials in Cambodia and Cameroon (UNAIDS, 2007a: 7).

Consensus was reached on a number of recommendations, including on the need for the development of guidelines on good community practice in this field and the updating of the 2000 document. A working group was formed, with assistance from AVAC, to develop those guidelines. Once developed in draft form, a broad consultation process was undertaken with a range of stakeholders (UNAIDS, 2007a: 7).

The *Good participatory practice guidelines* are designed to provide guidance in relation to the roles and responsibilities for those bodies funding and conducting biomedical prevention trials on engaging communities whereas the *Ethical considerations* document suggests standards for the conduct of such trials (UNAIDS, 2007a; UNAIDS, 2007b). These companion documents form the basis of the latest international guidance on such matters and, as noted above, the *Good participatory practice guidelines* provide a framework for analysing community involvement, which is the focus of this thesis.

The first of these documents I wish to outline here is the document entitled *Ethical considerations in biomedical HIV prevention trials* document. As I have previously stated, this document was not published or available to the consortium when it was undertaking its trialling in Australia. It is a response to the growing biomedical HIV prevention field which incorporates, but goes beyond, HIV preventative vaccine development (UNAIDS, 2007b: 6-7). Most of the points are very similar to other documents discussed in greater detail in the previous chapter and are merely providing more detail relevant to this context. I do not intend to discuss in great detail those similarities again here. The key features of these points are that:

- * There ought to be support for the development of biomedical HIV prevention strategies;
- * Capacity building ought to occur within affected communities;
- * There is a rigorous scientific and ethical review;
- * The risks of clinical trialling within the affected community should be fully outlined;
- * Appropriately rigorous research protocols should be developed with the study population in mind;
- * Recruitment procedures should be voluntary, fair and demonstrate respect for persons;
- * Greater care should be taken with vulnerable populations, women, children and adolescents;
- * The potential harms of the research should be fully explained;
- * The uncertainty of the benefits should be fully explained;
- * The standard of prevention in research populations should be high;
- * Treatment and care should be provided to trial participants acquiring HIV;
- * Control groups should receive all available HIV risk reduction methods;
- * Consent should be voluntary and informed and this should be monitored
- * Confidentiality of information must be maintained; and
- * The results of the trial should be readily available.

Of greatest significance for this thesis is guidance point 2. Guidance point 2 – Community participation, supports affected community involvement, in an early and sustained manner, in the design, development, implementation and dissemination of results of biomedical HIV prevention trials. This guidance point is discussed in

greater detail in the companion document, *Good participatory practice guidelines for biomedical HIV prevention trials*. In summary, the *Ethical considerations in biomedical HIV prevention trials* document states the involvement of affected community in trialling in a transparent and open process, helps ensure the ethical and scientific outcomes of the trial. The guidance point acknowledges that identifying the appropriate affected community for consultation and partnership is complex and evolving. Roles and responsibilities should be clearly defined and agreed to. Key to the ongoing engagement with affected community is consultation and engagement on relevant advisory structures and committees. In this way, improved literacy of both the researchers in relation to the community and community in relation to research design and concepts improves (UNAIDS, 2007b: 17-20).

Guidance point 4 – Scientific and Ethical Review, also suggests community representatives should be involved in the review of the trial protocol to “... insure that the research is informed for the concerns and priorities of the community in which the study is to take place” (UNAIDS, 2007b: 23).

The second of the UNAIDS documents I wish to outline here, and the one most relevant to this thesis, is the *Good participatory practice guidelines for biomedical HIV prevention trials*. The UNAIDS (2007a: 13) states there are ten fundamental principles which underpin the guidance for researchers, trial sponsors and onsite research staff on how to achieve standards in community engagement, input and participation during the life of the biomedical HIV prevention trial. Usefully for my research, UNAIDS states, these core principles form a foundation for evaluating existing community engagement efforts and creating new approaches. In summary, those core principles are:

1. Scientific and ethical integrity;
2. Respect;
3. Clarity in roles and responsibilities;
4. Towards shared responsibilities;
5. Participatory management;
6. Autonomy;
7. More transparency;
8. Standard of prevention;
9. Access to care; and
10. Building research literacy.

(UNAIDS, 2007a)

I will now comment on each of these principles in more detail.

1. *Scientific and ethical integrity*

Consistent with the other documents I have discussed in this chapter, this document suggests that maintaining the highest standard of scientific and ethical integrity is fundamental to the goals of the trial, advancing science and maximising the benefit for the trial community. It also suggests that this can be achieved only by adhering to "... the universal ethical principles of respect for persons, beneficence and justice,..." (UNAIDS, 2007a: 13).

2. *Respect*

The document suggests that the key to effectively communicating, fostering trust and developing partnerships to achieve mutual goals is respect among all stakeholders. It suggests respect in relation to communities includes respect for the community's values, its social institutions and, where relevant, abiding by the decisions of legitimate communal authority (UNAIDS, 2007a: 14).

3. *Clarity in roles and responsibilities*

This core principle states that in order to create an effective framework for community engagement, clear understandings of the roles and responsibilities of all stakeholders should be articulated and negotiated. These roles and responsibilities ought to be monitored and adjusted or refined throughout the course of the research undertaking and such mechanisms should be defined from the start of the endeavour (UNAIDS, 2007a: 14).

4. *Towards shared responsibility*

Core principle four suggests all stakeholders involved in the research enterprise, including funders, trial site staff, researchers, health authorities and the "community of people affected by a trial", must jointly understand the goals, risks and benefits of the research to develop and conduct ethical trials. The document states shared responsibility "commits all stakeholders to work in partnership towards the achievement of study goals and to honour the commitments they have made to one another..." (UNAIDS, 2007a: 14).

5. *Participatory management*

This principle articulates that communities affected by the research should play active parts in all aspects of the trial in conjunction with the principal investigator. There is an acknowledgement of structural power imbalances between the stakeholders and that such structural power imbalances should be overcome. It supports the attainment of the best possible representation in order for “parity for the values, norms, and behaviours of those affected by the research process”. Such an approach, it is claimed, builds community capacity, facilitates smooth trial functioning and assists in the resolution of concerns that may arise during the course of the trial (UNAIDS, 2007a: 15).

6. *Autonomy*

This principle highlights that established, independent community advisory structures are important to conducting an ethical trial. It also states that trial site staff and researchers must pay close attention, and seek to minimise, possible conflicts of interest by participating community members (UNAIDS, 2007a: 15).

7. *More transparency*

This principle states that fundamental to good participatory practices is open and honest communication. This includes the provision of access by the principal investigator and research staff to trial-related material by the communities affected by the research. Public documents, such as community education materials, protocols and communication strategies, should be made available to community partners in an appropriate format and summarised and translated where appropriate. Decisions taken elsewhere which affect the conduct of the trial should be communicated in a timely fashion. The plans for data analysis, interpretation of the results and the dissemination of such information should be agreed upon at the outset, paying due regard to the confidential or proprietary nature of such information. Communities have a “responsibility to raise issues with researchers and propose constructive suggestions for solutions to improve trial conduct”. Finally, communication should be multidirectional in order that all parts of the research enterprise are fully informed (UNAIDS, 2007a: 15-16).

8. *Standard of prevention*

The document suggests there is an ethical responsibility of researchers, research site staff and trial sponsors to ensure appropriate risk-reduction counselling and access to proven HIV prevention methods are provided to all trial participants throughout the course of the trial. The document suggests this is an integral component of the research protocol (UNAIDS, 2007a: 16).

9. *Access to care*

This principle is a reassertion of the core tenets of the Declaration of Helsinki and the CIOMS guidelines. The principle states that trial participants have “the right to access medical care for trial-related injury or harm, and to the experimental product under investigation should it prove go be effective”. In the case of biomedical HIV prevention trials, the document states that participants who seroconvert during the course of the trial have the right to access to a comprehensive package of care, including antiretroviral treatment, which is negotiated before the trial commences and defined in terms of its components and timeframe (UNAIDS, 2007a: 16). This and the previous principle seem to relate more to the more traditional ethical debates rather than community participation per se.

10. *Building research literacy*

In the interests of improved study design and a broader contribution to the development of the affected community, all stakeholders in the research endeavour have a responsibility to contribute to strengthening community research literacy. National and host governments have a responsibility to facilitate the conduct of biomedical HIV prevention trials by creating frameworks for HIV prevention research in country HIV prevention plans (UNAIDS, 2007a: 16-17).

The rest of this document deals with the mechanics of conducting, on the ground, biomedical HIV prevention trials. I do not intend to canvass those issues here. It is sufficient to note that, using the principles outlined above, the document discusses a broad spectrum of issues ranging from the development of the research protocol through to the dissemination of results and future access to HIV prevention technologies (UNAIDS, 2007a: 19-60).

Summary of this section

What I have undertaken to this point in this thesis is a brief discussion and outline of the international and national instruments that provide guidance and govern the conduct of clinical trials of potential vaccines. The guidelines are a manifestation of core ethical principles underpinning biomedical research in general, and in this instance, HIV vaccine research in particular. As such, the Australian consortium had to design its research to take account of these international and national standards and guidelines. Strictly speaking, since the 2007 UN documents were not in force at the time the consortium began its work, the provisions in the documents did not apply. However, the ethical issues addressed in them, and the idea that community involvement would help in ensuring ethical research, were very much current. From the outset, the members of the Australian consortium also needed to be aware of the core ethical principles which sat behind the guidelines, and the discussions relating to how they apply in HIV prevention research. The consortium, though based in Australia, needed to be aware of issues related to vaccine research in resource poor countries because the original plan was to conduct a trial in Thailand, as well as Australia. I will now explore the substantive ethical issues in greater detail.

Current relevant ethical issues in HIV biomedical research

In this section, I will explore how ethical issues in research may play out in resource poor countries. I do this by exploring notions of justice, in particular, the standard of care debate, the use of placebo controlled trials and I explore the concept of equipoise. Finally, I briefly describe some of the issues in relation to consent.

Research in resource poor countries

Some commentators have suggested, using the formal principle of justice, that it is ethically acceptable to use different ethical standards in resource poor countries (Macklin in Kahn, Mastroianni and Sugarman, 1998; Zion, 2001). This is most commonly associated with the 'best' vs. 'local' standard of care debate which I will discuss later (Angell, 1997). Although Macklin and Zion do not advocate for such notions, others do (see for example Lackey, 2001). Angell (1997: 847-849) strongly rejects such notions by suggesting that such ethical relativism may lead to widespread exploitation of vulnerable resource poor populations. Lurie and Wolfe (1997: 853-856) state this is an inherent double standard by accepting a standard in a resource

poor country that would not be acceptable in a resource rich one. They make the compelling argument that the standard of care is a normative standard not a relative one.

In discussing the issue, Angell (2000: 967-969) explores the defences for the 'local' standard of care approach, including that it is not necessary to provide better care for participants that seroconvert than is generally available in the participant's community and that it would be unsustainable to offer better health care as the local economic conditions cannot support this long term. This would seem to be using research populations as means to an end rather than valuing their unique humanity and personhood. As Hellman and Hellman (1991: 1586), in outlining rights-based moral theories on this issue claim, human beings "ought not be treated merely as means to an end; rather, they must always be treated as ends in themselves". Angell (2000: 967-969) asserts that researchers' ethical standards should not be dependent on the location of the research and that researchers themselves have an obligation to treat illnesses experienced by the participants even if those illnesses are not a result of the research. In particular, the nature of this obligation should not be influenced by the political and economic conditions of the region. To assume any other position, she states, risks leading to the exploitation of people in resource poor countries so that research unable to be performed in resource rich countries can be conducted.

Powers (1998: 161-164) believes a 'reasonable extension' of the Belmont Report's account of distributive justice requires safeguards against the abuse of vulnerable or disadvantaged groups or people. Restrictions on individual liberty to decide what acceptable risk and benefits are may be limited for the sake of avoiding injustice to the group. She further suggests that the focus of such assessments must not only occur in terms of the individual and group but also a separate assessment must be made of the benefits of the research and the burdens of the research, taking note of where the benefit or burden falls.

Macklin in Kahn, Mastroianni and Sugarman (1998: 143-144), in appealing to the principles of equity, procedural and distributive justice, suggests that a number of procedural steps can help to ensure justice in international research. First, she advises collaboration between researchers in resource rich countries with researchers in resource poor countries. This will aid in capacity building in local communities and within regions. Second, and importantly for my study, she advocates for community or regional involvement in the research process, including community consultation

before and during the conduct of the research and in distribution of the benefits of the outcomes. Importantly, Macklin assisted UNAIDS to draft their ethical guidelines on preventative vaccine research and is an executive member of the CIOMS board (http://www.cioms.ch/executive_committee.htm). Clearly, since both the CIOMS document and the UNAIDS document suggest such an approach, she has advocated successfully for such inclusions. Thirdly, she suggests that the setting of research priorities should be made in consultation with the local community rather than solely by pharmaceutical companies wishing to make a profit or “medical scientists hoping to win the Nobel Prize” (1998: 143).

On a much larger scale, Benatar (2001: 334) claims that “globalising forces create ever widening disparities in wealth, with important implications for health and well being” largely driven economically by the neo-liberal market place which funnels resources upwards, thus creating wider disparities in health and wealth. This has had the effect of increasing the poverty of third world countries resulting in unpayable debts to such organisations as the International Monetary Fund (IMF) and the World Bank and decreasing per capita spending on health.

The impact of HIV on resource poor countries is significant. It is proposed that ninety-five percent of the estimated 36.1 million people who have HIV are from resource poor countries. HIV/AIDS is seen as a threat to the development of these countries and has been identified as a significant threat to global security (Haire, 2001: 4). The development of an effective HIV preventive vaccine is said to be the only ‘realistic’ means of addressing the epidemic in these countries (Kirby, 2000: 435). Justice Kirby (2000: 435) suggests that even a low efficacy vaccine that protected some of the most at risk populations would have a significant impact and suggests that a recognition of the fact that *not* to act is to make an ethical decision.

Justice Kirby (1999: 18) also suggests that some risks are ethically acceptable in order that the energy, investment and interest of private sector entrepreneurs is not lost and so that populations in resource poor countries being decimated by HIV/AIDS can be assisted as quickly as possible. He does not advocate that these populations are exploited but that the ethical principles are applied in such a way as to produce the safest, most rapid response to the epidemic.

Benatar (2001: 338-340) also advocates for a paradigm shift in thinking around international research ethics toward reciprocal relationships “between individuals, society, and the notion of rational self-interest and long term interdependence”.

Utilising such an approach, he says, could advance human relationships to the “high moral ground” and promote long term solutions such as increasing dialogue, mobilisation of science and technology to address difficulties in resource poor countries, new institutional alliances constructed, a re-evaluation of intellectual property rights to avoid ‘ripping off the poor’, and long term financing for international human good should be planned. The current situation is onerous and favours resource rich countries.

One suggested resolution to these problems is community involvement. Kahn, Mastroianni and Sugarman, (1998: 170-172) suggest locating affected community as an integral part of the research process is a matter of justice and make a number of suggestions about how to implement justice throughout the research enterprise. First, scrupulous attention to justice fosters and maintains trust between researchers and participants. Second, attention to justice must occur throughout the research at each decision point from conception to outcome and must be explicit. Third, there should be a mechanism for coordination of decision making throughout the research enterprise and between agents in the research endeavour. Fourth, biases and incentives should be explicitly acknowledged and disclosed since decision making is not done in the absence of preconception or influence. Fifth, it is vital “... to incorporate a diversity of view and participation (e.g., gender, people of color, advocates) at each decision making point in the research process”.

Standard of care, placebo controlled trials and equipoise

In early 2000, when the consortium was originally granted the contract from NIH, the WMA released proposed changes to the Declaration of Helsinki for public consultation on their website (www.wma.net). Those proposed changes significantly weakened the provisions outlined in the then current Declaration through changes in the language of the text and omissions of both key words and key sections of the existing document. The proposed changes became a matter of great controversy and provide a very useful focus for exploring other important ethical aspects of research in resource poor countries.

There were three fundamentally important omissions in the proposed draft that drew attention to the underlying issues. The first significant omission was the removal of the word ‘best’ in relation to ‘best proven diagnostic and therapeutic methods’ in Sections 22 and 24b of the 1996 iteration of the Declaration. This

represented a significant erosion of the ‘gold standard’ or current best practice standard provisions of the 1996 Declaration. To provide less than ‘best’ available treatment to research participants, particularly in resource poor countries where health infrastructure is significantly compromised, is problematic at best. Fundamentally what this proposed change would have allowed is the provision of care in resource poor countries that was not the ‘best’ but only what was locally available (which may have been little or nothing). Later in this chapter I will propose that this is an ethically dubious proposition. This requirement for best methods was eventually re-inserted into clause 29 of the new revised Declaration which states the “... benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods”. Prophylaxis is defined as the prevention of disease or preventative treatment (Miller and Keane, 1983: 920). For example, the provision of antibiotic therapy may be a useful prophylactic measure to prevent respiratory infection. In the context of HIV preventative vaccine research, prophylaxis may take the form of high quality, regular HIV prevention education, making available condoms and water based lubricant and regular sexually transmissible infection (STI) testing. This issue of comparison between a new method and best prophylactic, diagnostic, and therapeutic method will be discussed later when I discuss the importance of equipoise in clinical research.

There is, however, a fine ethical distinction between providing health infrastructure and coercing participation in clinical trials to access that infrastructure. Bastian (2001: 1420) suggests that the “reality is that participation in trials has effectively become a way to access new treatments, and in poor communities it is often the only way to get any formal health care”. In particular, she says, if ongoing treatment at the conclusion of the study is routinely established, the impetus for access to participation, as well as the coercive potential, rises considerably.

Use of placebos was another contentious issue. Clause 29, in particular, was the source of some consternation within the medical and pharmaceutical research community.

In full, clause 29 states:

The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude

the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.

(WMA, 2004: 4)

The debate around this clause prompted the World Medical Association to include a clarifying note about it as an inclusion in the Declaration. The note states:

The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:

- *Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or*
- *Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.*

All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.

Tollman (2001: 1417) suggests “... clause 29 may impose demands on local and national health systems that, without massive additional investments, simply cannot be met” particularly in resource poor countries where inadequate health and public sector systems exist. Other commentators suggest that placebo controlled trials (where an inactive substance is tested in humans against the proposed new method) may be ethically acceptable “under certain well defined circumstances” and will enhance the scientific design, thereby protecting human subjects. Critics of clause 29, the United States Food and Drug Administration (FDA) among them, applied sufficient pressure on the World Medical Association, the authoring body, to force the explanatory note in relation to the clause as a first step to reopening the debate at the 2002 WMA meeting (Rothman, Michels and Baum, 2000; Hirsch and Guess, 2001).

Schuklenk (2001: 299) suggests this is more of an economic argument than a science over ethics debate because lower standards of care are cheaper. This is of particular relevance to HIV vaccine development since most of the trialling will occur in resource poor countries. In any case, the reopening of the debate failed to achieve the weakening of clause 29 as its critics wished. This question of standards of care will be one of the issues relevant to the role of community involvement in trials.

Closely related to the conduct of placebo controlled trials is the notion of equipoise. Equipoise is the condition where researchers believe, in comparing two treatments for a disease, there is no good reason for believing one is superior to another (Angell, 1997: 847). Angell asserts that “[o]nly when there is no known effective treatment is it ethical to compare a potential new treatment with a placebo” (1997: 847). This theory of equipoise can also be expressed as a null hypothesis (Freedman, 1987: 141). London (2001: 314) suggests it is based upon two interlocking ideas. The first idea is that it is permissible to randomly assign an individual’s treatment because no judgement exists to suggest one treatment is superior to another and the second is that trials are designed to enable the medical community to improve its clinical practice.

Freedman (1987: 141-145) suggests that there is a difference between theoretical equipoise and clinical equipoise. He suggests that theoretical equipoise is fragile because if the researcher’s personal state of genuine uncertainty is disturbed, the state of equipoise no longer exists. Clinical equipoise, on the other hand, is the state of uncertainty in the clinical community about whether treatment A is more beneficial than treatment B. Once researchers become aware of data from the study that one treatment is clearly favourable to the other, the state of clinical equipoise is disturbed.

London (2001: 312-332) reframes the equipoise principle into a broader conception and states that the broad “...interpretation is not the degree of clinical comparability that *already exists* between two treatment settings, but the degree of clinical comparability *that is practically attainable and sustainable*.” In other words, he believes the broad conception of equipoise is dependent on whether a proposed treatment, if found to be efficacious, is sustainable in a particular community. If it is, to trial any other treatment against a placebo in preference to the proposed treatment is unethical. By requiring clinical comparability that is sustainable over time, the broader conception of equipoise provides constraint against exploitation of resource

poor populations that do not have the same clinical comparability. It also addresses questions that relate to the specific needs of the participant population.

In the case of HIV vaccine trialling, no known effective treatment exists at the moment but, if at some stage in the future, existing trials produce results that suggest a degree of efficacy, this has significant implications for trials that are ongoing if they have incorporated a placebo arm. Incorporating the efficacious candidate into an existing trial has significant implications for the methodology and numbers of participants required. In other words, the way the trial is conducted may need to change and the number of participants enrolled in the trial will need to increase dramatically in order to make the sample of participants statistically significant. There appears to be no consensus about how to address these concerns at present in the HIV vaccine research community. Indeed, in London's view, it may depend on whether the efficacious vaccine is sustainable in the host country.

In October 2000, the World Medical Association ratified the modified Declaration at their 52nd General Assembly. As a result of a high degree of public scrutiny and criticism of the proposed changes, some of the more contentious issues, such as those I have mentioned above, were modified to take account of the concerns of the people who wrote, faxed and emailed. Since that time, the declaration has been ratified three further times in 2002, 2004 and 2008.

There is a clear emphasis in the ratified 2004 Declaration that the protection of the "life, health, privacy, and dignity of the human subject" is paramount. This change in emphasis occurs in both clause 2 and the first of the Basic Principles in clause 10 (Barry, 2001: 27). Clause 2 states that "[i]t is the duty of the physician *to promote and safeguard* the health of the people. The physician's knowledge and conscience are dedicated to the fulfilment of this duty" (my italics). Clause 10 states that "[i]t is the duty of the physician in medical research to *protect the life, health, privacy, and dignity* of the human subject" (my italics) (WMA, 2004: 1-2). In order to avoid "cherry-picking" (choosing one site or population over another because the structural or ethical requirements are less stringent at that site or in that population) by sponsor institutions, the Declaration includes a statement in clause 9 which says "[n]o national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration." This has the effect of limiting (to the extent that this Declaration limits) sponsor researchers from searching for the resource poor country with the most relaxed human

research regulations and is an attempt to internationally standardise the approach taken by researchers (Barry, 2001: 27-28).

Barry (2001: 28) also suggests that in reviewing the “standard of care” issues within the Declaration, the resulting position of the WMA is that “the Helsinki guidelines relating to the standard of care and the ethical use of placebos will apply only to patients who are participants in clinical trials” and that healthy volunteers may not be afforded the same protections. He does make a separate distinction of volunteers who, in the course of an HIV vaccine trial, seroconvert and ought to be provided with optimum care.

As can be seen from the above discussion, the related issues of standard of care, equipoise and use of placebo are contentious and open to interpretation. The relevance of the social context of a trial to what counts as ethical practice is a major point of contention. All of these issues were pertinent to the consortium in planning its vaccine trial in Australia, and in considering the Thai arm.

Consent

In order to make an informed decision in relation to participation, volunteers need to provide informed consent which is also open to some debate within the scientific community. There is even debate about the necessity for informed consent if it requires researchers to compromise the research methodology and possibly cancel the research. Doyal (1998: 1000) makes the claim that proponents of such a course of action “fail to respect the autonomy of competent people” and “inflict harm on them that is just as morally unacceptable as direct physical or mental harm”. But, as Power (1998: 1003) says “[t]o improve the practice of obtaining informed consent”... “there must be a number of changes in attitude” including participants as a legitimate voice in the design and approval of trials that is meaningful and not tokenistic. Lansang and Crawley (2000: 778) support this view by advocating “the need and value of consulting local communities and involving potential participants in research early and in the process of designing research protocols”. Power says that situating participants at the centre of the process may require additional resourcing and time but that it leads to better trials (1998: 1004). However, there is a social aspect to consent because individuals are influenced by their social relationships and personal influences (Lewins, 1996; Alderson and Goodey, 1998). The complexities about

consent relate to how it can be meaningful in the particular social setting in which the research takes place. This was also an important consideration for the consortium.

Community involvement in research

The exploration of the literature to this point suggests two rationales for community participation in research. The first is that the documents discussed to this point seem to present community involvement as a partial solution to the problems raised by research in resource poor countries and corresponding concerns about standard of care. The second rationale is that community participation is a mechanism for improving informed consent. These are both universalist arguments which, while valid, do not take into account the social context in terms of any past history or practice of involving affected community. Such contextualisation is important to tailor different approaches to such matters. The Australian context provides a powerful example of why this is so.

In Australia, there is an additional, very powerful, rationale for community participation. As I highlighted in chapter one, there is a tradition and social practice of involvement of affected community in matters to do with HIV prevention, research and treatment and care.

In seeking to understand community involvement in the consortium, it is, therefore, necessary to understand that involvement both in theoretical ethical terms (the ethical rationale and objectives) and in grounded practical terms as part of a wider social practice. The theoretical ethical objectives of community involvement can only be pursued in a real-life setting, involving real people operating together as part of a social practice. Therefore, we need a good idea of what a social practice is, what constitutes a social practice and how it operates.

Social Practices

Just as ethics is an examination of people's relationships, so too are social practices. In order to meaningfully explore how ethical principle or ideas are put into practice in these relationships, it is necessary to have a good model or understanding of social interactions in general. One particularly useful way of understanding the interaction of people in social groups, is the concept of a "social practice". By social practice, I am not meaning family groups or intimate personal interactions. I mean the

types of interactions between practitioners, teachers, community advocates, health educator, nurses, doctors, and their social practices.

A number of authors (Bourdieu 1977, Giddens 1984, Taylor 1971) have explored social practice theory, however, Langford is the most useful to explore the ethical domain because Langford has usefully outlined key features of social practices that is explicit and easily operationalised. Much of the consortium members also come from professional backgrounds that are different but related.

Langford (1991: 22) argues social practices are comprised of individuals who exist in social situations. Social practices occur in the broader context of society and persons provide the society with its members. Social practices are comprised of a number of defining characteristics and can only be examined by exploring the relationship between these characteristics (Langford, 1991: 27).

First, social practices are “constructed and constituted” by persons. They do not exist in abstraction from the individuals that make them up and can only be identified through the behaviour of the persons who are their practitioners (Sunderland, Muirhead, Parson and Holtom, 2004; Isaacs, 1993; Langford, 1991). McCall (1990: 7-17) distinguishes between person, self and human being as concepts related to individuals which helps differentiate the characteristics and properties of the individual. The individual as a person, they suggest, is conceptualised by others. Therefore, the individual as a person can only exist in the context of the social. McCall (1990: 12-13) argues the components which characterise personhood (agency, accountability, responsibility for actions etc.) only operate within a social framework. Similarly, the granting of rights (the right to vote, the right to be heard, the right to autonomy and self-determination etc.) can only occur within the social context and cannot exist for an individual in social isolation. There would be no need for the granting of rights to an individual absent from the presence of others. For example, much of the rights of a person in life lapse upon their death. Similarly, the notion of personal identity can only be achieved in the context of the social. Therefore, the nature of individuals as persons is essentially social and, as such, ethical in nature. As Langford (1991: 23) states, the behaviour of persons is purposive, guided by beliefs and directed by intentions. Beliefs, in turn, are guided by perceptions which are themselves dependent on appropriate sensory receptors and conceptual schemes or ways of seeing. Persons also situate themselves in a spatio-temporal context relative to the things they perceive. Such beliefs guide behaviour and give purposive behaviour “... an intrinsic temporal dimension

which directed behaviour does not have” (Langford, 1991: 23). Similarly, intentions are also spatio-temporally located. Persons can form intentions, “... only insofar as that way of seeing allows them to do so”. Together, this provides persons with a sense of where they have come from and where they are going to (Langford, 1991: 24-25).

The concept of the self refers to those aspects of an individual constituting self-consciousness. Reflection upon one’s actions, thoughts and intentions examines the experience of those actions, thoughts and intentions through a subject which is conceptualised as the self. The self is the location of experience, “...the aspect of an individual which can reflect upon experience, which ‘has’ those experiences, but which is not identified with the experience” itself (McCall, 1990: 14).

Human being refers to the individual as a biological entity who is a member of a certain species and may be identified as a member of that species. The individual may be identified from others of the species, for example by having unique fingerprints and DNA, and recognised as the ‘same’ by means of spatio-temporal criteria (McCall, 1990: 15).

Langford (1991: 26) suggests that persons who see others as persons are guided by their own beliefs and their beliefs about the beliefs and intentions of others. Those beliefs may also include “... beliefs about the other’s beliefs about their own beliefs, beliefs about the other’s beliefs about their own beliefs about the other’s beliefs about their own, and so on”. Persons are, therefore, related to each other by what they describe as a reciprocal self-awareness. It is because persons have a reciprocal self-awareness that they can become practitioners in social practices. Because the relationship with others is an inherently ethical interaction, later in this thesis I investigate and interpret the relationship between the affected community (as represented by AFAO on the consortium) with the other consortium members in these terms. Such interactions inhabit the ethical domain.

Langford (1991: 27-31) indicates that a social practice is directed towards an overall purpose. For example, the overall purpose of a receptionist is quite distinct from that of a waiter, which is quite distinct from a researcher etc. Indeed, it is the overall purpose upon which the social practice is dependant for its existence and identity. Subsequently, each member needs to be aware of, and have a clear conception about, the overall purpose of the social practice (Sunderland et al, 2004; Isaacs, 1993; Langford, 1991). In the course of pursuing the social practice, the individual is called on to make judgements regarding what actions would best serve its overall purpose. Individuals

would be unable to make appropriate choices if the overall purpose of the social practice is not clearly articulated and understood (Langford, 1991: 29). That overall purpose is one that develops over a period of time.

Social practices, therefore, have a unique history and tradition. Indeed, the social practice of biomedical research has a distinct and well documented history and tradition which I have outlined in previous chapters. I have also described the history and tradition of the Australian HIV/AIDS Partnership in chapter one. The individuals within that practice have their own internal unity with their past. Therefore, as individuals constitute a social practice, the social practice itself will have its own internal unity. It has, as Langford (1991: 30) states, its “view of how things were done in the past...”. This provides a historical framework that allows understanding of the purposes and goals of the practice, allows choices to be made in light of the past and provides direction for it into the future. This is a tradition and history that allows for continuity and change.

The members of the social practice need, also, to be reciprocally aware of sharing this purpose. Reciprocal self-awareness is described as practitioners being aware of seeing themselves and each other as sharing the overall purpose and goals of the social practice. A reciprocal relationship exists between the social practice and the individuals within it, for the social practice cannot exist without the individual and the individual has no point or direction without the social practice (Langford, 1991: 28).

Social practices are constituted with members who teach and socialise new members of the social practice into shared ways of seeing and doing which flows out of reciprocal self-awareness. Such learning and socialisation can occur both formally and informally to assist new social practitioners about what to do, what not to do, what is valued, what is not valued etc. Sunderland et al (2004: 35), paraphrasing Isaacs, highlight that social practices are produced and reproduced over time via such learning and socialisation and emphasise the extent “... to which social practices are created and recreated in ways by persons in positions of power and authority and also by informal dynamics of power within the practice itself”. They suggest the knowledge required to participate in any social practice may range from highly specific and specialised knowledge (e.g. research design and implementation) to unrecognised, everyday and commonsense knowledge.

Social practices have an institutional dimension. This dimension ensures the cohesiveness and continuity of the social practice by authoritative mechanisms such as

by way of power and hierarchy as a means of interpreting changing practice, compliance with the overall purpose and interpretation of tradition. Persons inhabiting such positions within (or from without) a social practice may be in both formal and informal positions of authority (Sunderland et al, 2004; Isaacs 1993; Langford, 1991).

Finally, for the social practice to exist and for it to be recognised as a social practice, there needs to be a societal legitimisation of that practice. Social practices are embedded within relationships with other practices, communities and society. The social practice may both shape and be shaped by the context within which it exists but for it to survive, it must be recognised and valued by the broader community and be seen to be making a valued contribution to that community (Sunderland et al, 2004; Isaacs, 1993; Langford, 1991). For example, before the 1980's, the need for specialised nurses in the care of HIV infected persons would not have been perceived because society was not aware of the disease and therefore no conceptual framework was in place.

Society places certain obligations upon the person involved in the social practice. Individuals are required to behave in certain ways within that practice consistent with its overall purpose. It would be seen as contrary to the social practice of biomedical research, for example, if a researcher malevolently inflicted harm on a participant. Indeed the international guidance documents discussed in previous chapters explicitly prohibit such behaviours.

The overall purpose, in turn, is governed by society as a whole because it is society that is served by a social practice. Therefore, society has an obligation to sanction social practices that do not serve its needs. Codes of conduct, investigative bodies, practice standards and legislative restrictions serve to regulate the actions of individuals who are part of a social practice. For example, adherence to the *National Statement on Ethical Conduct in Human Research*, complying with Therapeutic Goods Administration requirements, obtaining research ethics committee approval for the conduct of trials, all regulate the behaviour and conduct of trials to ensure that researchers do good.

Social practice

In the previous section I explained that social practices are comprised of a number of defining characteristics and can only be examined by exploring the relationship between these characteristics. I said that the direction of a social practice determines its overall purpose (Langford, 1991: 27-31) and that each member needs to be aware of the overall purpose of the social practice. As such, as Isaacs (1993: 3)

states “[a]ll professions are social practices, but not all social practices are professions”. For the purposes of this discussion, I use the term social practice in the sense of professional practices. I am not referring to social practices such as drug use, which do not serve society in the conventional senses used here and indeed are sanctioned by society. In the course of pursuing the social practice/profession, the individual practitioner is called on to make judgements regarding what actions would best serve its, the social practice’s, overall purpose and such practices evolve over time (Langford, 1991: 29). It is not merely an aggregate of the individuals which make up the social practice but each of the practitioners has a reciprocal self awareness of sharing the overall purpose, identity and direction which gives unity to the practice as a whole (Isaacs 1993: 4).

Social practices, therefore, have a unique history, individuals within that practice have their own internal unity with their past through the medium of the social practice and because of this, the social practice itself will have its own internal unity. Therefore members of the social practice *need* also to be reciprocally aware of sharing the overall purpose, tradition and identity of the social practice (Isaacs 1993: 3-4).

Society places certain obligations upon the person involved in the social practice/profession. Individuals are required to behave in certain ways within that practice consistent with its overall purpose which gives rise to the reciprocal awareness of its practitioners. In the case of biomedical research, “two sets of primary interests can be identified: the subjects’ welfare and the scientific integrity of the data” (Morin, Rakatansky, Riddick et al, 2002: 79). It would be seen as contrary to the social practice of biomedical research if a researcher malevolently inflicted harm on a participant or falsified research results. Indeed my previous discussion of the international guidance documents explicitly prohibits such behaviours.

Finally, I stated that the overall purpose of the social practice/profession, in turn, is governed by society as a whole because it is society that is served by the profession. Therefore, society has an obligation to sanction professional practices when they fail to serve its needs.

Relationships of a social practice with others

Mount has distinguished three kinds of relationships between social practices and the community at large: the philanthropic, contractual and covenantal relationship

(Isaacs, 1993: 4). Indeed, many different social practices may exist within a single institution.

The philanthropic relationship is often characterised by self-interest both of the institution and the individuals within the institution. In the foreground of any relationship of this type is the concern for institutional benefit. The institution is also guided more by survival than by the provision of the service for which it is responsible. This relationship is seen as one which is characterised by *optional giving* in the sense that it is the giver who decides who benefits, how much the other benefits and whose interests should be served in the giving (Isaacs, 1993: 4). To use the example of the pharmaceutical company, the company may donate money to charitable organisations both to derive the taxation benefit from doing so and to derive the community kudos and publicity from the donation rather than have any genuine regard for the charitable organisation or its work.

The contractual relationship is one where the service provided is paid for. For example, if one goes to a mechanic to fix a car, one expects to pay for it. With all such work, there is a certain profit margin involved and it is this that the mechanic or service station is concerned with. Not only do they survive and indeed prosper, but they also provide the customer with some benefit. This is essentially a *sharing* relationship. It is characterised by economic considerations as well as considerations of survival. It is structured by the contractual obligations of the marketplace and motivated by profit (Isaacs 1993: 5).

The covenantal relationship is, perhaps, most suited to that of health care provision and, by extension, biomedical research. It is a *giving* relationship and as such more closely relates to vocational professions or those professions which individuals are called to do. As Isaacs (1993: 7) states, it is the covenantal bond, expressed by an overriding commitment freely given for the benefit of others, which is the central consideration for all professions. Mount (1990: 57) argues this ultimately indicates a religious founding. The health care professions have a rich tradition of values such as beneficence and non-maleficence, advocacy, the right to privacy, confidentiality and autonomy which indicate its commitment to this covenantal relationship. Mount asserts institutions should and must be held accountable to a violation of public trust and the covenant which is their very reason for existence (1990: 62). In the context of biomedical research, Lemmens and Singer (1998: 961) suggest that physicians “who have conflicts of interest risk damaging the

trust between them and their patients” and patients “expect that physicians will not be led by motives other than the pursuit of” their wellbeing. They assert that this loss of trust with the particular physician would lead to a loss of trust in the profession as a whole. Were this a widespread phenomena, the public would lose trust in the medical profession as a whole (Lemmens and Singer, 1998: 961). Put in a biomedical research context, the “...application of high ethical standards is essential to ensure that societal trust in research is not eroded, and that subjects enrolled in trials do not become merely a means to an end...” (Morin, Rakatansky, Riddick et al, 2002: 79). Indeed the covenantal relationship between society and academic medicine is said to be so special and different from other academic disciplines, that even “the perception that faculty investigators or their institutions have financial interests that might compromise their independence and credibility cannot be tolerated” (Korn, 2000: 2235). Conflict of interest situations damage the covenantal relationship social practices have with society. It is worth noting that damage to the covenantal relationship can occur whether the conflict of interest is actual, potential or perceived. In particular, perceived conflicts of interest, because they are generated by third parties, may have serious consequences for the covenantal relationship. In all cases, however, the conflict of interest must be actively managed by the social practice. This is another reason why conflict of interest is problematic for AFAO in the consortium because it damages the covenant it has with both its constituents specifically and with society more broadly.

The way in which practitioners fulfil their primary purpose is, as Isaacs (1993: 4) has suggested, through four fundamental dimensions: the temporal dimension, the political dimension, the environmental dimension and the ethical dimension. For the purposes of this discussion, the dimensions have been made into distinct entities. However, in reality, the boundaries of such distinctions can often blur.

The concept of a social practice has considerable significance for this research. The most significant affected community in Australian society in relation to HIV is gay men and other men who have sex with men. This type of community will differ from heterosexual injecting drug users who are the primary affected group in Thailand for example. As such, the approaches used to engage the community, and the community’s response to those approaches to participate in research, may differ. And even if community, however that is identified, is engaged with the research, how do collaborators ensure that those community representatives are effective? Liberati

(1997: 499) claims that even if lay people (for the purposes of this argument read community representatives) are members of research ethics committees, there “is a widespread belief that they are rarely influential”. Therefore, conceptualising HIV biomedical research, in general, and the consortium in particular, as a social practice highlights the importance of looking at the nature of the interactions involved when the ideal of community involvement is put into practice. It also facilitates an understanding of how the inclusion of affected community as an important and integral part of the research enterprise from the start of the research process may play out in practice. The overall purpose of the Australian consortium is the development of a preventative HIV vaccine. All of the consortium members are aware of that purpose and have an awareness, to a greater or lesser extent, of the traditions and social history upon which the consortium was built. However, the consortium also exists as part of the social practice of the Australian HIV/AIDS Partnership and the social practice of the affected community response to HIV. The consortium sits at the intersection of these three social practices, existing as a part of the social practice of HIV biomedical research, the social practice of the Australian HIV/AIDS Partnership and the social practice of the affected community response to HIV as represented by AFAO. This will have implications for the way the consortium operates and will be explored later.

The benefits of conceptualising research, in general, and the consortium in particular, as a social practice is that the framework provides a theoretically and intellectually useful means of making sense of the complex ethical relationships between the actors and, for the actors themselves, a mechanism to enable affected communities to build their capacity and knowledge of biomedical research and for biomedical researchers to gain an understanding and appreciation of the ways in which the affected communities operate and make decisions. Use of the theoretical frame of the social practice will be a key feature of this thesis from this point on.

Conclusion

I have described the specific national and international documents relevant to HIV vaccine development and paid particular attention to the UNAIDS documents which state there should be community involvement in such research, in part as a means of addressing some of the ethical concerns of such trialling in resource poor countries. Because vaccine trialling often occurs in resource poor countries due to

their often high incidence of HIV, I have briefly discussed the ethical problems and challenges raised by those trials such as justice, exploitation and informed consent. In particular, I have discussed the difficult issue of standard of care in such countries as it relates to knowing what counts as acceptable standard of care in terms of what should be provided to trial participants both on the active arm of the trial and on the placebo arm of the trial. Part of this discussion involved the notion of equipoise. I have argued that community participation is a possible way of resolving and addressing some of these issues and that it is ethically required in principle as a matter of justice.

While these ethical concepts aid an understanding of the complex considerations affected community makes as part of the biomedical research endeavour, it is only part of the story. My argument within this chapter is that the consortium I am investigating can usefully be understood as a social practice and that the ethical rationale for community participation can only be applied within such a social practice. As such, I will draw on the concept of a social practice in interpreting the interview data, in addition to considering the more obvious ethical concepts discussed earlier in this chapter.

5

Research Methodology

Introduction

As I demonstrated in chapter 1, affected community is central to the HIV response in Australia and has been for many years. It is unsurprising, therefore, for affected community to be a full partner in the Australian vaccine consortium developing a prime-boost preventative HIV vaccine. As I showed in chapter 2, the science surrounding HIV and vaccine development is highly complex and technical. Given this level of complexity, it is important to determine whether community involvement is achievable in that context. I have outlined the theoretical ethical argument for community involvement in biomedical research by referencing the underlying ethical principles inherent in all human research ethics and outlined both the international and national documents regulating the conduct of research on humans. I have also explored the HIV specific international documents that promote community involvement. So, given this context, my research is important as a means of exploring how community involvement in a particular research context occurs and works in practice and what effect that has on the ethical approach by the consortium to the research being conducted. This is especially significant in Australia, since community involvement was borne out of a socio-political context rather than as an explicit research ethics decision. In this chapter I outline the methodology of the empirical research component of my study.

Aims of this research

The primary aims of this research project were to explore:

1. How community involvement as a full partner in vaccine research works in practice;
2. What effect that involvement has on the ethical approach adopted during the course of the research by the consortium;
3. What implication that has for community involvement in biomedical HIV prevention research; and
4. What implications that has for community involvement in biomedical research generally.

Theoretical framework

This research is not designed to produce a sociological theory explaining personal interactions within the consortium. It is designed as an applied ethics project, aimed at investigating the nexus between the theory and the practice, and ethically evaluating what has occurred there. The theory to be generated in this research will aim to explain how the ethical ideal of community involvement in HIV vaccine research plays out in practice.

Constructionism is an epistemological approach highly relevant to the study of ethics, and applied ethics in particular. As an approach, constructionism suggests there is no objective truth per se but that meaning comes into existence through our engagement with our world. In other words, meaning is not discovered but constructed. In this approach, subject and object (and in this case researcher and participant) “emerge as partners in the generation of meaning” (Crotty, 1998: 9). As a theoretical approach falling within constructionism, symbolic interactionism is described by Hansen (2006: 62-63) as the idea:

... that human actions are a result of the meanings they give to things...; meaning arises out of social interaction; people modify their meanings through an interpretive process.

This approach informs data collection and analysis in my project. It is not an arms-length process of collecting ‘facts’. For example, Paget (1983: 70) described her experience during the course of an interview where she identified with her respondent’s narrative. The questions she asked were congruent with that identification: in other words, this empathic relationship influenced and guided the questions she asked. She reflected that the interview was being controlled by the interviewee and that this encouraged searching, reflective, and extended responses. Put another way, I am an “agent in the text”, which, given my background, may assist in the exploration of themes and issues embedded within the context of the accounts provided by the informants in my research (Reissman, 1993: 14).

This empathic approach may lead to questions of bias in the generation and analysis of the data. However, the concept of bias is not relevant in this approach to research. As the interviews were semi-structured, the participants and I entered into a conversation with one another. Subsequently, we both developed “meaning together” (Reissman, 1993: 55). Thus, by developing meaning together, we were both agents in

the formulation of an account. This shared meaning provided a framework from which we both could interact and inform; it does not “bias” the analysis.

Such accounts (and it is important to note that they are subjective accounts articulated retrospectively within a research context) will provide an insight into the way participants frame their involvement in relation to affected community as members of the consortium and provide the groundwork for further research into this important subject area. It will also provide an indication of how participants understand the notion of community participation, how they may operationalise it and how they perceive its connection with ethics.

Reflexivity

As explained above, the researcher is an active player in the generation of data, so reflexivity is an important consideration to ensure this is handled appropriately. Rice and Ezzy define reflexivity in research in the following way:

Reflexive research acknowledges that the researcher is part and parcel of the setting, context and culture they are trying to understand and analyse. That is to say, the researcher is the instrument of the research.

(1999: 41)

Hanson (2006: 59-60) suggests reflexivity has a number of benefits. It encourages a researcher to consider their role honestly thereby improving their study design and the way they conduct themselves over the course of the project. It also provides a useful framework for questioning the researcher’s own (and their participant’s) underlying assumptions and interpretations. Hansen (2006: 59) argues that “in the interests of establishing researcher credibility” information about the researcher should be contained in qualitative reports. Examples of information she suggests is relevant are age, sex, training and background, any relationship to the research participants or funding bodies or any personal connection with the research topic being explored.

At the time I performed the interviews reported within this research, I was 34-37 years of age. I am a gay man and have been an AIDS Council volunteer in Queensland and Victoria for many years. As a result of that engagement with the HIV sector, I have followed the development of preventative HIV vaccines both nationally and internationally. I am a Registered Nurse Division 1 and have specialist training in

oncology and palliative care nursing. At the time of the data collection, I worked for the Australian Government in aged care complaints resolution. I hold a Bachelor of Nursing and a Master of Arts (Research) in which I explored nurses' accounts of oncology and palliative care using an applied ethics analytical framework. This means that on the one hand in some aspects I am an 'insider' who is known in the community sector but not part of AFAO's decision making bodies. Since undertaking the interviews, I have been nominated as one of the two AFAO voting delegates from Victoria. I also bring 'outsider' perspectives, for example in terms of being able to comment on the governance arrangements in the consortium without experiencing a conflict of interest. As a result of my 'insider' status, I am sensitized to the ways in which the community sector operates which may provide me with greater insight into what is occurring. Liamputtong and Ezzy (2005: 178) suggest this may help formulate meaningful questions and to assist in making the result of this research more useful. However, as Hansen (2006: 82) also suggests, this may lead to discomfort or feelings of disloyalty to the researcher's friends or, as Liamputtong and Ezzy (2005: 179) state may cause me to feel uncomfortable about the information obtained. So, while I may derive rich accounts from the participants in my research, I may self-censor the results. As I describe later in this chapter, there are a number of approaches to rigour which mitigate against such censorship.

As I have previously stated, because the participants in the research and I are agents in the text and develop shared meaning from our participation, a grounded theory approach was the best choice as the research methodology to employ.

Methodology

A grounded theory approach was first articulated by Glaser and Strauss in 1967 which provided a link between the concept of symbolic interactionism and a qualitative research approach (Hansen, 2006: 63). Crotty (1998: 71-78) suggests symbolic interactionism "... explores the understandings abroad in culture as the meaningful matrix that guides our lives". He suggests that, as conscious and self-conscious entities, our very sense of being arises from the process of symbolic interaction. We consider our situation from the perspective of an actor, in the place of the other. We give significant meaning to the 'symbols' through which we communicate, like language and dialogue. Ethnography is a powerful example of a

form of enquiry in the symbolic interactionism tradition. Grounded theory may be viewed as a specific type of ethnographic enquiry.

Grounded theory methods arose from a collaboration between Barney G. Glaser and Anselm L. Strauss during their studies of dying in hospitals. During this study, they developed systematic methodological strategies that other social scientists could adopt in other settings. Their approach, which was cutting edge at the time, joined epistemological critique with practical guidelines for action. They intended to construct theoretical explanations for social practices. They provided a powerful argument that legitimised qualitative research as a credible methodological approach, rather than as a precursor for developing quantitative instruments. Glaser and Strauss came from different and competing traditions. Glaser came from Columbia University and the epistemological assumptions, logic, and systematic approach of grounded theory reflect his positivistic roots. Strauss, coming from the Chicago school, viewed human beings as active agents, rather than passive recipients, in their lives. He assumed process, not structure, was central to human existence and that humans developed structure through engaging in processes. Subjective and social meanings emerged through our use of language and action. Thus, Strauss utilised both symbolic interactionism and the Chicago legacy of ethnographic research. Since their ground breaking work, they have each taken grounded theory in divergent directions. Glaser has remained consistent with both his tradition and earlier statement of grounded theory method by defining it as a method of discovery, treating categories as emerging from the data, relying on direct empiricism and analysing a basic social process. Strauss moved the method towards verification and, with Juliet M. Corbin, furthered this direction. The notion of verification can be considered as the comparison of qualitative data against the emergent or established theory under examination to validate that theory (Charmaz, 2006: 4-8).

Strauss and Corbin (1998: 12) define grounded theory as theory "... that was derived from data, systematically gathered and analyzed through the research process". Hansen (2006: 62) defines it as "... an inductive technique that involves highly descriptive accounts of social interaction and a focus on the meanings and interpretations of research participants". The approach I take in this study is largely Straussian, relying on the interview text as the primary data.

Grounded theory, in its purest sense, states that the researcher "...does not begin a project with a preconceived theory in mind" but, rather "... begins with an area of

study and allows the theory to emerge from the data” (Strauss and Corbin, 1998: 12). Meanings and interpretations emerge as themes from the obtained data during analysis, enabling the researcher to categorise them in such a way as to yield a theory (Bowen, 2006: 2).

Bowen (2006: 3-4) suggests that part of a grounded theory approach includes what he states are “sensitizing concepts” whether they are explicitly identified or not. He states that “[s]ensitizing concepts draw attention to important features of social interaction and provide guidelines for research in specific settings” (2006: 3). Taking a grounded theory approach, researchers may use sensitizing concepts as a framework for research analysis or in examining major codes in the data with a view to developing thematic categories (Bowen, 2006: 2-3).

In the context of my research, the sensitizing concepts that exist include those social history concepts outlined in chapter 1, the scientific concepts outlined in chapter 2, the general ethical theories in chapter 3 and the specific ethical theories and issues outlined in chapter 4. In particular, the social practice concepts and the core principles espoused in the *Good participatory practice guidelines for biomedical HIV prevention trials (2007)* provide a useful framework for analysing the data generated from the interviews with consortium members.

My theoretical framework of symbolic interactionism and the grounded theory approach provide the basis for my choice of conducting individual interviews. I employed what Patton (1990: 280-290) describes as the informal conversational interview. Berg (1995: 31-35) also describes this type of approach as a semistandardised interview.

This approach enables the formulation of predetermined topics or questions by the researcher but also allows for probing in light of the responses received from the research participants. This helps in allowing the participant to frame and structure their responses so that the phenomenon of interest unfolds as the research participant views it, not as the researcher views the situation (Berg, 1995; Marshall and Rossman, 1999). As Marshall and Rossman (1999: 110) suggest, “... interviews allow the researcher to understand the meanings that people hold for their everyday activities”. This approach has been chosen over a survey type questionnaire as these meanings will be important to the analysis of the accounts obtained and it is important not to “... do violence to the respondent’s meanings” (Dingwall in Miller and Dingwall, 1997: 59). Questionnaires also limit the researcher’s ability to “...delve into tacit

belief and deeply held values...” and do not elicit patterns of interaction or social relationships, which was critical for my work (Marshall and Rossman, 1999: 129-131). Those social relationships exist within the constraints of the Australian HIV Vaccine consortium.

Research Plan

Sample:

In order to elicit answers to the questions posed in the aims of the research, I endeavoured to interview all members of the consortium. The names, positions and organisational membership of each of the consortium members (except for the community representatives) were published on the National Centre for HIV Epidemiology and Clinical Research’s website. I obtained consortium membership details from there. Determining who represented community on the consortium was a matter of writing to the Executive Director of AFAO. Given the commercial-in-confidence nature of the enterprise, members of the consortium are the only ones with direct personal experience or involvement of community participation as full partners in the vaccine research enterprise. All consortium members, not just the community representatives, were invited to participate in my research as I wished to know about the process of community involvement and its effects on the vaccine development enterprise as a whole, not just the personal experience of the community members. The numbers able to be interviewed, therefore, are self-limiting to the number of consortium members. As such, the sampling approach taken in my research was purposive.

Throughout this thesis, the term ‘consortium’ refers to two related concepts. The first meaning refers to the contractual relationship between the organisations developing the prime-boost preventative HIV vaccine. The second meaning of consortium refers to the group of people participating in the governance of the vaccine trial. The second meaning of consortium is the predominant meaning used throughout this thesis. The consortium members included representatives from:

- * The Australian Federation of AIDS Organisations (AFAO)
- * Australian National Council on Hepatitis C, AIDS and Related Diseases (ANCHARD)
- * Australian National University (ANU)

- * Commonwealth Scientific & Industrial Research Organization (CSIRO)
- * National Centre for HIV Epidemiology and Clinical Research (NCHECR)
- * National Centre for HIV Social Research (NCHSR)
- * University of Melbourne
- * University of Newcastle
- * Virax Immunotherapeutics Inc.

The representatives participating in the consortium remained stable throughout the course of the life of the consortium with one exception. Virax Immunotherapeutics Inc. withdrew from the consortium.

The sampling approach adopted in this research is an elite interviewing approach. Elite interviewing is described by Marshall and Rossman (1999: 113-144) as a specialised case of interviewing that focuses on individuals that are “influential, prominent, and/or well-informed people” who are selected on the basis of their expertise. They suggest elite participants are able to provide valuable information about the organisation to which they belong and that organisation’s relationship to other organisations. As vaccine research is highly publicised and competitive, participants in the vaccine development endeavour are prominent in their field and fall into the ‘elite’ category.

Recruitment

As I have mentioned, the names, positions and to which organisation members of the consortium belonged were published on the NCHECR’s website. Once I determined who to invite to participate, I obtained their postal addresses and sent letters outlining the research aims, the types of questions I might pose and the limits to confidentiality of their participation in the research (discussed later in this chapter). I sent twelve letters of invitation and received responses back from six of them, one of which was a letter declining to participate. Two letters were sent to AFAO, one to the Executive Director and one to the International Policy Officer. Two letters were also sent to NCHECR, one to the Director and one to the Head of Therapeutic Research. I received responses from AFAO, NCHECR, NCHSR and the University of Melbourne. The refusal came from the head of the consortium who was also the principal researcher and the Director of NCHECR. There was no response from the University of Newcastle, ANCHARD, ANU, CSIRO and Virax Immunotherapeutics. At a later stage in the research, I sent a second letter of invitation to the consortium

members from the ANU and the CSIRO after the first invitation indicating the initial findings of my research so far and offering a final opportunity to participate as a key informant. At this stage, Virax Immunotherapeutics was no longer involved in the vaccine research. I determined that both ANU and CSIRO consortium members may provide perspectives different to the other participants I had already obtained interviews from. They again did not respond. I also invited the CEO of the consortium to participate as an alternative means of obtaining the perspective on the consortium I was unable to obtain from the Director of NCHECR. That offer was accepted and an interview with the CEO occurred.

Of those participants who did not respond, the perspectives of the consortium members from the ANU and the CSIRO would have made an interesting addition to this research. Both consortium members have not, historically, participated in the Australian HIV/AIDS Partnership and are not familiar with working with community representatives in such key roles. Those insights may have added to the results of this research.

Data Collection

Prior to commencement of interviews, I ascertained whether the participants understood the consent form and were freely consenting to the interview process. I also verbally reinforced that the participant could withdraw from the interview process at any time and that, due to the discrete nature of the participant pool, it may not be possible to maintain absolute confidentiality of their participation. I conducted nine semi-structured interviews, using six key questions to guide me. Those questions were:

- * How are you involved in vaccine research?
- * How have you found the general experience of working in the area of vaccine development?
- * Do you see any value of having community representatives involved?
- * Why do you think that?
- * How important is it relative to other things?
- * Have you changed your view over time?

Reflective questioning occurred thereafter to enable the exploration of issues encountered and identified by the respondent. This is consistent with Bell's (in Riessman, 1993: 34) approach of listening with a minimum of interruptions and relating questions and comments to responses by using the participants' words where possible.

Exploring the issues already mentioned by the participant was designed to limit the extent to which I, as the researcher, directed the answers obtained. The intention was to allow the participants to structure their account as much as possible rather than a structure being imposed on them. Other questions specifically targeted at eliciting participants' views on community participation in the process of vaccine trialling were raised at appropriate times throughout the interview process to focus participants on the subject of this research. The approach also allows the researcher to probe the particular foci identified by the participants concerning the relationships identified within this research. These relationships were explored only if the participant had identified them previously in the course of the interview. The interviews were informal and proceeded in a conversational style (Field, 1984: 62). Notes were taken at interview about the key themes or phrases emerging from the participant's account. These were utilised as points to return to if the need arose and as prompts during the transcription of the interviews.

The interviews were recorded on audiotape by a recorder placed in an unobtrusive position. The tape recording approach was adopted for accuracy of transcription and to limit any tendency for personal interpretation at interview when using a note taking approach. Once recorded, the tapes were transcribed and printed.

The participants were given a choice regarding the location of their interviews both for ethical reasons and methodological reasons. For methodological reasons, my preference was for interviews to be conducted at their place of work. This required travel interstate to conduct some of these interviews. This was important because the participants were describing interactions in their professional lives and I wanted them to be at ease when describing their roles in the consortium and able to feel as though they were in control of the interview. All interviews occurred at participants' places of work except two. The other interviews occurred in one participant's home and the other at a café nearby. I sought and obtained permission to record the interviews which went from between 30 and 60 minutes duration.

The participants were very willing to participate in the interviews and were interested in the results once they became available. I did not detect any discomfort or reluctance to be open and frank with me, although this was situated in the context of commercial-in-confidence considerations. Being part of the social practice being researched lessened the "asymmetric power relationships between interviewee and interviewer" (Sarbin, 1986: 248-249). My own knowledge and experience, both as a

member of the affected community and as a former clinician assisted me in being able to relate to both community and non-community members alike. This shared context and understanding encouraged a more conversational style of interviewing and elicited richer information from the interviews. I conducted two follow up interviews with two participants approximately 18 months after their primary interview to clarify specific aspects of their first interview. Preliminary analysis of the interviews indicated some ambiguity on matters arising from the data which were central issues to this research, and I decided that this made it important to seek clarification.

Data Analysis

As Riessman (1993: 5) indicates, there are many ways that discourse may be analysed and interpreted. Some approaches use a reductive method to transcription and analysis, for example, reducing a lengthy transcript to one or two core sentences. Others look for the characteristics of the discourse, for example, the orientation and the complicating actions (Reissman, 1993: 25-53). In order to retain the meaning of participants in this research, I have retained large sections of transcript so that the rich descriptions of the participants in the consortium are not lost.

Hansen (2006: 148-149) describes thematic analysis as an inductive process where the researcher is guided by the data rather than an existing hypothesis. She qualifies this by stating a researcher might have some interpretive idea about what might be occurring in the data they collect as a result of their training, experience and knowledge, but the researcher approaches the analysis of the research with an open mind. This is consistent with the notion of sensitizing concepts describe previously in this chapter. Rice and Ezzy (1999: 194) describe thematic analysis as a means of allowing researchers to generate themes as they perform the research. There are two important characteristics in a thematic approach. The first is that it is an iterative process and the second is the coding of data (Hansen, 2006: 149).

Hansen describes the iterative approach as immersing oneself in the data. This is undertaken by collecting, transcribing, reading and analysing the data obtained during the course of the research (2006: 149). During the course of my research, I conducted the interviews over time and transcribed the accounts obtained from the participants as I received them. This meant that ideas arising from earlier interviews were used to inform later interviews.

The second important aspect of thematic analysis is the coding of data. Coding refers to the identification of “interesting sections or ‘chunks’ in the qualitative data so that they can be identified and sorted” (Hansen, 2006: 149). I coded my transcripts by using various coloured highlighter pens to identify different aspects of the accounts that were interesting or raised important issues.

I did not strictly follow coding in the traditional way, that is, line by line open coding followed by axial and selective coding (Liamputtong and Ezzy, 2005: 268-269). As applied ethics predominantly deals with the relationship between people, and affected community participation in the consortium is the novelty, I used affected community as the central point of reference and sought to describe and identify the relationships they have with others. The common major themes that emerged from the first phase of analysis concerned the relationships of the community representatives with the other consortium members, with the affected community and with society more generally. The second analysis phase involved the identification of relationships between each of these major themes. The final phase of analysis identified the key theoretical ideas to emerge from all of those accounts across all of the major themes.

This analysis sought to accomplish two aims: the description, illumination and portrayal of the nature of community participation as a participant in vaccine trialling from a variety of different perspectives; and, drawing on the ethical frameworks such as those articulated in Chapter 3, the interpretation and appraisal of that participation which interrogates the ethical challenges faced by both the affected community and other members of the partnership.

Rigour

As Hansen (2006: 49) states, a “... researcher should provide a clear account of the research process, allowing the reader to judge the dependability of the research”. The notion of rigour in qualitative research such as the type I have described in this chapter differs from the understanding of rigour in quantitative research. In quantitative research, importance is placed on validity and reliability. Validity is concerned with the extent to which the measurement used in the research measures what it claims to measure whereas reliability is concerned with the consistency of the research findings and whether it, the research, can be repeated and obtain similar results. Validity and reliability are achieved through the strict adherence to rules of

sampling, measurement, statistical methodology and statistical power of the data analysis (Hansen, 2006: 47-48). Such rules do not apply to qualitative research. This does not mean that qualitative research is not concerned with rigour. Rice and Ezzy (1999: 35-41) offer a useful framework for examining rigour in qualitative research.

Theoretical rigour refers to the clarity of the theoretical framework used in the research and the ways in which data are collected. In this chapter, I have outlined the theoretical framework I have adopted in this research and have described the way in which I have collected data, consistent with that theoretical and epistemological approach.

Interpretive rigour is the idea that a research approach has rigour if "... it accurately represents the understandings of events and actions within the framework and worldview of the people engaged in them" (Rice and Ezzy, 1999: 36). This is also described as confirmability (Hansen, 2006: 49). In the next chapters, I make extensive use of quotes from the participants in my research which allows them to describe their experiences of working in the consortium and allows the reader of this research to form a judgement of my interpretation of those quotes for themselves. In addition, my supervisor and I undertook an independent thematic analysis of the data obtained in the nine interviews and there was a high level of concordance of the themes identified between us. These two approaches combined point to high levels of interpretive rigour.

To "...avoid unwarranted overgeneralisation and unsubstantiated conclusions", methodological or procedural rigour is required (Rice and Ezzy, 1999: 36). This type of rigour is described as one which promotes interpretations of the research that are understandable. As I have done in this chapter, an explicit account of how the research was conducted and how the findings in the research were arrived at are critical.

Evaluative rigour refers to the need for ethics in practice and a high level of reflexivity on the part of the researcher. This type of rigour also takes into account the political dimension of the research. As Liamputtong and Ezzy (2005: 283) say, the "... positivist utopia of independent objectivity is unrealisable" and the "... results of the qualitative data analysis clearly exhibit and represent the desires, hopes, and theories of the researcher". I have described my personal connections with this field of research earlier in this chapter. I also had a theoretical position, which grew and developed during the research. My position is that biomedical research is a social

practice, the Australian HIV/AIDS Partnership is a social practice, the affected community response is a social practice, and the Australian Vaccine Consortium is both a sub-set of those social practices and an emergent social practice in its own right. Therefore, it is vital to get comprehensive and accurate accounts of the socio-political dimensions of that practice.

Prior to commencing this research, I sought and obtained approval from the School of Population Health's Human Research Ethics Committee. As I have noted previously, because the sample size of this research was small and the participants so well known, there is a possibility that confidentiality of their participation cannot be absolutely maintained. Prior to commencing the research I raised this issue, both verbally and in the plain language statement and consent form, with the participants. None refused to participate in this research as a result of concerns for a possible breach of confidentiality. As I have described, it was important to obtain accounts from individuals with experience and knowledge of the workings of the consortium and the only people able to do that were consortium members themselves. Therefore, I was required to balance the need for absolute confidentiality with the method of obtaining relevant accounts for my research. In later chapters I have also labelled quotes attributed to community representatives with a (C) and from non-community representatives with (NC). I have assigned each participant with a number within that group and have indicated whether this is the first or second interview for the informant. For example, the second interview from the second community participant would have a label of C22. The first interview from the third non-community participant would have a label of NC31 and so on. This approach is designed to make the data presented more meaningful to the reader but it also adds to the risk of a loss of confidentiality. So, in order to address the potential breach of confidentiality, I have alerted research participants to that possibility and obtained consent from them prior to the interview taking place and I have also labelled the accounts in such a way as to minimise the possibility of the participant being identified.

Despite careful efforts to ensure rigour, there are limitations in any research. The research is limited because, as a result of having the invitation to participate declined or not responded to, those individuals who did not participate may have brought interesting and key perspectives to community involvement in the vaccine development enterprise. The participants from the CSIRO and the ANU did not respond to my invitation to participate. Interestingly, neither of these groups have

traditionally been part of the Australian HIV/AIDS Partnership so may have had interesting insights, both positive and negative, into community participation in the consortium.

Another limitation is that the situation with the Australian HIV vaccine consortium was so unique. Participants' views and experiences cannot be directly transferred and applied in other settings. However, my analysis and discussion take account of the unique nature of the context. The recommendations from this research do not assume that the Australian context will be mirrored elsewhere, but rather are intended to be applicable in a range of settings, for a range of different styles of community involvement.

Conclusion

In this chapter, I have described the aims of this research and described the theoretical, epistemological and methodological approaches used to achieve those aims. The way in which the data were analysed is clearly explained and the limitations to the research described. In the next chapters, I will present and discuss the research findings.

6

How Community Involvement Works in the Consortium

In previous chapters, I suggested, based on a theoretical understanding of social practices, that the consortium is a particular type of social practice and that it was constituted by practitioners of the social practice of the Australian HIV/AIDS Partnership, of the social practice of the affected community response and practitioners of the social practice of biomedical research. In this chapter, I draw on the interview data given by the informants to highlight the key ethical considerations which the informants refer to in their accounts of the consortium's work. As part of this, I provide a description of how this particular social practice works, particularly in relation to the way community involvement plays out.

I describe the ways the representatives of the community participating in the consortium interact with other members of the consortium and highlight in-practice examples of the three distinct social practices coming together. This analysis shows how the intersection of those social practices affects the work of the consortium and the consortium members. Of the six characteristics of a social practice, described in a previous chapter, of particular relevance to the community members on the consortium are the institutional dimension inherent in a social practice, the unity of purpose and the reciprocal self-awareness of the practitioners of a social practice. A fourth characteristic also highlighted in the following accounts is the learning and socialisation aspects of a social practice.

How the consortium works on scientific and ethical integrity

One key component of all international documents on biomedical research is that the research must have both scientific and ethical integrity. These are broad headings and need to be worked through for each particular project. In this section, I provide an insight into how the consortium worked through aspects of the scientific and ethical integrity of their project. A large proportion of what the consortium discussed related to achieving this objective. I discuss in particular, informed consent, data monitoring and safety, balancing competing interests and the scientific complexity of the consortium's work.

Informed consent processes/education processes

One major aspect of ethical integrity is informed consent. The understanding of what informed consent is all about differs between the different social practices from which the consortium members came. The involvement of community changed scientists' understanding of consent, but the community also learned much about it. The following quotes show the complex nature of the issues they worked through. Part of the way in which the biomedical scientists' behaviour changed is reflected in the rigour or otherwise of the informed consent processes and education programs in the trial. In particular, this informant sets out the ways in which informed consent is ensured during the trial process. The emphasis is not only on the process itself, but on flow on effects of the trial in terms of behaviour and attitudes of both the trial participants and the affected community more broadly.

C21 ...So the work that we've been doing recently is preparing the, you know, the participant information and particularly the recruitment information with the aim of, you know, ensuring informed consent, a high level of informed consent. So we've been producing, a website, booklet... So there's that range of work. The other thing is monitoring the interest and any possible impact, hard to measure, within the community, within the gay community primarily... Oh, yeah, so that's, you know, engaging with gay media through AIDS councils in terms of education that's provided to, you know, community and things like that. And that might not be a lot of work because we've not, what we don't want to do is create an issue there that isn't one. But what we want to, I guess, the main thing we're looking at is that there isn't a level of vaccine optimism that's gonna have a negative impact in terms of people's behaviour... Well, I mean, the very first task is ensuring that the gay community understand what this trial is and what it isn't... So, that kind of information about people understanding having a good understanding of what the trial is and what it isn't.

C22 But I think, one thing that brings up, I guess, turning to a bit of a community perspective, is the issue of informed consent. And

informed consent meaning that any participant in the trial understands what the full risks are and is told and has access to the results of any relevant previous trials. So that anyone going into a subsequent trial is aware of what the results are.

AFAO's focus on informed consent and education processes is borne out by this non community informant. The inference from the following extract is that the processes are more comprehensive as a result of AFAO's involvement.

NC11 ... so the most, I guess, tangible benefits of being run, um, AFAO have helped design our consent forms so, you know, with a sort of a public community perspective on that. They've helped with recruitment of subjects to the trial. Sort of put the word out, held information sort of nights and things. They've certainly helped with media both for starting the trial and when it was the results were announced, helped media statements and what this means for the community... And they've been linking with Thai, similar Thai community organisations, sort of imparting their, sort of wisdom from the process into the Thai community partners who will be participating in the Thai trial, so. No, it's been tremendous.

This informant describes the proposed process in Thailand and particularly emphasises the notion of a group informed consent process as opposed to an individual consent process.

C11 Yeah, well, I think informed consent's quite interesting there. I was, in one of my trips, I sat in on one of the sessions where they were, you know, kind of explaining to me the, the centre that's doing it HIVNAT [The HIV Netherlands Australia Thailand Research Collaboration], about general practices about clinical trials, not necessarily for vaccines. And, kind of an interesting Thai model where they are prefer to be in groups rather than individually... You know, like four-six people where the Thais figure that they really like to have someone else there, buddy there,

and have everyone ask questions and have this group process where they feel much more open and confident and able to speak. And then, after all the questions are answered and, you know, they've talked and discussed the issues and run over the informed consent thing, then they have the choice to sign it. So I think it's a different model...HIVNAT already have an informed consent process and they, I believe, are sanctioned internationally by some sort of clinical trials network that they work to international acceptable standards, and I imagine that if the community folks wanted to tweak that, then they would alter it but not too much.

This next informant outlines the comprehensive nature of the informed consent process developed for the trial. Of particular note in the following account is the tested and repeated checking on participant's understanding of their participation in the trial and continual access, via a variety of methods (face to face contact, discussion boards, newsletter etc.) to information about the trial. The comprehensive nature of the informed consent process used in this trial would seem to be a useful model to adopt in other biomedical trialling processes.

C21 Well, I guess, briefly the way it's working is that we're sending people all to the one source. If people have questions, send them to the trial coordinator. We don't want the information to be given by a whole range of people. So, people will go direct, their first contact will be with the trial coordinator and if they are interested in the trial and participating, then they'll be sent an information package. Which is a detailed booklet. They'll get a self questionnaire which goes through risk factors so people can see, you know, is this trial for me or not? So at that stage they can see whether they're eligible or not. Then the next phase is they will come in for an interview. So they'll be interviewed where their eligibility will be, will go through in detail. And that's health as well as risk status of major health issues and things. And, then there is a period where, like a cooling off period, I guess, before they actually consent. And throughout that time, the trial

coordinator is available to ask any questions at any point. We also, on the website, which is, a whole, a range of information, is also a discussion board. Which is something we're sort of trialling as well, so that people can ask questions, people can talk about..

...

So we've got two discussion boards. One before people enrol for anyone so you and I can just go on and talk about, you know, the issues and ask questions. And then we've got a closed discussion board which is just for participant on the trial.

...

GD So how are you assessing what people know, have a level of knowledge in this consent process.

C21 They do a test.

...

Yeah, so, before they consent, they need to, they'll do a test, which will kind of ask questions, you know, don't know what they are but a crude question of you know this vaccine will protect me from HIV? True, maybe... And, you know, having done this whole list of questions, some decision will be made of, yes, no, we need to sit down and discuss some more things with this person. To ensure that they've properly understood, so yeah.

....

C22 ...So, we set up a web based discussion group, we have a face to face, set up a monthly face to face discussion group, a regular newsletter and occasional information sessions. So there was a discussion group but then occasional information forums as well.

And also access, the regular clinical contact with the nurse and access to a counsellor whenever it was requested.

GD Ok, so the consent process is the same in Thailand?

C22 As far as I'm aware, it is. I've had a quick look at the consent document and what would be included in the formal consent meeting, and yes, it's pretty much the same. I think what would, were it would differ slightly is the information materials that are provided to interested people... So the information that's provided to them, would include results of the Sydney trial.

The decision to include the poor interim results from the Sydney trial may have had an impact on recruitment of participants in Thailand, however, inclusion of the Sydney results is consistent with the high value of informed consent which the informants espoused during the course of this research. The Sydney results are a relevant piece of information potential trial participants should have in order to make a fully informed decision about their participation in the trial. Withholding such information diminishes the possibility of fully informed consent for those participants.

Balancing competing principles/ethical analysis

As demonstrated in the previous chapters, biomedical research ethics is based around core principles. In certain circumstances, those principles come into conflict with each other and require balancing. The consortium dealt with this too, as is demonstrated in the following quote. This informant is the only one to have explicitly mentioned the way in which the principles involved in making decisions in the consortium involve a balance of competing principles.

C31 ... but applying those principles to the circumstances that arise is often extremely complex and requires you to balance areas where your principles are competing with a range of other principles and values that drive your organisation.

- GD Due you think there's a degree of tension between those specific areas like ethics, law, science, community? Due you think they can be contiguous, contiguous in terms of...
- C31 Well no, obviously they can't because if they could, you'd feed all of this into a computer program that would balance your interests in line with some formula. I mean what makes this interesting work is that there are a set of competing principles there as there are with all difficult decisions and it's about finding a path that doesn't do violence to, that does violence to as few of those as possible. Adding to that the kinds of egos that are around in this area and it makes it a really interesting area to work... That confronts a whole range of things that we stand for and we say yes that's there sitting right in front of us, we can't go under it or over it or around it so we have to find a way of working through it. This has raised a number of those issues. And I think one of the benefits in having a consortium approach to this is that a range of people come to that table with a range of different perspectives. And there have been a whole set of discussions in the consortium, most of which I can't talk to you about, where that issue's arisen and isn't surprising that it would.

Of interest to note in this extract is the imagery elicited by this informant in relation to 'doing violence' to as few principles as possible and 'finding a path' through those competing interests. This is consistent with the process of ethical decision making described in principlism.

Principlism is described as that position that holds that "*a priori*, there are generalizable principles and rules which should universally determine one's ethical stance" in a particular situation (Mitchell and Lovat, 1991: 15). However, as Beauchamp (1994: 49) suggests, principles are abstract rallying points in health care ethics, rather than "solely sufficient or final appeals". The most common criticisms of such an approach is that it is not possible to apply dogmatic rules to every situation encountered because every situation is different with different variables and nuances. However, principles in research ethics (as in other contexts) are not rigid rules.

Principlism envisages exactly the type of balancing described by this informant. The balancing, however, is complicated by the social context of the situation (Lewins, 1996, 21-36). As Lewins (1996: 35) states, "... we bring to social situations certain moral implicit assumptions, even if these do not end up shaping our moral responses". In other words, the nature of the social situations we find ourselves in influences the way we ethically respond to those situations. Beauchamp (1994: 52) states "... there is no escape from the exercise of judgement in circumstances of uncertainty..." but that the infringement of a principle must be justified given all the circumstances and must constitute "... the least infringement possible". And that would seem to be the approach being described by the previous informant.

Challenges of the work :Grappling with the scientific process

For the consortium to ensure scientific integrity, it has to deal with scientific complexity and the frustrations and set-backs that go along with it. While the development of a preventative HIV vaccine is novel and enterprising, the following informants explain the difficulties in motivation around such endeavours.

C11 Ah, over time. Hmm. Well, you know, I mean, I'm surprised how slow HIV vaccine work is. You know, I knew that we'd be missing timelines here and there, but it has been a long, drawn out process and I think for administrative, scientific, so many different reasons, we're more behind schedule than we expected. And, you know, that's been interesting to observe, how complicated the science is and how many checks and balances they have to go through which is good.

The complicated nature of the work reinforces the views expressed previously in this chapter in relation to the informed consent process. As I discussed in chapter 2, the development of a preventative HIV vaccine is a complex, challenging task involving highly complex science. Obtaining informed consent and developing a plain language statement dealing with those complicated issues is challenging.

C12 It's really depressing in some ways. I think it's interesting how the question of how we manage to continue to do work which is

important but have realistic expectations and what we use to do our work. You know, the prediction about a vaccine in 10 years if we get enough funding etc etc. Well, you know, I don't think that's going to happen and that's what people are, kind of, saying. We're in it for the long term. The idea of vaccines is so exciting to people and the idea of an HIV vaccine is so exciting that it's probably not going to go away. And it's too sexy really as a concept. So, you know, and I don't think that people should give up on it entirely. I think that it does sound like that there has been scientific progress and the other thing is, well, you know, they made vaccines for things that they didn't know how the disease worked in the first place or how the vaccine was going to work in the first place either. So, I don't think it's out of the realm of possibility that an HIV vaccine, either therapeutic or something that slows the progress of the disease might come up some time. However, at the moment, we need a scientific breakthrough which isn't necessarily about money at all. We need a scientific or conceptual breakthrough in order to go somewhere. So much hope being placed in, I find is, technology and the theory and it's not really being born out at the moment.

NC21 ...the notion of an AIDS vaccine, the reality is an AIDS vaccine at the moment is a pipe dream... I'm disappointed. I thought, as I said, there were some moments during the, earlier, particularly during the monkey trials, the Macaque trials, where it looked like we had something that might really work. And, the excitement in the men themselves was actually quite obvious, I mean, it wasn't as though they were pretending, I mean, a couple of them were really quite excited and that was very infectious. I mean you could tell. So I think there's disappointment but I think there's still some sort that maybe, I mean, they're going to do the trialling in Bangkok with a much smaller group of people. And I think they're doing that and NIH at the moment are going along with it

but I think there may be some advantage in changing the dosings and how often.

Interestingly, inherent in the previous extract is another balancing of competing interests. On the one hand, discontinuing with trials that show little promise or, on the other hand, continuing the trialling with different dosages. This raises concerns in relation to whether there is ethical justification for conducting further trials. One of the fundamental concepts in human research trialling is the notion of equipoise as I have discussed in a previous chapter. As I discussed, equipoise relates to whether there is genuine uncertainty in relation to the therapeutic outcome of two treatments for a disease (Angell, 1997: 847). If that notion of equipoise does not exist, or there is not a genuine scientific question to answer, conducting the trial may be difficult to justify on ethical grounds.

In the current case, the trial in Sydney found no immunogenic response to the trialled preventative HIV vaccine. There was, however, a slight immune response in some participants (mentioned by an informant later in this chapter). On that basis, therefore, some of the scientists involved in the consortium believed that increasing the dose of the vaccine might elicit a more favourable response. Is there a genuine scientific question to be answered? Yes, probably. However, the scientists have invested many years developing the vaccine construct and may not be entirely objective in considering whether to trial a different construct in Thailand or not. At the time of this interview, the NIH was prepared to entertain a different construct being trialled in Thailand. The NIH, also, has invested considerable funding in the development of the vaccine construct but is one step removed and less likely to be invested in the outcome of the trial.

Data Safety and Monitoring Board

In accordance with standard scientific practice, the consortium established a Data Safety and Monitoring Board (DSMB). A DSMB receives the interim results of a trial, often unblinded, to determine whether the participants are at risk from the drug that is being trialled. This is done to determine whether the trial should continue or be stopped on safety or resource allocation grounds. One particularly problematic area for biomedical prevention research is that risks to participants include changes to their protective behaviours, not just the physical effects of the drugs. The following

informant highlights the need to consider behavioural as well as biomedical data when Data Safety and Monitoring Boards consider whether trials ought to continue or not. This raises a further question about what expertise the Data Safety and Monitoring Board ought to have.

NC21 Amongst populations from where the participants are drawn. Like treatment optimism, it's a sort of vaccine optimism and one needs to keep an eye on it. And I certainly remember having an argument, not an argument, a discussion with Jose Esparza from WHO some years ago, many years ago, saying that I thought in fact that if you were trialling a vaccine and what you discovered was the populations at large, that their safe sex began to fall apart and increases in HIV began to occur, then that should be a reason for perhaps, maybe not stopping the trial but actually responding to what was going on in the population and I thought it should be built in to the safety monitoring board.

This informant believes that behavioural outcomes in the trial participants should be built into the information triggers for the Data Safety and Monitoring Boards. It is unclear how such triggers might work or whether, indeed, they are legitimate triggers in the first place.

C31 Yep, I don't know whether there's been a DSMB that's been established but I expect again, there'd be a community person that would sit on it because, I mean, that would be quite uncontroversial that there would be because it's so much of the way in, as the interaction between community and drug companies who are doing clinical trials. And that means that by sitting on the DSMB actually get access to more data than the researchers have got because you actually get to look at unblinded data before a trial's completed. Now, that's just been so much of how we've operated.

What is clear from the preceding extracts is that there was an expectation that a community representative would sit as a member the Data Safety and Monitoring

Board for the trial. It is unclear whether such a position was brokered but certainly, there was an assumption by this informant, that it would occur.

Level of efficacy

The affected community needs to understand and become familiar with the issue of the level of efficacy at which it would be acceptable to endorse the introduction of an HIV vaccine/biomedical prevention approach. The following quote from the informant demonstrates the complexity in this task.

NC21 Yeah, well, my understanding is that you'll get HIV but it won't replicate. But they don't know how effective it will be and whether it'll be 20% effective or 90% effective or, and when you ask someone what does 20% effective mean and what does partial efficacy mean, it's actually very complicated. And I don't think they know and I'm not suggesting they shouldn't be trying to find out. But that also raises enormous issues around safe sex. Huge issues. Because, I suspect, unless people are really aware of that, if you get vaccinated, you're not going to use a condom and it's going to be very hard, if the world does produce or virology does produce a partially effective vaccine, which may in fact in high prevalence countries be very useful in terms of bringing down prevalence, it may be a disaster in the developed world where in fact we haven't got the prevalence, high prevalence. And that's sort of, that issue really needs to be really opened up and discussed I think... I mean, there are medicos that are saying well there's a big question mark here about whether people with a partially effective vaccine of the type being tested now, if they're effective but only partially effective, there's a big question mark about transmission... But I think there are models that people are developing that attempt to estimate the usefulness of rolling out a vaccine that's say, 30% effective.

This informant raises some critical issues. At what level of efficacy would it be acceptable to market a preventative vaccine to the *developing* world? At what point

would it be acceptable to market it to the *developed* world? The analysis of those questions will depend largely on the incidence level in the target country. Hypothetically, a country with a 40% HIV incidence may benefit from a vaccine that was 30 % efficacious because the pool of infection is sufficiently large enough in that country that such a low efficacy would still have an impact on preventing the spread of HIV in that population. However, it may not have an effect on a population where the incidence of HIV was 5% for example. Such a decision would rest largely on the mathematical modelling used to answer such questions, an in-depth discussion of which is beyond the scope of this thesis. A further series of questions raised by such a discussion is how might that decision be made? What principles and frameworks would be used to make such a decision? Affected community clearly has a stake in such discussions. A statistician might develop the most beautiful model regarding this issue that exists but unless the affected community accepts that model, the uptake of vaccination might predictably be limited. Indeed, the involvement of affected community in such decisions is consistent with the assertions earlier in this thesis that affected community ought to be involved in all aspects of the vaccine development. The best way to incorporate such involvement may be a point of some debate. How affected community might make decisions in relation to this issue is in no way straightforward either as this information suggests. How the community representatives might make decisions around a poorly or moderately efficacious vaccine was of concern to this informant both in terms of how decisions might be made within the consortium itself and how that decision might be advocated to government.

C31 ... they thought they might be on to something here that would be, maybe, 40 or 50% efficacious, we then had to think, well, what position are we going to adopt, both within the consortium and to the government, because, again, we've got a role in urging the government to take certain positions about how would we deal with that and I think that plays out slightly differently if you're sitting completely outside of the process and don't have, only have the capacity to influence it instead of having an active role in the decision making. And, even the decision about whether we'd be in or out was one that needed to be balanced.

In Australia, the Therapeutic Goods Administration (TGA) has a number of committees which provide advice to both it and the Minister responsible in relation to therapeutic goods. Three TGA committees have consumer representatives as a member (http://www.chf.org.au/consumer_reps_program/committee_list_orbody.asp#T). The Consumer's Health Forum (CHF) is a national, member based, non government organisation that "helps shape Australia's health system by representing and involving consumers in health policy and program development" (http://www.chf.org.au/our_chf/index.asp). In order to become a consumer representative, a nomination must be received from an individual who is part of a member organisation. Once that nomination has been received, a sub-committee of CHF will select a representative for that committee from the pool of nominations (http://www.chf.org.au/consumer_reps_program/how_become_a_rep.asp).

Hypothetically, a situation may arise, however, where the consumer representative on the relevant committee approving the use of a preventative HIV vaccine may have no knowledge of HIV at all. In the event of antiretroviral therapeutic goods, one would expect AFAO, as a member of CHF, to advocate on the affected community's behalf through the CHF's internal structures and with the TGA more directly. It is unlikely that AFAO would advocate for a particular drug rather than advocate for a class of drugs. In the event that a preventative HIV vaccine is seeking approval from the TGA for licensure and AFAO is a partner in the consortium that developed the vaccine, it would represent an irreconcilable conflict of interest for AFAO to undertake an advocacy role on the affected community's behalf. This is particularly so since, in the event of an efficacious preventative HIV vaccine, it will be the only therapeutic good available in its class, thereby placing AFAO in a position of advocating on behalf of the construct it helped develop. A more comprehensive discussion of conflict of interest will occur later in this thesis. A solution to this would be for AFAO to lobby the government, as a member of the consortium, for approval and a quick decision by the TGA. But what of the long term effects of participation in the trial? In the next section, an informant raises a hypothetical situation which may impact on both informed consent and the nature of participant's involvement in trialling.

Long term effects of participation

The following informant raises a critical issue. Does participation in a trial now potentially affect the effectiveness for participants of a more efficacious vaccine in the future for individual trial participants? What this informant does not raise is the effect this consideration has on the informed consent process. Should it be raised in the informed consent process for this trial? However, as this informant points out, because of the nature of the trial, low risk participants are enrolled and are unlikely to encounter such dilemmas. Had the trial demonstrated a level of immunogenicity and it proceeded to a phase IIb or phase III trial, high risk individuals would have been enrolled and such considerations would have been important considerations to take into account.

C21 ... is this the right trial for gay men in terms of, you know, participation this trial may exclude you from future trials which might be more relevant. The possibility that exposure to this candidate vaccine may impact on future vacc, the efficacy of future vaccines on your immune system. Like, you take this vaccine, it may have negative, may have a positive impact, who knows. But it may impact on your immune system's response to future vaccines. So, for this trial, which is purely about safety and immunogenicity, so the way the immune system responds. Low risk individuals are the best participants.

Interim results

Interim results go to the Data Safety and Monitoring Board, but then the consortium (or its funder) needs to decide whether those results justify continuing. It is often not a clear-cut matter. The following informant highlights the decision making process in relation to whether the trial continues in the same or a different form.

C22 ...Fifty two week study. Interim results are the results from the first twelve weeks of the study. That being since the twelve weeks from the last recruitment. At that point, each of the participants or the volunteers that had all of the vaccine injections, of the three,

and that's the point at which an immunogenetic response should have peaked... It looked at the safety of the vaccine at that point in time. There were no serious adverse events. It showed a good safety profile. There was some not unexpected results of pain at injection site, that was not high or long lasting. But they were the main, kind of, outcomes. In terms of immunogenicity, the comparison between the group receiving the active vaccine and the placebo showed that there was no difference in immuno response. The summary of that is that the vaccine, at that dose and within that schedule, the schedule of vaccination, did not produce immunogenicity... The numbers range between one and four depending on what you actually measure, but there were a number of individuals who did show a low level response. Immunogenetic response... So, one thing that indicates is that possibly the dose of the vaccine is an issue. That the dose in this trial was too low... Yeah. So from here, the trial continues as a monitoring of the participants, primarily for safety. There's not going to, the immune response is not to improve from here on in. We're at that point where it would peak, so it's really a continuation of the trial to continue looking at safety and also any behavioural changes which are part of the study we're looking at; behavioural changes in the trial. So that's where we go with the Sydney trial.

NC11 [The Principal Investigator] presented some of our Sydney trial data. That's an ongoing trial but the initial look at the data showed some immune responses but only in a minority of the patients, at the first look. You know, that was a little bit disappointing but, you know, there's some hope that some activity from the vaccine. So now we're looking at increasing the dose to use in subsequent studies. The first study that you do with vaccines in humans is always, tends to be with lower doses because you worry a lot about safety. And the vaccine was very safe so that was a good outcome but, you know, it's not good being safe but not doing anything.

GD In bumping up the dose, does that have any... Like, when you're talking about dose, you're talking about the prime or the boost or both?

NC11 Well, both. We don't really know which one or both were sort of the culprit in being too low a dose so we're going to bump up both. We suspect it's probably the boosting vaccine. The fowlpoxes might be on the lower side, but we're going to increase the dose of both, get them up.

GD In increasing the dose, is there likely to be any, kind of, increase in those?

NC11 Yeah, that's a possibility. We've done some animal studies with increasing the doses and we haven't seen any bad reactions but, certainly, we could run into that but, you know, this is one of the challenges of vaccine development in that, often, some of the reaction to the vaccine is actually your immune response to the vaccine. So, sometimes for vaccines to work effectively, they have to produce something and, in fact, that was one of our concerns in the vaccine study that they were just simply not producing enough reaction. They weren't immunogenic enough. Not stimulating the immune response enough. So, you know, all vaccines tend to cause a little bit of a sore arm for a day or two so, we'd expect that. What we don't want to see is, you know, whopping big swollen arms or, you know, really reactions that would stop people taking the vaccines essentially. That would be too great, but certainly, there is that risk in trialling.

On the basis of those poor immunogenic results, a trial, using a different vaccine construct and dosing, has proceeded to be developed in Thailand. The interim results referred to in the following informant's account were disappointing and show limited immunogenicity. There was a result in one vaccine research participant which the consortium viewed with some interest. That gave rise to the following reflection.

C22 Not just unique to the Thai trial situation, it's also the situation in the Sydney trial. There are, and I think there's a lot of issues which are challenging or testing that because of the results of the interim, the Sydney trial, the interim results of the Sydney trial, it does raise questions about should the Thai trial continue? But there has been questions raised. But quite openly within the PEC, it was like on the table. It was like, well look, we have a range of options, one of them is to cut the, stop the program now or you know, other options are to, the modifications of the Thai trial, what are we wanting to do in the Thai trial? But, it was on the table that the Thai trial not proceed. So, that does kind of raise a bit of a sense of that. Yeah...

This account raises both an issue within the trial and an issue more generally for the type of prime-boost approach used in other trials as they relate to the notion of equipoise. I described equipoise in the previous chapter dealing with ethical theories specific to HIV. At what point does equipoise become disturbed during the course of a trial? In other words, at what point does the level of genuine uncertainty about the outcome of the trial diminish to the extent that it is known that the approach does not work? And who makes that assessment and the decision to discontinue the trial? Similarly, with the prime-boost approach generally, at what point do funders no longer fund prime-boost approaches on the basis that such an approach to vaccine development does not work? And, if such approaches are already in a human trialling phase, who makes the decision to discontinue the trial on the basis that the approach does not work? These are all issues which the consortium needs to grapple with.

Negotiating roles and responsibilities

As well as dealing with the substantive issues of the trial design and conduct, because the consortium generates an intersection between different social practices, the members need to negotiate how they interact with each other. This section illuminates that process of negotiation of roles and responsibilities. I will cover the following areas in my discussion of that negotiation: governance structures; disagreement and conflict; participatory management; and particular issues for

AFAO, including tensions with other social practices, suspicion about its involvement, and issues about the AFAO representative's representativeness.

Governance structures

As I have previously outlined, the consortium was contracted by the National Institutes of Health (NIH) to develop a preventative prime-boost HIV vaccine. As the funder of the trial, the NIH has a legitimate interest in the performance of the Australian consortium. The way in which the consortium successfully obtained the contract is described by this informant in the following way:

NC41 The NIH is I think in a very well made out process for managing these types of programs. Effectively, it's sort of the other way around really, looking at it. That they put out a request for proposals. They asked for people to come to them with ideas. And this group got together and put a proposal and particular work plan to them. So in a way, it was what we were going to do we described to them and they accepted it. So when they gave funding for that, the expectation was that we would enter into a contract with the NIH for the delivery of what you said you would deliver.

Interestingly, the relationship between the consortium and the NIH is described by the following informant in terms of the different power relationships inherent in a funder/provider arrangement. Of particular interest is the notion of being at the 'mercy' of the NIH and the informant's desire to then reframe that statement into a more moderate statement about the reasonableness of the reporting requirements. This is an example of the institutional dimension inherent in the social practice and demonstrates that this dimension can be perceived as problematic by some members.

NC41 So, it's not really a process of, you know, you know, we're at their mercy effectively. I mean, you know, they ask for anything that one can only consider reasonable which is frequent updates, reports of what's happening, when timeline or a certain milestone is met that they're notified of that. But, you know, there's an

active process really, provision of information. But they really do leave it to us to deliver the workplan that we said that we would for the budget that we said we would do it in.

NC41 No... Well, you know, in various consortia we've changed that name so PMC on this particular occasion is effectively the Board....Because, remember, the PMC is, they have institutional representation rather than necessarily, people who are practically doing the work itself.

Disagreements/conflict within the consortium

As with any cooperative venture, there will be a level of conflict or disagreement among the participants as to the best approach to take. Those disagreements were described in various ways by the informants in this study. Such accounts highlight consortium members negotiating clarity in members' individual roles and respectful working relationships. One informant described those disagreements in the context of the Australian partnership approach as minor 'tiffs and miffs' as you would find in any relationship.

C11 It's nice to see the old Australian model which they talk about of science and government, government's not particularly involved in this but the scientific establishment and AFAO working together. You know, it's generally small little tiffs and miffs here and there, like any relationship but generally it's quite a positive one.

Another informant described the conflict as being more serious but constructive. They stated that such conflict helped to achieve good outcomes. Of interest in this excerpt is the description of being on the outside and being on the inside both in terms of participation in the consortium itself and AFAO's interaction with other consortium members.

C21 Yeah, yes. There's that thing about being on the outside and being on the inside. But I mean, the way it operates, I see that there is a lot of conflict, like good conflict, within the consortium. I think

that there's a lot of, not always, but often there's a lot of rigorous debate about the direction of the programme. And, so, that, the internal process I think is there that produces good outcomes, there's that level of conflict that actually means that the decisions made are considered from a number of angles. And AFAO has I think, has put itself in a position where we're able to participate at a good level in the scientific level but also our role is not seen as tokenistic.

The informant has highlighted that through AFAO's involvement within the consortium, it has been socialised into the shared ways of seeing by biomedical scientists in order that the AFAO representative might participate more meaningfully in decision making processes. This has the effect of both helping AFAO understand why and how decisions are made but also increases the transparency of the decision making within the consortium. Perhaps the best description of the group dynamic is this:

C21 So there were rigorous debates about what was necessary, what was unnecessary, what was being, you know, over cautious, what was, that need to streamline. But there was never any sense of competing as to what people wanted out of it I think.

What this informant may be referring to here is the overall unity of purpose of this social practice and a reciprocal awareness of sharing that purpose. This informant further elaborates on the way in which issues are raised in the consortium, described by them as 'the partnership'. Most interesting is that it appears such issues do not factionalise along professional grouping lines, but along individual opinion.

C31 Because it's commercial-in-confidence. So, there are some issues that have come up in terms of the development of getting as far as we've got so far where there have been different views being expressed about how that ought to be resolved by different parts of the partnership. That isn't a surprise to me and interestingly, the divisions aren't into social researchers, epidemiologists, finance people, bench scientists, medical practitioners, community people

which is kind of the loose mix, they cut across those groupings so it's very seldom factions that are at work, but it's a range of different perspectives that people bring to the way in which the kinds of problems that are inherent in doing this kind of research that it throws up all of the time, how they are best resolved and which set of competing values you will favour at any given time.

The informant gives the clearest indication of the complexity involved in agreeing to a consensus course of action within the consortium. This highlights participatory management in action, which is one of the core principles outlined in the UNAIDS document. Participatory management may be defined as "... a commitment to carrying out a set of strategies that involve workers in organizational decisions" (Pine, Warsh and Maluccio, 2003: 117). Clearly, this is not an easy process as the informant further highlights.

C31 So I imagine, well, having just seen a program on the mars expedition, where there were people who were saying, it's really important that this thing actually gets on the ground, that's the primary objective, and there are another bunch of people who were saying well if it gets on the ground but it's going to take 100 years to get to were it's going to find anything interesting, then that's a waste of time. Now watching how that worked through was something that although I've never been involved in that kind of research, I could see happens all of the time in my organisation about what's the best line to take when the line isn't clear and you're trying to reconcile a range of variables, a lot of which you don't know how they're going to play out. So you're anticipating how something might go and then trying to factor in that to a complex equation. Watching that discussion between engineers, who are the ones who are having to get it on the ground and the geologists who are the ones who wanted it on the ground in a position that was pretty impossible to get it on the ground in, watching how that played out was something that I could

absolutely relate with both from being involved in this project and in a whole range of things I do in my job all the time.

The informant clearly identifies the way in which the community representatives interact within the consortium, including the use of a veto power on fundamental issues. This is particularly different, as identified by them, from most other structures involved in HIV vaccine development. As I have outlined in previous chapters, community representatives are not usually full partners in vaccine enterprises. Because they are not partners when they are members of Community Advisory Boards, community representatives' bargaining positions are significantly weakened and their capacity to change the outcomes, once reached by the consortium, are limited. AFAO's position of relative strength is illustrated quite starkly in the following excerpt. Indeed, this informant believes because community was a full partner, other consortium members' ways of justifying particular approaches changed as a result. Rather than a highly hierarchical approach, all members of the consortium have an equal capacity to influence the direction of the consortium's work. So, the institutional dimension within the consortium is such that each individual on the consortium has, in practice, equal power to other members.

C31 And I think the benefits, having looked at the models that operate elsewhere, are way more beneficial, and on some of those issues where I'm not able to give you the details, where there were issues that for us were very fundamental ones, we were able to say no this cannot proceed until we're satisfied... And who knows how the times when those types of discussions were happening, how it would have been resolved otherwise but my view is that it meant that the people who were advocating an alternative position had to look at the way in which they approached it quite differently from if they could then engage with us where we were saying this is a fundamental matter of principle that it should happen this way, and they would then potentially say well, we understand what your position is but we've decided that we can't accommodate it.

As I have highlighted previously, various structures within AFAO authorise, in as much as any representational model authorises, the AFAO representatives to

represent the affected community in the consortium. The way in which that representatives faithfully represent those views are described in the following way.

C31 The consortium members brought it to the PRG [Policy Reference Group of AFAO] to say this issue's arisen, the Board's going to need to make a decision on what the position is, particularly if we're going to dig our heels in here and say we need to be persuaded of the alternative point of view and for us to change our position, these are the things you would need to do. That needs to be made by the Board because it has implications for the way in which the conduct of the research is going to happen.

Because AFAO is an incorporated body governed by a Board of Directors who are elected by the membership and legally accountable for the conduct of the organisation, the Board of Directors is the highest decision making group in AFAO. The Board is assisted in that decision making by a variety of policy reference groups or PRGs. These PRGs are made up of individuals, from both member organisations and from outside the membership of AFAO, who have expertise in the particular policy area or a discipline related to the policy area. As the issues being discussed in the Vaccines PRG were in part commercial-in-confidence issues, PRG members were required to sign confidentiality agreements in order to provide that advice to the Board (AFAO 2008). So, by the time representatives of AFAO came to the consortium decision making committees, most issues had been considered and a position agreed upon within AFAO. So the institutional structures of AFAO influenced the way in which the consortium operated through the AFAO representatives.

One informant suggested that the consortium members acted more along disciplinary lines than other informants have. Interestingly, even the Principal Investigator is bound by the collective agreement of the programme management committee (PMC) which is a further demonstration of the flat, consensus institutional dimension of the consortium. This account also indicates the intersection of a number of social practices and the internal negotiation that entailed.

NC41 You've got very fundamental researchers who are very laboratory focused, you've got people who are community focused and

you've got clinically focussed and frequently those groups have very differing opinions of the world and view of the world. It's come together really well and I think a lot of that's a credit to David because of the sort of person that he is. He's a chiefly respected individual and there isn't an individual that you would speak to who would give you a contrary view. He's just one of those people that people run around and for a pretty good cause.

GD Well, just to give you a hypothetical, if David says "I think you should do this" and the PMC says "well I think you should do this" that seems to me to kind of leave you out on a bit limb.

NC41 It does so the, we would under a collaborative agreement that clearly defines how disputes will be handled. And disputes are handled at the PMC level. And, so the process of dealing with that is it's a documented way if David had a certain perspective and the PMC had a different one, the PMC would address that conflict and, you know, create a ruling for it.

How much is the community component worth? Participatory management and clarity of shared responsibilities

Some of the informants pointed to the poorly defined nature of AFAO's contribution to the overall workings of the consortium. For example, while a particular consortium member might bring gene shearing techniques to the consortium and another might bring the prime-boost vaccine construct, what community brings was not particularly well articulated by the informants.

C11 There will be some conflict trying to figure that out if there is something called a community, ah, community component. How much of those responsibilities might go to the community component or not.

NC11 I think our consortium is pretty unique in that we have the sort of community and social researcher component built into the budget of the whole program but that doesn't mean there are not

discussions about you know, well, how much and what's the value of this compared to that and, you know, I guess we're obliged to spend the money wisely and in a, sort of, goal directed manner, but.. So there are, that's, they're the main sort of issues around that.

GD Did that create some tension though, around the table?

NC11 Oh it does, it does. Certainly, and it's a little bit easier for me being a clinician and a basic researcher but some of the basic researchers, for example, don't, haven't worked ever with community groups before so they kind of see the.. They might see these people as not being particularly helpful and when your trying to test a vaccine in an animal, manufacture it, make sure it meets all its specifications and get it through, you know, the TGA or the FDA so that you can do a clinical trial with it, they don't always see the value of having the community people along all the way, spending money on them, you know, supporting salaries all the way along. So, you know, having said that, the costs associated with bringing community people on board are not massive in the grand scale of things but, you know, they're costs and whether you could, you know, it's an issue of whether you could use that money more wisely somewhere else...

It would seem from this account that AFAO's continued involvement needed to be justified to the other consortium members in a way that other members were not required to do. While some consortium members needed some justification for AFAO's presence, the overall view of the consortium was that AFAO was a vital member. Had there not been the social history in relation to HIV in Australia, it could be argued that those objections would have been difficult to surmount. The learning and socialisation of the Australian HIV/AIDS Partnership social practice was persuasive on those members of the consortium new to it.

A major theme to this point is that there was in-principle agreement, through reliance on the social practice of the Australian HIV/AIDS Partnership approach, for AFAO's involvement as a full partner in the consortium. In practice, that agreement

needed to be worked through by the other members of the consortium and AFAO itself.

Tensions in AFAO's roles

NC11 ... I think, sometimes they feel like that they don't have enough independence in viewing things because they're, sort of, part of the process and so that there's a natural tension between wanting to be rigorously viewing things from the outside and being so closely involved that they hear about it all the time, they become, sort of, you know, becomes sort of the doctrine if you like, this is how things are going.

What this informant highlights is the consortium's socialisation effect on new participants. The 'they' being referred to in this account are the community representatives in the consortium. While I have discussed that learning and socialisation of new practitioners is a core characteristic of a social practices, this account also describes obliquely, the institutional aspects of the consortium in terms of the power and influence being exerted on the consortium participants through confidentiality agreements. What this account also demonstrates is the intersection of the social practices of the Australian HIV/AIDS Partnership and biomedical research.

NC41 And any [indistinct] of that intellectual property aspect. So again, the intellectual property that's generated within the program is further defined by this collaborative research agreement. What happens to it. Who owns it. So the collaborative research agreement specifies that, what background intellectual property will come into the consortium for the use of the consortium, and then the stuff that arises during the conduct of this is shared equally amongst the consortium members. And then, NIH has a kind of, I guess, a get out clause that basically if we really aren't doing our jobs very well that we fail a number of, you know, we're basically incompetent, they have the right to step in, take the intellectual property that arises during the course of this that's owned by the consortium, and then develop it... And if they think

that we're, you know, complete time wasters, or that we're a commercial company, which we're not, but if we were, commercial company who were failing to develop something that was commercially viable. They have funded a certain amount of that work and generated intellectual property, they want the right to take it and develop it themselves. So, it's completely reasonable I think and that's the sort of two levels of course. One is within our collaborative research agreement and the second is overarching by the NIH if we really fail to perform... Yes it would. Essentially because the consortium was formed for this piece of work and this piece of work will conclude in June of this year. So then the consortium will go back to being just individual institutions. The materials go back to, the materials being the vaccine, go back to their original owners... that gave us the DNA which we've modified but they still own that construct. And Virax. So if we want to do continued work in the future, we being say the Thai Red Cross, if we want to do the trials in Thailand or any other groups who would like to do the work with that needs to be done, we need to get back to the owners of those for the rights to use those materials.

There are two aspects to this account. The first aspect concerns the way in which institutional control is exerted by the NIH over the work of the consortium. The NIH reviews whether the funding they provide in the contract they have with the consortium is being used in an effective manner, and if it is not, they assume control of the research from the consortium. Secondly, each of the consortium members brings a particular skill or technique to the work of the consortium. The example given by the informant, the DNA construct, highlight the collaborative nature of the consortium is limited to just this vaccine enterprise and new agreements would need to take place in order to access those skills or techniques again in the future. What is unclear from this excerpt is what intellectual property items are associated with AFAO. This had the potential for down stream effects in relation to profit share of a successful vaccine by AFAO etc.

Suspicion about community involvement and commercial-in-confidence information

C31 CSIRO has no history of community involvement and was extremely reluctant at times to have community privy to information that was coming to the consortium. But a view of a large number of other people around the table was that they've seen far more sensitive information and it's not ever been revealed inappropriately so we would have no problem with providing them with that information because they have a track record of being able to use that information confidentially and appropriately.

Another artefact of the social history of HIV in Australia is that most members of the consortium, having worked and interacted with affected community beforehand, have no concerns about the confidentiality of information provided to community in confidence. Tellingly, according to this informant, the CSIRO had concerns about that process. In the absence of the type of social history we have in Australia, would such suspicion prevent the inclusion of community in vaccine trialling elsewhere? I was unable to explore that perception with the CSIRO member of the consortium since they did not take up my offer to participate in this research. What might be worth exploring is why they believed the AFAO representatives posed more of a risk to breach that confidentiality than other members of the consortium. Also of interest in this account is the claim by other non-community members of the consortium to a tradition of working with community and, as a consequence of that tradition, having no concerns about the confidentiality of information being provided to the community members.

Community Representation

Community as a term is used throughout this thesis. It is generally a poorly defined term and one examined in much social research deliberation. As Greirson (1998: 24) states, it:

... has a long history of definitional ambiguity, flux and contestation, from early usage denoting groups of people with

geographical, social and political interdependence;... to contemporary usage that seems to be more about shared identity, interest or dilemma.

The term 'gay community' is also problematic (Greirson, 1998: 24). I have described the emergence of what has been called the affected community in describing the social history of HIV in Australia in chapter one. I described how the AIDS Councils, and AFAO, emerged out of the social activism of gay men in the early '80s. As Dowsett (1998: 175-176) states, the men who constituted the AIDS action groups at the time were, in part, experienced campaigners working in anti-gay law reform and the gay liberation movement and professionals within the emerging gay communities.

What is clear is that the notion of representation and the definition of community is contentious. It has been explored in much more detail by others. It is not the phenomenon I wish to explore in this thesis. For the purposes of this thesis, however, I assume affected community authorises AFAO to act on its behalf in relation to its participation on the consortium. One informant clarified their understanding of AFAO's authorised role in the following way.

C31 Well, it's the community of people who are affected by HIV to the extent that the organisations that we're involved with have views in relation to that and have raised issues. But, for example, one of the reasons why AFAO was bought on board, was that its role is to do the community education component so in the process of doing that work in Sydney, they come into contact with a large range of gay men and are then able to talk to them about what the issues involved around HIV vaccine research and what views do they have? If it's can we say we know what the community thinks? No more than any politician can, well, no less than any politician can, probably more than any politician can because we have in fact run a range of focus groups in Sydney but we've also had the vaccines issue on the Board agenda which means it's gone out more broadly to the membership and we've run sessions on vaccines at the half yearly meetings where people have had an opportunity to raise

questions, throw in their point of view. Because in a sense Sydney is the epicentre of gay community in Australia, although nobody else wants to kind of admit that, the reality is that what goes into the gay media in Sydney ends up being diffused outwards and so in a sense the information sessions that are run and the information that's available for gay men in Sydney when, for example recruiting for the Phase I/II trials was starting, ends up being disseminated around the country and the AFAO processes of consultation mean that, that information in draft form gets circulated fairly widely for people to, kind of, comment on, raise questions about, say this is how that'd play out in my State if it turned up here. So, to that extent we can say we're able to reflect community views in relation to it. We've got a charter and part of our contract is to go out and find out what those views are.

The following informant clearly sees AFAO's role as one of moderating competing interests between the rights of participants in the trial and the practicalities of running a clinical trial of the nature of a preventative HIV vaccine.

NC41 So, they understand that there are limitations and it's not like you're always getting someone who's belligerent about, you know, just focussing exactly on what the participant needs. There's an understanding of the balance between participation in the trial and limitation of what it is we can do.

While competing interests are a consideration for this informant, the positive aspects of full partnership are tangible in terms of AFAO's capacity to influence and be effective negotiators. This account also highlights the 'newness' of AFAO's full involvement and that it is unusual for such a situation to occur but that it is a positive experience for this informant.

GD So, they're relatively effective negotiators?

NC41 Yes, very effective negotiators. It's been a very positive experience and, yeah, when it's formalised in this way as well. It's unusual to have it formalised as a, you know, community to be

active and a full member with voting rights as part of the consortium.

Different social practices coming together in the consortium

Underlying all of these specific issues are the points of intersection between different social practices. In this section, I discuss those intersections more explicitly. I show that there are tensions and differences which are dynamic and produce changes in understanding and behaviour. This informant highlights the intersection of the biomedical research and Australian HIV/AIDS Partnership social practices within the consortium. They argue in favour of the Australian HIV/AIDS Partnership approach, which is unsurprising because they come from the community sector.

C11 Ah, hmm, well, you know, I think some of the scientists have got, you know, pretty strong opinions so they'd disagree with anybody no matter what the concept it was... they disagree among themselves and are always quibbling about different points, so, you know, they're quibbling about us or community, you know, I don't know, it could be anything, it could be excuse, it could be community. I think that the way that Australian community based organisations work is a very particular style and, these scientists are used to it. Still might have problems getting, understanding a bit of it but generally get it. But, you know, for example, it's not necessarily the conflict between science and community. If I am working with particular agencies outside of AIDS, for example, for example hypothetically, with development agencies, who have a different modus operandi than the AIDS sector, those conflicts could be exactly the same because they don't understand how the Australian community based model works which is, one of great consultation. You know, it's definitely a model which demands that there is a representation from at least a number if not a larger number, if not an entire membership of people and a structure where people are basically in agreement with something to go forward. And if there's no agreement reached, then, you know, I think the, you know, the Australian community response in HIV

says no, we'll stop, we will not go forward on that and I think the leaders of the CBOs and the movement understand that well and that's how they operate. So there's that, kind of, given understanding which other sectors or other people might not understand. I find it frustrating 'cause it's not the way their organisation works... You know the structural stuff is all about negotiation and who has, you know what votes there are and who has, you know, that's all a bunch of politicking so I think everybody's background and experience as partners on the consortium have an equal, maybe an equal influence.

The next informant, however, who does not come from the community sector, argues in favour of it too.

NC11 Well, it is a critical step but if you didn't do it, in theory, you could still get it into clinical trials but it would come at a cost of not having community involvement and having a lot of disgruntled people and, you know, your left with this, sort of, public relations problem at the end of the day.

There are two interesting perspectives here. This first perspective from the first informant portrays community involvement as the norm rather than the exception and that that 'norm' is something that bench scientists ought to accommodate. Such an account highlights the intersection of two social practices, that of biomedical research and affected community involvement in the Australian HIV/AIDS Partnership. The second perspective is that not to include community would bring with it a "public relations problem" for the trial. This informant believes that not to include community would be an error because, as a result of the Australian HIV/AIDS Partnership approach, affected community has always been central in the response to HIV and excluding them may present difficulties in achieving the trial outcomes if the community in which you are wishing to trial is disgruntled and unwilling to participate. Inherently, this may have an effect on recruitment to the trial which would be an undesirable outcome.

Researcher's roles/perceptions/views

This informant also suggests the interaction of scientists with community 'grounds', or makes more relevant, the application of the science in a successful candidate vaccine. The meeting of the two social practices, according to this informant, enhances the outcomes of the consortium in terms of making information associated with the trial more understandable and accessible to the trial participants.

C12 And both the researchers for that trial and our trial they feel that they've got a very clear role which is to inform communities and education communities and not force them into a position one way or the other... Well I think the sad thing in terms of figuring out how to proceed in the world of vaccines is that, you know, vaccinologists and the scientists do have so little contact with community members and with social researchers, that when they do come to those questions, you know, there does need to be this, whether it's yearly at the vaccines conference meetings or some other mechanism, for these folks to be reminded constantly of what are the real issues about getting a vaccine into a population if there is going to be one. It's not realistic to have a vaccine that takes, you know, six doses, to get into somebody.

Having been explicitly asked about the ethical awareness of consortium members, this informant suggests merely by participating, consortium members would be aware of the issues.

C21 Look, yeah, probably. And probably to varying degrees throughout, you know, that have been exposed to it. But I think that anyone who's been involved in the programme so far has not been able to ignore the issue. That the issues have, you know, are raised and discussed. I think, I would say, pretty much with the same level of, you know, given the same level of importance and the same, kind of, rigour of debate, those kind of ethical issues and conduct of the trial issues as the scientific, that animal and the, sort of, lab studies. I think. So, I think everyone who's been involved

has been exposed to that and they would, to varying degrees, have some kind of understanding. Not necessarily that they might apply it to their way of thinking from now on into the future but they've certainly been exposed to it.

This informant expresses surprise that scientists who are also clinicians tailor some of the scientific development and approaches to trialling to how that development or approach might be applied or affect individual trial participants.

NC21 And it's quite interesting because clinicians are very thoughtful about, you know, in some ways more thoughtful than I would be, they worry about how many injections and how big the injections and, you know, they're very careful about, and rightly so, but I mean, to an extent that actually surprised me. I mean, they're more caring than I think, than I think I might be or that I would have thought about being if I'd been in their shoes. So they're, but they're very individualistic. I mean, they're dealing with individuals so they're very concerned about each of the participants and their welfare and for their safety.

The informant goes on both to use the inside/outside analogy they previously used to describe community participation, to describe social researchers who they viewed to be 'outside' the biomedical scientific paradigm and also suggested social researchers' experience with biomedical researchers indicates significant rigidity in approach along professional lines. The following excerpt is a very good example of how the traditions of the social practice of biomedical research influence its practitioners.

NC21 But he also said that, maybe what you need, you need to tell people they're using the vaccine because you need to know what the impact is on their behaviour. You shouldn't be second guessing. So, in other words, there's quite complex arguments and I'm not sure he's, I mean, I think he is right at one level and I think there needs to be, I think there needs to be if you like, as well as people like me working in there, there needs to be a critique of

some of the tools or the models that are just imposed on some of these vaccine trials because the thing that's always struck me right from the very beginning is that actually it's a very different disease from polio or from cholera or from, you know, small pox. You can, I mean, I think women in Africa have limited control, or some women have limited control, but most of us, to some degree, have some control over whether we transmit it or in fact become infected by it. And because we have some control over it, it makes vaccine trials quite different and I think that is absolutely essential. And I think, well that's what Doherty saw when I talked about it, and, you know, it makes a difference. It is not the case that you're just dealing with a whole lot of people who, you know, can't do anything about being infected or infecting somebody else. You're actually dealing with a disease or a virus over which we have some control and I think that control varies enormously from country to country and from population to population in different context. But to pretend that we don't is very, very foolish and I think that's why it's a social context. So I suppose what I've, I think it's just being in the trial, in the consortium has actually strengthened my view of how important it is to have both community and social researchers, but indeed people who have, who can sit on the outside as well and actually start to look at some of the assumptions that people take into these trials. I can certainly remember having a big argument years, not in this vaccine trial, but a long time ago there was a trial in Sydney, you know, and having a real argument with someone who I now get on with very well, who, and I was making arguments about randomised control trials and placebos and double blinds, and this guy finally in absolute irritation with me said, you might be right but that's not how we do it. And I thought, that's very interesting. There was a sense in which, he knew, it wasn't quite as straight forward but it's actually quite scary for them in some ways if their tools aren't clear cut. And, I mean, running a huge trial is a, I mean I've learnt to admire these guys, I mean, they work really hard and they work

really well and they're extremely competent and they're very bright. So it's actually watching this science unroll that's actually quite remarkable.

Indeed this informant is almost condescending in their views about how rigid scientists' are in relation to the ways in which they work and how they adapt to different models of working.

NC21 There was a sense in which, he knew, it wasn't quite as straight forward but it's actually quite scary for them in some ways if their tools aren't clear cut.

The following informant highlights that the academic process of trialling is the same whether it is a vaccine being trialled or a prospective antiretroviral agent. However, they make the distinction in vaccine trialling in terms of a vaccine being a part of an overall HIV prevention package and that, for such an approach to work, community and social research are vital components and participants. The informant also highlights the tradition and ways of doing in the social practice of biomedical research.

NC31 ... there is nothing, actually different to the discipline of evaluating and design of trials. Vaccine trials are trials and they need to sit in a framework of academic rigor... So, academically, in experience terms, there's a great deal of difference between clinical trials of candidate vaccines or of candidate treatment. I think, you know, they're one and the same thing as an academic, developmental exercise. I think the thing that is very, very different between the two, and where I would reflect on different, much clearly is in the perceptions associated with the conduct of vaccine research... And really, that we see vaccines as a component of an overall package of prevention rather than being seen or perceived as being in some way a substitute or a replacement or in some way deemed to be better than education programmes, behavioural interventions.. Which are very much

more the property and domain of the community sector and social research.

This informant also comments on, in a somewhat colourful way, the rigidity of scientists' approaches. They suggest that this rigidity is far too entrenched to be overcome by some of its practitioners. While a social practice has a tradition and ways of seeing and doing which all of the practitioners subscribe to, it would seem that the adherence to those ways of seeing and doing may vary from practitioner to practitioner. As I suggest later in this thesis, while Langford (1991) implies that ways of seeing and doing change over time, the dynamic nature of the ways of seeing and doing by practitioners is not explicitly described. In other words, the ways of seeing and doing are not static and may traverse a spectrum for each of the practitioners. Inherent in this account is that, while there are core ways of seeing and doing that are not negotiable, for example the way statistical methods are used to investigate an outcome, there are other non-core ways of seeing and doing that are able to be tailored to particular situations. This is an important finding in this research and adds to the body of knowledge as it relates to the Langfordian model of social practices.

NC31 Cause lab jockey's right there. They are committed to HIV vaccine development because that's where they as scientists have spent years fiddling with these bits and pieces, think they can make a contribution. And that's, whether you like it or not, that's fine... you know, they have generated this incredibly interesting technology. And, you know, it needs to be evaluated properly. But where they have the disconnect in understanding the role of a community representative or organisation in that process of ongoing development. They just don't get it. And they never, ever will.

GD ... do you think they'd be quite as critical if the dollar was going to another scientist in the field rather than AFAO?

NC31 I think that if AFAO weren't there, then they would find another target to vent their frustrations on. But, I think that also there's also an issue of just complete lack of understanding of what a

community organisation does. They've just got no insight.... They're not anti, they're not homophobic, they might come across as being both of those on occasion, sometimes quite frequently, but they're not, they just don't understand... This world is not part of their world. It's just not part of their thinking, their lives, their whatever.. so.

The informant also provides some intriguing historical context to the way in which community involvement has developed over time in Australia compared to the United Kingdom.

NC31 In the context of the current consortium, this is a perspective that's grown over the passage of our two and a half years... Certainly in the UK, the community sector in the early nineties was not the same, very visible, engaged, productive constituency. It was a very passive and almost charitable rather than representative. And in Australia, it was quite the opposite. It was incredibly politicised, very well connected and very strong, forthright views, incredible power base and the experience from that was that we did things very badly in terms of consultative aspects, in terms of engagement, discussion, whatever. And there was no way I was going to go into the current project in isolation of a constituency that, rightly or wrongly, could completely scuttle the whole bloody thing. So, I mean, I actually see great merit in the contribution from the community sector, but like I said, even if it was just tokenistic, prevented those public, hostile, destructive sort of clashes, it would be worth its weight in gold. And it's actually far, far more than that...but at the end of the day, the consortium is the consortium and, you know, whatever goes on inside that consortium, doesn't necessarily reflect where I come from or my view and we have to move forward on some common ground rather than continue to try and find differences.

Almost exactly the same perception was held by another informant.

NC41 ...The researchers have been very well motivated, they want to do this for all the right reasons, it's not only purely financial aspect, it has a financial aspect to it of course, funding the research but it also has a very important community and, you know, world wide impact if things go well. So I've found that people have been tremendous to work with. I mean, really genuinely tremendous to work with. The effort that people put in has been well and truly over the top that was to be expected and the program has gone extremely well in terms of its conduct. So it's been a group that have worked well together. It's not necessarily a group of people who are aligned necessarily. You've got very fundamental researchers who are very laboratory focused, you've got people who are community focused and you've got clinically focussed and frequently those groups have very differing opinions of the world and view of the world.

Indeed, this is a clear description of the intersection of the different social practices involved in the consortium but it also highlights the emergence of the new social practice that is the consortium. The different members of the consortium, given the type of work and the stakes involved in the development of a potentially efficacious HIV preventative vaccine, have been forced to work together and to develop shared ways of seeing, and doing which is an amalgam of different aspects of the various constituent social practices. As will be explained in the next section, such a merging is obviously, not without its challenges though.

Learning to work with community

The 'foreignness' of working with community has a flow on effect in terms of the behaviours of scientists as highlighted in the following extracts.

C31 Well, yeah, having community there means that scientists need to be able to explain to community what it is they're on about.

C11 I think around some of the issues, the scientists have been forced to wait for us to consult with our constituencies and develop a community standpoint. There have been a few issues that we've

had a difficulty getting our heads around because we're not scientists and then to figure out the scientific implications. And then for us to decide what the community implications are and then to feed that back into the process sometimes has been stressful because we haven't had enough time to do that, or it's been quite difficult trying to figure out what information there is... it is a difficult relationship for scientist to have to explain to community what is going on and, however annoyed we might be with scientists, sometimes for speaking in impenetrable language, or, you know, being impatient. They're, in some ways, incredibly patient because no-one else has to do it, you know, they're willing to do it and they've been, I think very good in general. So I can't remember, you know, there's not been particular impasses.

And that change of behaviour has occurred over time, despite the inherent tensions and rigidities highlighted in the previous extracts.

GD And do you see that as having changed over time?

C21 Ummm.. Yes I think so. I mean I wasn't involved at the very beginning, but my understanding is that yes it has. There's a lot of people who are a part of the consortium that, part of the meetings and who had no idea, or had never considered, what AFAO is as an organisation or the kind of work we do or HIV prevention education or social research. What it does, how it operates, what its value might be and how it might add value to a vaccine development programme. So I think that that has been something that has probably been, you know, a number of people have begun to understand or now understand where they probably didn't at the beginning.

GD Yes, Ok. Have you changed your views over time? Is it something that's kind of evolved or is it..?

NC21 I think it's evolved. I haven't, I mean in some ways, although, you know, I do, I always thought from the days I went to one meeting I went to at the very start with UNAIDS, that it was important to have social researchers there, I think the only, I think really, I think my view has strengthened. I mean, I think, I now believe that even more than I did then, although I think it's difficult. I mean I think. I mean I also think there should be people who, and they're not there now, people who can actually, you know, I suppose it's strengthen, and I'm thinking about a man called Julian Meldrum, I don't know whether you know him... So I suppose what I've, I think it's just being in the trial, in the consortium has actually strengthened my view of how important it is to have both community and social researchers, but indeed people who have, who can sit on the outside as well and actually start to look at some of the assumptions that people take into these trials.

What does the above informant mean by constantly referring to the 'outside'? It seems that this is an artificial construct designed to inoculate the informant from the 'contamination' of working with bench scientists. Or, perhaps it says more about this informant feeling marginalised rather than being 'sullied' by biomedical empiricism. It may also be, albeit unconsciously, an acknowledgement of the social practice of the consortium and an acknowledgement of the reciprocal self awareness that arises from participation in that social practice. There is a tension between the participatory management model in the consortium and the capacity to act autonomously. As will be describe in the next section of this chapter, such positioning foreshadows the conflict of interest issues experienced by AFAO. This and the next accounts are indicative of the challenges experienced by the new social practice of the consortium which the previous informant appears not to have fully embraced.

The strongest indication of the way in which scientists have been required to change the way they operate as a result of community being a full partner in the vaccine enterprise is by the following informants. The first sets out the practical considerations in terms of having to explain processes in order that informed consent and the plain language statement can be understood. The second participant describes

the 'sea change' experienced by biomedical scientists, and the third describes their personal experience and the resultant change in the way they desire to operate.

C31 Community is able to say, sorry, we don't know what you're talking about, turn it into concepts that we can understand... Because, our position is, if you can't explain it to us, then you certainly can't explain it to punters who you're asking to come and participate. So, the plain language statement, if you can't get what you're proposing in plain language, then you're not going to get it into a plain language statement and if we can't understand it, as people who have some level of, who've developed some level of expertise in the area, then you're not going to be able to get it past people who you want to participate and you need to go back and rethink your communication strategy. And that's been a very effective thing to be able to do.

NC11 ...but I think the big change has been probably some of the more basic scientists who have never had much interaction with community groups and certainly they've learnt a lot about AIDS politics and how, you know, how having these groups is important but, you know, it's a little bit time consuming and a little bit educative but, you know, ultimately very helpful at the end of the day in terms of education and recruitment and retention in the trial and support and all that sort of stuff. So, I think, so yes, I mean, I've learnt a lot but probably not had a lot of surprises but other members of the group probably had a bigger, sort of, sea change in their attitude and things, knowledge about things.

NC31 Oh, I'd, you know, my learning experience came in the early nineties with the very first trial that were conducted. And, it was given to me to run shortly after I'd arrived in Australia. Leaving a position in industry to go into an academic appointment and it was like a baptism of fire. Certainly in the UK, the community sector in the early nineties was not the same, very visible, engaged, productive constituency. It was a very passive and almost

charitable rather than representative. And in Australia, it was quite the opposite. It was incredibly politicised, very well connected and very strong, forthright views, incredible power base and the experience from that was that we did things very badly in terms of consultative aspects, in terms of engagement, discussion, whatever. And there was no way I was going to go into the current project in isolation of a constituency that, rightly or wrongly, could completely scuttle the whole bloody thing. So, I mean, I actually see great merit in the contribution from the community sector, but like I said, even if it was just tokenistic, prevented those public, hostile, destructive sort of clashes, it would be worth its weight in gold. And it's actually far, far more than that.

The previous accounts highlight not only that community representatives have been socialised into and learned the ways of the social practice of biomedical research, they also highlight 'bench scientist's' learning and socialisation into the social practice of the Australian HIV/AIDS Partnership. As such, both groups have been socialised into the social practice of the consortium.

AFAO's involvement, however, while perceived as beneficial by consortium members, brought with it a set of other issues, not least of which, was a potential conflict of interest between AFAO's obligation to act in the best interests of the consortium and its duty to advocate on behalf of its members.

Conflict of interest

One of the most significant issues to arise from all of the discussion in this chapter is the potential for a conflict of interest when affected community is involved in the consortium as a partner. The following quotes give indications of how conflict of interest could arise. After I have explained what the potential competing interests are, I will show how these constitute a formal conflict of interest as conventionally defined, and why conflict of interest is particularly problematic in a consortium of this type.

C21 Oh well, I guess, I mean, the key issue is as a member of that consortium, AFAO has a vested interest in that we are, will have, a

percentage of the profit share from any product that results as a part of the programme. So, that raises for us, I guess, the issues of how we are, how we balance the objective advocacy on behalf of the community within that programme when we have that conflict of interest. Now, it doesn't, it's not actually problematic for us but it's an issue that we've raised and occasionally just, kind of, comes up. And I think, I believe it works well. I believe we do maintain a level of independence in how, you know, we participate and the way that we represent community. And I think that as a model, although I'm not intimately familiar with the way other models have worked, generally my understanding is that the community, the level of community involvement in many other programmes is, sort of, less than adequate and doesn't always work well. Whereas this seems to be a model that works really well. So I think the benefits far outweigh some of those concerns around independence of community in a programme like this.

While such conflict of interest is unlikely to be realised in a safety/immunogenicity trial, with small numbers of people who are not drawn, in the main, from member organisations, the likelihood of an actual conflict of interest arises once efficacy or proof of concept trials begin. How can AFAO discharge its duties to act in the consortium's best interests if a member organisation raises a complaint about the conduct of the trial with it? Or, once a commercial partner is engaged to manufacture an efficacious product, how does AFAO respond to the legitimate commercial interests of the consortium and also seek to minimise the amount of profit gained from the distribution to its member's constituents? I contend that in both instances it is an irreconcilable conflict of interest. Interestingly, this informant raises the issue of profit share but immediately discounts it as not an issue now but that it may become one in the future. Of immediate concern to the informant is what they describe as a balance between the scientific imperatives of the trial and the way in which the trial is conducted ethically. One way of understanding this is not as a conflict of interest as such because these are ethical principles that clash. Instead, as Taylor (in Smith, 2002: 107-120) suggests, it is a conflict between competing moral

goods rather than between self-interest and the interests of others. This idea of competing principles was discussed earlier in relation to principlism.

C21 Well, first of all in terms of profit share, I mean, that's a long way down the track, so it's not, you know, it was something that we, you know, had to consider I guess, but in reality it's not something that's with us at the moment and won't be for a long time, so it's not an issue we're gonna gain from this because we may not. No one may, depends how it goes but that's, I guess that's I guess one that may later on that may become a conflict. More currently, I guess it's around the decisions of the conduct of the trial that there are, I guess, scientific imperatives which are about ensuring that the trial meets its objectives and gets the data that is required so that we get, you know, the volunteers, the process produces the data that is required scientifically. And the other balance of that is the ethical issues around conduct of the trial which could be argued, can be seen by some, that the two aren't dependent on each other where our position is that it does. You know, the conduct of a good trial is, underpinning that is the kind of ethical and conduct of the trial is gonna impact on the quality of the data that's produced. So I guess that's one area of conflict of the trial can be seen as having one purpose of being a scientific trial about producing data so, I guess, people may question AFAO's role in terms of where's our key purpose in this. I guess sometimes there's a thought that it's a, it needs to be a kind of an adversarial role that the community plays. Which is just, I think that's, historical in some ways but, or people see it in that sense that the way you're a good advocate is because you play an adversarial role. And it's harder for AFAO to do that when we're, you know a part, when we're in there amongst it. Yeah, yeah.

GD You don't see any potential conflicts in being, like having a fiduciary duty as a full partner in the consortium and...

C22 Oh, look, there are. But there always has been.. I mean....

GD You mentioned it last time.

The informant perceived the community's role as being adversarial because AFAO undertakes an advocacy role and flags a potential conflict of interest as a result of AFAO's involvement in the consortium. Interestingly, the same type of conflict of interest exists with University Human Research Ethics Committees (HREC) in terms of complaints. Any complaints about the conduct of the trial generally go to the Registrar of the HREC that approved the trial in the first place. This gives rise to a reasonable apprehension of bias in terms of that complaint process. So too with AFAO, there would be a reasonable apprehension of bias if a complaint about the trial process was received by the consortium since AFAO, as pointed out by this informant, has an interest in the outcome and was involved with the trial design. A fuller discussion of conflict of interest will occur in a later chapter.

On the one hand, this informant was concerned with the perception that AFAO be seen to be advocating on behalf of affected community but, on the other hand, acting in the best interests of the consortium. The informant was clear, however, that AFAO should not be a mediator or arbiter in relation to the Thai trials.

C22 That the communication relationships in Thailand are there, that it's not, that the community and the clinicians in Thailand are working together. And I don't want the fact of, I don't want AFAO to become an arbiter between the two of them.... And, I guess, I mean, if the Thai partners said we don't agree with the trial going ahead. We think that it's, you know, unethical for the trial to go ahead, then whilst they have made a decision on that, I would say that we would probably have to support that and go to the PEC and say we believe that the trial should not go ahead.

GD That would be a very interesting position for AFAO to take, I suspect, if they've been involved with agreeing to the process at the PEC in the first place. You see the inherent conflict...

C22 Ah, yes it is. Yeah, it would be.

GD How would.. I mean, is it resolvable?

C22 Is it resolvable? It's not out of the questions for AFAO to say we no longer support the trial and we withdraw from the trial. I don't think that's really out of the question.

While this is speculation from this informant, an equally valid and arguably more strategic approach would be for AFAO to exercise its partnership rights and seek to either change the approach by influencing the other members of the consortium or exercising its veto power.

C22 Yeah... I mean, I think it would raise a conflict and I think that AFAO would form its position through involving the people and processes that we've put in place from a, you know, the organisational processes that we have in place for making those decisions being the Vaccines Policy Reference Group, the Board of AFAO, plus we would ensure that CAR and ACCESS and the Thai community, that the processes that had happened in Thailand were sound, that we could support their position, I guess.

The informant speaks of AFAO as something separate from the Board of Directors. The inference in the preceding text is that the operational aspect of AFAO is somehow set apart from the ultimate decision making body in the organisation. Legally, the Board of Directors is the ultimate decision making body in the organisation so, in effect, they would be trying to influence the Board's decision rather than the Board shaping theirs.

C22 Yeah. But I think, and it would raise a conflict, but I think that, and you know, AFAO would need to make a decision, I would say that the type of organisation that AFAO is, we would fall on a position that we could not, if the Thai community did not support the trial, then I don't think AFAO could support the trial. I think, because the kind of organisation that AFAO is, we would probably need to, hypothetically, to say we don't support the trial.

- GD Let's run this out to its logical conclusion, if you did do that, what sort of consequences for AFAO would there be to their partnership in the consortium?
- C22 Well, I think we'd need to withdraw from the consortium, probably. Although what I, I think that what, if that was the situation, I think what we would try to do would be to resolve the issue. So, if the Thai community don't support the trial, look at why is that... You know, rather than just withdrawing support, looking at, are there reasons why the Thai, you know, is it a situation that can be mediated, are there issues that the Thai community are concerned about that can be answered?
- GD Do you think AFAO could mediate that?
- C22 Yeah, I think we could, I think we could advocate that they be mediated. So whether we act as mediators or whether we say that this is the issue that needs to be solved, if this trial.... If the trial is to go ahead, then these issues need to be solved and so the consortium needs to find a way of solving those and we would facilitate those issues being resolved. We may not necessarily act as the mediators, but we would facilitate a mediation process.
- GD I think it may be problematic for AFAO to be the mediator. They're not coming to the table without a vested interest. Are they?
- C22 No and that's why I don't think perhaps we can be the mediator but I think that what we would do is advocate a mediated process to try and answer the faults or concerns of the, if the community had concerns, then let's see if we can answer the concerns of the community.
- GD So that kind of works against, your advocacy role though doesn't it? If you can't mediate on behalf of, if you can't mediate in that

situation, then there is a conflict that's not resolvable. Do you see what I'm driving at?

C22 Well, yeah.. What do you see as.

GD You're the community representative on the consortium. CAR and ACCESS informally feed into you. You said that you advocate on their behalf to the PEC, but you've just said that if there's a conflict in terms of your duty as a member of the consortium and to act in the best interests of the consortium, and advocating on behalf of CAR and ACCESS, then you'd, what I'm hearing you say is that, what I think I'm hearing you say is that is that you would fall on the, you'd tend to fall on the side of the consortium duty rather than the CAR ACCESS duty.

C22 Look it would certainly be a position of the Board, what position we took, but I would think that if it was unresolvable, then we would need to act on what we thought was in the best interest of the community, Thai or Sydney, rather than the best interest of the consortium. I think that, I would say, that that is our prime position. Yeah.

Admittedly, this is speculation on this informant's part, however, it is interesting to note the stated primacy of the interests of community in this matter. On first consideration, this may not be a controversial thing to say. After all, AFAO has its origins in the community response to HIV in Australia but other considerations, such as profit sharing or allocation of resources, may play a part in the decision making process.

GD Just one last question on this, ... we've spoken about the conflict of interest, but there seems to me to be issues around profit sharing. You mentioned profit sharing in your last interview I think...

C22 Yep.

- GD How would that play out with say the Thai Red Cross and CAR and ACCESS?
- C22 The situation that there is currently is that the Thai Red Cross is a partner in the consortium. But, CAR and ACCESS are contracted to AFAO. So they're not members of the consortium. So, they, while the Thai Red Cross would have a profit share, CAR and ACCESS don't have a profit share.
- GD Would Thai Red Cross devolve some of their profit share hypothetically to CAR and ACCESS or would it fall to AFAO to do that?
- C22 Look, I don't know. It's not really been discussed. Like I have no idea what Thai, because it's become even more hypothetical regarding a profit share. For a while there was a glimmer of, well, what does profit share mean? It could mean, this much, and it's, kind of like, people...
- GD I don't think anyone is addressing any profit type talk at the moment.
- C22 Look, there hasn't been any rigorous discussions about that but it has been raised about, is there a role for CAR and ACCESS, set up a division of CAR and ACCESS in terms of profit sharing. But, the position at the moment is that their involvement in the consortium is as a contractor, a service that is contracted to AFAO.

So, a further area of potential conflict might be AFAO's advocacy for the community partners in Thailand competing with AFAO's desire to reap greater profits for itself as part of the consortium. The following informant describes AFAO's conflict of interest in an "inside-outside" construction. And not only does the informant conceptualise the conflict of interest in that way, but abdicates responsibility for addressing the ethical issues that arise from that conflict.

- NC21 But what the community actually gets the clinicians to think about is, or what AFAO in this case actually get them to think about the

population as a whole, you know, about what, how one might deal with the population, how one might improve the understanding of vaccines out there, and the possibility, how one might help recruitment. That's were, if there's any conflict of interest, that's where it might arise, but I don't think it has... Well, you know, if you've got really.. Let's just say there was a Nobel prize or a vaccine on the horizon, that we're working on that's really going to, you know, save the world, it's really exciting and there've been moments in the consortium, at meetings when some of the early Macaque, I think, were looking extremely positive and it was a real buzz, I mean a real excitement about being part of something and AFAO, like the social researchers like all of us, you get caught up in that buzz. I mean, it hasn't happened, but I can imagine, and I'm sure they can too, where the worse that buzz gets really, if things got really exciting, it's not so much about money I don't think, it's about the fame or the ... but you might do something that maybe in a different context you might not. I don't know... and I think for them there is a bit of a conflict of interest. I mean, they're inside it, they're not outside on a data safety and monitoring board who can actually say hey, because they're in there. So I think there are both pluses and minuses for them in there and they themselves have discussed that quite a lot. I mean, they've actually both within the consortium but outside it, I mean, they have discussed that amongst themselves and with their constituent members. So, you know, and I mean the subjects, the social researchers get the tradition as the ones looking after the ethics and I just keep saying, no, no, no, you know, we're not looking after the ethics, we're there as researchers. You need a proper safety monitoring board outside this that will actually, and you need social researchers on that, but I'm not going to look after ethics, I'm part of it. You know, I'm not going to, I can't wear two hats and I'm not an ethicist anyway, I'm a researcher.

This begs the question, is it an acceptable position to take the view that because one is wearing the ‘hat’ of a researcher, one necessarily cannot wear the ‘hat’ as an ethicist, notwithstanding the fact that this participant was not an ethicist? I would argue that it is not. While a member of the consortium as a researcher, it is every consortium member’s ethical responsibility to raise issues of ethical concern. To remain silent on matters that raise such concerns effectively consents to those matters. Being an authentic ethical agent requires of the consortium members no less.

What I have provided to this point is a discussion on the informants’ views as they relate to the potential conflicts of interest arising out of the consortium. However, do these views conform to the conventional definitions of conflict of interest?

What is a conflict of interest?

A conflict of interest may be defined as “a set of conditions in which professional judgement concerning a primary interest tends to be unduly influenced by a secondary interest” (Thompson 1993: 573). There are three types of conflict of interest discussed in the literature, actual, potential and perceived conflicts.

In the health care research context, a good example of an *actual* conflict of interest would be the payment of money to physicians from a particular pharmaceutical company to increase the prescription of a drug manufactured by that pharmaceutical company. Using the example of antihypertensive medications, the physician’s primary interest, that of providing best standard of care to their patients, may be unduly influenced by the cash incentive offered by the pharmaceutical company such that the physician prescribes the pharmaceutical company’s drug over that of a more efficacious one from another company. In this type of conflict of interest, a situation arises which brings into conflict competing interests. In other words, the situation is in the *foreground* of ethical concern. It is the emergent situation which gives rise to the conflict of interest.

To extend further the example I have used, a *potential* conflict of interest may exist when the physician is approached by the pharmaceutical company in the first place. The potential not to act in the best interests of their primary interest, best standard of care to their patients, is high when faced with the secondary interest of a cash incentive. While the physician may not have been in the situation where the conflict of interest emerges, the potential for such a situation to occur is high. In

potential conflicts of interest, the actual interests are present but the situation to bring them into conflict has not arisen. The previous two examples can be described as 'real' conflict of interest situations. The interests exist that give rise to both the potential and actual conflict. The situation is in the *background* of the ethical concern and the interests are the focus of enquiry.

A *perceived* conflict of interest arises where the pharmaceutical company offers cash or non cash incentives as 'gifts'. Using the current example, the company may fly the physician first class to their headquarters for an 'educational' on their product, paying for five star accommodation and paying a per diem travel allowance. While the company's gift does not provide direct incentive to prescribe its product, a reasonable apprehension would exist on the part of a reasonable patient that the company's largesse might influence the physician's prescribing habits. This type of conflict of interest does not rely solely on the interests or the situation but the *perception* of third parties observing the individual's or social practice's actions. In other words, it is the *perception* of third parties which is the focus of the ethical enquiry.

The question arises that, if such situations are so common, why then do individuals and organisations not recognise the conflicts of interest and avoid them? Sometimes they can but it is difficult, if not impossible, for individuals and organisations (through the agency of individuals) to make an objective assessment about their own interests. Indeed, individuals cannot be completely objective about their own interests. They are, therefore, inherently biased in favour of those interests and, as such, cannot determine objectively a conflict of interest about themselves or in which their interests play a part. That is why the scrutiny by third parties is such a critical part of assessment, avoidance and mitigation of conflict of interest.

While I have used a financial conflict of interest as an example, a conflict may occur between the clinician role and the research scientist role and, as highlighted by the informants in the previous section, in the case of AFAO, there may be a potential conflict of interest between its primary role as an advocate for the affected community and its duty to act in the best interests of the consortium as a partner. Such potential conflict clearly meets the definition of a potential conflict of interest.

So while these are the types of conflicts of interest that may arise, why does it matter?

Why does it matter?

Conflict of interest considerations matter because such situations affect the functioning of a social practice, particularly when (as is the case with the consortium) it is a fledgling social practice with all of the inherent difficulties, as shown in previous sections, associated with the emerging social practice.

Chapter Summary

In this chapter, I have highlighted, using the informants own accounts, how the consortium operates as a social practice with a particular task, namely the task of ensuring that the vaccine trial which it is running has high standards, both scientifically and ethically. I have paid particular attention to the ways in which the consortium demonstrates unity of purpose, learning and socialisation of its new members and the practitioner's reciprocal self-awareness of each other. While the consortium operates as a social practice, it is one in its infancy with all the inherent tensions and positioning that comes with the emergence of new, shared ways of seeing and doing. This is not unexpected, and on the basis of the data I have been able to collect (the CSIRO and ANU did not participate in this research), it appears to have come to a mutually beneficial outcome. However, conflict of interest issues do need to be explicitly acknowledged and managed. This will be addressed in my final chapter.

7

Maintaining Autonomy and the Covenant

In order for AFAO to bring a community perspective to the consortium authoritatively, it must have an ongoing relationship with the community it claims to represent, and it must negotiate the needs and desires of the community within the consortium.

In this chapter, I explore how AFAO maintained its relationship with its membership and, more broadly, with the affected community in the context of its participation as a partner on the consortium which, as I have pointed out in the previous chapter, is not straightforward or simple.

AFAO's relationship with its members

In the previous chapter, I argued that the professions have a covenantal relationship with society and that biomedical research is a type of profession which also has a covenantal relationship. AFAO has a relationship with its members that goes beyond merely contractual or philanthropic but is not a profession and, therefore, not, strictly speaking, the type of covenantal relationship defined by Mount and Isaacs. However, while it is true to say that AFAO has it and its members benefit in mind (making it a type of philanthropic relationship), it also advocates on behalf of affected community (making it a type of covenantal relationship). This gives it a significant covenantal aspect. It is worth noting that a large proportion of both the Board of AFAO and the membership of the Policy Reference Group are volunteers and unpaid, giving further weight to the covenantal nature of the relationship.

Costs and Risks to AFAO

Negotiating relationships both within the consortium and within its own organisation has required AFAO to incur costs and undertake risks that it otherwise might not have as a result of its involvement. These costs and risks come in a variety of forms, as demonstrated below.

Transparency, roles and responsibilities and internal governance structures

This section describes the ways in which AFAO organised and re-organised itself internally in response to the demands of consortium membership. In doing so, AFAO relied on the strength of its covenantal relationship since this involved changes to the way AFAO did things, and potentially risked disagreement or disaffection from its members.

First, it is worthwhile to get a sense of the many aspects of AFAO's involvement in the consortium. AFAO's representative roles on the consortium involve participation in a number of different committees. This informant highlights AFAO's involvement in that range of capacities on the consortium. Of additional interest is the comment in relation to AFAO always being the community partner. AFAO, being the national peak community based organisation for the community response in the HIV/AIDS sector, is the natural choice for community partnership in an undertaking such as this. The social history of HIV in Australia, and community's response within it, has facilitated the seemingly effortless choice of AFAO being the community partner from the start.

C11 ...So, AFAO has been, is part of a consortium from the beginning that was bidding for the, to develop, receive funding to develop an HIV preventative vaccine and first of all, I mean, the bid did go into the NIH, but there were also backup plans that if money wasn't accepted, that it would approach and work with other partners such as IAVI. But AFAO was always the community partner in terms of that. So AFAO's been involved in the bid process and then further developing the further proposal and so we've been involved in that since the beginning and we have various people on our secretariat who attend different meetings. Either the management committee, programme executive committee, clinical programmes committee. So, the completely scientific ones we leave to the scientists but the other ones we are representative on them.

This informant has a more structured view of the way in which the community inputs into the work of AFAO on the consortium and clearly articulates the governance structures at play within AFAO.

C31 Working from the bottom up, I'm [a senior member of an AIDS Council], so we've had an interest in following what was happening with vaccine research as a component in the overall approach to HIV prevention. I'm also, through my involvement with the ... AIDS Council, that organisation's a part of the

Australian Federation of AIDS Organisations and AFAO's a part of the Australian Consortium. But the interest, AFAO's interest pre dated that bid being there. Working up from that, I've been a board member of the Australian Federation of AIDS Organisations through the entire period that it's been involved as a member of the Australian consortium and was part of the discussion at the board that suggested that prior to AFAO getting involved and subsequent to it being involved, we needed a separate policy reference group to look at providing advice to the AFAO board about issues that arose from its participation. So in all of those ways, I've been involved.

The previous informant describes that as a result of AFAO's proposed involvement in the consortium when the bid was being developed, the way in which AFAO sought advice changed to meet the demands of the highly complex and technical area of vaccine development. I highlighted how just how complex and technical in Chapter 2. The changed advisory structures in AFAO also meant that advice to the Board of AFAO was received quickly rather than needing to wait for a Board meeting or a general meeting or seeking informal advice. The changed structures also facilitated research literacy in the processes of HIV preventative vaccine development. Members of the Board of AFAO are either elected officials or paid staff of its member organisations who report back to those organisations. In this way, the membership of AFAO has the capacity to input into the decision making process. Because it may be possible to identify the informant from this extract, I sought and received permission from the informant to use the extract.

C31 But I was aware in general terms of what were the kinds of issues that might arise and my view was that as a community organisation we were going to be facing a range of areas that the governance structure of the organisation didn't allow everybody in the organisation to get across those issues and there needed to be a reference point for the board where a smaller group of people could develop a degree of expertise in sorting through those questions. That then meant that the board would be in a position

to make informed decisions on those issues that it needed to. So the Policy Reference Group's made up of people who are on the board, people who are on the staff of the organisation and a range of people from outside of the board. And that process of specific purpose policy reference groups is one of the ways that an organisation, where the board meets every two months, where the members meet twice a year, is able to deal with and provide advice to, both the management structure and the board, on particular areas of interest..... So they tend to be relatively technical in their nature and they're designed to be able to unpack the issues in more depth and more detail than the board would be able to do meeting for two days every two months.

C31 Well, the Policy Reference Groups are set up so that they draw on the resources that are available in the membership. They don't have any decision making powers at all. So there would usually be a link from the PRG back into the Board, because, in a sense, what comes out of the PRG goes to the Board in relation to decisions, so it makes sense to have somebody in the PRG who's then sitting at the Board and able to take that discussion forward. It has the staff who are working on it because they're key sources of information for the Policy Reference Group and then it has a range of people on it who come from outside of that who have particular areas of expertise or who represent various parts of the membership of the organisation. So, they're kind of a mixture of representative and skills based.

They also explicitly mention the social history in Australia and the partnership approach as being the mechanism for informing both the community representatives and those they are trying to influence. Consistent with the characteristics of the Langfordian model of social practices, there is an explicit acknowledgement in this account that the social history shaped the consortium's acceptance and approach to AFAO's involvement and that such an approach may not have worked in other settings. In other words, the shared ways of seeing and doing as a member of the

Australian HIV/AIDS Partnership social practice assisted with AFAO's acceptance as a partner in the consortium.

C31 In terms of needing to marry, the law, the science, the ethics and bring a community perspective into those discussions, that's part of what the HIV sector in this country's done since the early days of the epidemic when, depending on whose version of the story you believe, we either got ourselves a seat at the table or somebody said there's one there do you want to take it? But certainly the partnership approach has been one where our role has been to take community views, make sense of them and take them to the table where policy and other kinds of decisions which can be made. So it's not as though this sits in a bizarre place in the history of the epidemic in Australia the way it might, for example, if this model had been used in the UK or the US where there'd been much less history of people sitting around decision making tables as opposed to fairly remote sometimes when you look at them, advisory tables. But it has required us to get across a whole range of issues that we had never had to consider before.

This informant states that, unlike other consortium members, there is a high level of voluntary work put into developing AFAO's positions or assisting in AFAO's role on the consortium. This is beyond the budgeted staff time for consortium work, however, while this informant frames this discussion in terms of a high level of contribution not costed out, they also state the benefit, because having that discussion has contributed knowledge. This is consistent with the covenantal nature of AFAO's involvement through the desire for effective advocacy on behalf of the community it claims to represent. It is also further evidence of the capacity development required of the affected community sector in terms of research literacy.

C31 In terms though of the volunteer hours that the consortium gets for free, enormous, in the same way as everything that the community gets from the community sector. I mean, if you costed my hours that have gone into this in my own time at my hourly rate, if you costed [the layer's] hours at what he gets as a senior counsel, if

you took into account the, whatever [the ethicist is] getting paid as a consultant ethicist and added that in, you start ending up with a huge number of hours but there are benefits. I mean, I now have a much better understanding of how patent law works than I needed to know, we've got a better understanding of the role of intellectual property in steering this sort of stuff. We have a much greater understanding of how, the difference between good and bad clinical trial design, so I mean, there's a whole range of, like everything else, there's a whole range of spin off benefits that come from that as well.

Interestingly, the AFAO Board does not operate on a 'majority rule' approach but, rather, on a consensus approach to decision making. One would expect in an organisation the size of AFAO, a majority rule approach would be the most expedient means by which to make decisions. This is not so in the AFAO model as the following participant highlights. This is perhaps reflective of the covenantal nature of their relationship with their members.

C31 So it's not a Board that operates on the basis of needing to get a majority. It's a Board that operates on the basis of consensus and that if there are still people who are opposed on the board and are able to mount significant arguments, it's a bit the way in which the consortium had to deal with us when we've got some fundamental objections to something that's going to happen, that appears that it's going to happen, if I said, or if any Board member said I've got fundamental objections, the question would be, not well, you're one and there are five or six or seven other people who have a different view, but what would we need to be able to do to persuade you and there's then a process of trying to find a position that would satisfy everybody.

This informant elaborates further on the way in which the internal structure of AFAO assists the Board in its decision making. Interestingly, this informant suggests the Policy Reference Group made decisions during AFAO's involvement with the consortium. However, the governance structures within AFAO do not lend

themselves to that approach. It is more likely the informant means the Policy Reference Group provided authoritative advice in relation to decisions that needed to be made by the organisation. Given the complex nature of vaccine development I highlighted in previous chapters, in-depth discussions would have occurred within the Policy Reference Group who then, after discussion and exploration of the particular issue, would have provided advice to the AFAO Board who would have made a final decision on the matter. This may have given the impression that the Policy Reference Group was making decisions. Also of importance is that one or more Board members were also members of the Policy Reference Group which enabled direct involvement in such discussions by representatives of the Board, and the capacity to directly feed back to the Board the discussions held by the Policy Reference Group.

C21 Yeah. I think the only thing I didn't mention was we have at AFAO a vaccine policy reference group. I was trying to think what the acronym was. Vaccine Policy Reference Group, which is a, drawn from our membership and community which is another method by which we get a broader community perspective on a whole range of issues. And we've used them to assist in making decisions. Like throughout the process, some scientific decision have been made of whether we drop some constructs within the vaccine and, I mean, that was one area where we've had to get the scientists in and talk about it and explain it to us and we've used the PRG for making that decision as well as a whole range of things around the process of informed consent. So, it's kind of a bit broader than just the staff in the secretariat. Yeah.

C21 ...So there's a range of member organisations plus outside community people as well. Epidemiologist, lawyer, ethicist.

C31 ... But I was aware in general terms of what were the kinds of issues that might arise and my view was that as a community organisation we were going to be facing a range of areas that the governance structure of the organisation didn't allow everybody in the organisation to get across those issues and there needed to be a reference point for the Board where a smaller group of people

could develop a degree of expertise in sorting through those questions.

The next informant provides some insight into the early internal discussions at AFAO in relation to participation in the consortium and the types of considerations taken into account in those discussions. The discussions appear to have set to one side discussion of profit share in the event of a successful vaccine in favour of the capacity to influence the consortium through affected community's participation. The following informant suggests this decision was made because profit share was a remote outcome whereas the opportunity to participate as a partner in a consortium developing a preventative HIV vaccine was immediate and it was important for AFAO to seize the opportunity. The informant also gives a sense of feeling that any problems encountered would be able to be resolved along the way.

C31 I think one of the things that we have had to say in the early days of this discussion, where some of the discussion was about how would we make decision about what we would do with the profits if there were profits, and was it legitimate for a community group to profit, was that the likelihood of there being profits was highly remote and it was about where could we best fulfil the role that we saw of being able to make sure that the decisions that were being made appropriately took into account community's views was what ought to guide the decision about whether we went in or not, not how would we make a decision about what we would do with the profits if there were any, in X number of years time. As it's turned out, that's a sensible approach to have taken.

All of the internal consultative processes and governance structures were noticeable to other members of the consortium. This non-community informant appears to have an understanding of the internal consultative mechanisms in AFAO and the way in which AFAO members of the consortium might bring issues to the consortium's attention.

NC41 I think it's probably easier with community no matter what because scientists always do have, they're opinionated and the

have their own perspective on things, so smaller groups are always more effective. I think AFAO is the peak organisation in Australia is a helpful thing for this work, because then you can, then they can go out and seek additional information and advice from their constituency and then bring that to the table as a consolidated view. And I hope they felt that they were bringing views to the table even if they weren't the views of the person bringing them that they were getting appropriately aired and discussed. And I think that was the case. So, yeah, I think it does help to have that kind of structure here and being a small country, with a well organised group, it helped.

Conflict within the community: about participation; about process

AFAO's involvement was not without some tensions. Conflict within AFAO could not always be avoided, however, conflict in itself, is not necessarily problematic. In fact, in this instance, I suggest that better trial outcomes came from this conflict. Indeed, the capacity to present alternative points of view encourages a comprehensive examination of issues from different perspectives and may lead to better policy decisions as it did in this case. This informant states that the internal debates about participation were in no way straightforward at the start of AFAO's involvement.

C31 There were certainly people in the community sector who said, no we should not be involved as a partner in the consortium and those views are still being put.

GD Do you see any conflict in AFAO being part of the decision making body in the consortium and actually being the educators as well?

C31 No

C31 Yeah, the reality is that there's a degree of separation between the two, and if that, if pressure was being applied to do it in a, the way

it's set up, if pressure was being applied to do things in a particular way, that would be very transparent.

GD To whom?

C31 To the staff who are doing the work and to the Board who are watching that work being done and to the community who are watching that work being done. So, for example, the team of people who are doing the work, who are actually charged with rolling out the work, don't sit at the consortium table. Management of the organisation sit at the consortium table, so if, for example, the consortium was to say to [the AFAO representative] we don't want this education program to be rolled out in a way in which the educators are saying it needs to be using their skills as community educators, then [the representative] would need to say to them I don't want you to do it that way, I want you to do it this way and they would say why. And if he just said because I'm telling you to, that would cause an immediate ruckus....So, it's not impossible that that influence could be bought to bear but it would have to be extremely subtle and it couldn't run counter to what was good practice as determined by the educators without it causing a blue. So the notion that somehow, someone could be, in a Machiavellian way pulling strings off to the side and that then made a difference to how [the health educator] and people actually worked on the ground, is pretty impossible.

While this informant has said the influence would be very difficult to get away with, what this extract also highlights is the self-regulating capacity of AFAO's internal arrangements. This is consistent with Langford's idea of institutional regulating effect on social practices. While I have argued that the Australian HIV/AIDS Partnership approach adopted in Australia is a social practice, and the consortium, as a physical example of that partnership is, in part, a manifestation of that social practice, the way in which the community is organised to respond to

HIV/AIDS in Australia is a social practice also. As a social practice, it is unsurprising that such structures exist within AFAO itself.

C31 To some extent though, that depends on the Board and the PRG being kept informed of what's going on and I see my role as a Board member being to ask questions about that stuff and expecting that I'll get answers... And if I don't, I keep asking. So, I mean, my view is, as happens in my own organisation, the operational stuff gets left to the managers to do that, that's not the board's role, but it does keep an eye on what's going on and if it looked as though influence was being exerted to do things that weren't appropriate, then those tension would emerge very quickly I would think.

This next informant also highlights the internal conflict and dialogue within community. This informant, who is not from community, also puts faith in the self-regulating effect of AFAO's structures to "sort out" its internal conflicts.

NC31 I think that within the community itself, and this is pure speculation, I think there are conflicts between the infected community and its representatives and the affected community and its representatives about where resources go in terms of research and development. And I tended to hope and regard that as an internal issue. But one that there is an expectation that the community will sort out internally. But it's pretty clear that there's quite a diverse range of perspectives within that sector.

It also was not just locally that AFAO encountered potential conflicts which required them to change their approach or institute new structures. Had the trial shown a level of efficacy, there was a proposal to undertake a larger trial in Thailand. This required AFAO to both identify the relevant community organisation in Thailand to liaise with, and required consideration of how those community groups might have some influence in the trial itself.

C22 Right, in term of the consortium, AFAO as a member of the consortium is subcontracting them for services....While ensuring that AFAO can represent the interests of the Thai community at the PEC level.

But how does AFAO represent the interest of the Thai community partners (sub-contractors) if that interest comes into conflict with decisions made by AFAO as a partner in the consortium? This potential conflict of interest was a risk to AFAO. It was a question I put to this informant.

C22 ...I mean, we AFAO needs to represent the community which is both the community in Sydney, you know the stakeholder community in Sydney, as well as the community in Thailand. Now we can't directly, I don't feel that AFAO can directly represent the interests of the Thai community because we're not part of the Thai community, so we need to know what [the Thai community organisations'] position is on certain issues so that we can represent that position at the PEC....Well, how they could would be directly through their representation on the CPC [Clinical Programme Committee] or to me and I would raise it at the PEC [Programme Executive Committee]. So, if they raised it with me, I would make sure that they also raised it at the CPC. And I would raise it at the PEC. Like, I think it's really important that the relationships in Thailand are maintained. That the communication relationships in Thailand are there, that it's not, that the community and the clinicians in Thailand are working together. And I don't want the fact of, I don't want AFAO to become an arbiter between the two of them. So, I would encourage it to be raised in Thailand at the bodies that are established in Thailand to deal with those issues. But, I would also raise it at the PEC as an issue...And, I guess, I mean, if the Thai partners said we don't agree with the trial going ahead. We think that it's, you know, unethical for the trial to go ahead, then whilst they have made a decision on that, I would say that we would

probably have to support that and go to the PEC and say we believe that the trial should not go ahead.

The previous informant speculates about what AFAO might do should the situation arise where the Thai community partners disagree with the trial going ahead, on whatever grounds, and suggests they would advocate that position to the Programme Evaluation Committee. While AFAO may do that, this seems to be a somewhat uncritical way of approaching this particular problem. A likely alternative scenario is that AFAO would determine the exact nature of the issues, work with the Thais around suggested ways of addressing or mitigating those issues, and advocating those positions to the Committee, rather than simply suggesting the trial not go ahead. This, clearly, is an option, but would probably be the last option available to AFAO.

What the previous and the next extract suggest is that little consideration has been given to the types of conflicts that might have arisen had the Thai arm of the trial proceeded. In both cases, AFAO has an actual or potential conflict of interest. The first, as described above, relates to the advocacy role they have and the duty they have to act in the best interests of the consortium as a partner, and the second is a potential conflict of interests between AFAO's financial interest and the Thai community partners' interests. While AFAO is a full partner in the consortium with a full share of the profits, the Thai community organisations, the next extract suggests, seem to get none.

C22 Look, there hasn't been any rigorous discussions about that but it has been raised about, is there a role for [the Thai community organisations], set up a division of [the Thai community organisations] in terms of profit sharing. But, the position at the moment is that their involvement in the consortium is as a contractor, a service that is contracted to AFAO.

While there may be a potential conflict arising from the way the trial was structured to incorporate the Thai community organisations as 'contractors', the wisdom of participating in significant levels of community preparedness work in Sydney was by no means universally agreed.

Waste of community resources/Educating communities prematurely

The following informant expresses a view that it is a waste of time preparing and educating communities in relation to vaccine trialling when it is highly unlikely such trialling will actually occur.

C12 ...I'm sure I said this in the last interview that this community focus on preparing trials, preparing communities to have vaccine trials when there was never going to be a vaccine trial in that community, to me, doesn't make any sense. I think it's a much better use of resources to, you know, look at what the real questions are which would be prevention and treatment and care. Rather than spending any resources at all trying to get a community active in vaccines work. So, you know, from that view which I probably express, could have gone even further, to involve communities now in something which just isn't even vaguely looking like it's going to have a successful. There might be a few trials around the world that their have to be community involved in those trials, the community have to be prepared, so there's a role for organisations to play in that as before, but in terms of broader remit, educating communities about vaccines and promoting in communities about vaccine research, I'm not certain, it's so pie in the sky. I think generally, I mean I would probably agree with what I see as happening with colleagues with people who [indistinct] microbicides had a huge resurgence in Bangkok. People are starting to talk about them again because they think, well, this is a better route.

Given the lack of progress in efficacious vaccine development, this informant expresses frustration and suggests funding could be better spent elsewhere. Microbicides, and indeed biomedical HIV prevention generally, is an emerging area of research interest. Microbicide trials, circumcision trials and Pre-Exposure Prophylaxis trials all have similar structures to vaccine trialling. At the time of this interview, such trials were only being contemplated and few were occurring. More recently, such trials are gaining momentum and funding as a more cost effective

approach and as vaccine development is proven to be unsuccessful. As I have previously stated, the results of my research may have benefit to such trialling.

Benefits of AFAO's participation

The previous section illuminated some of the risks and costs associated with AFAO's involvement in the consortium. This next section describes the benefits that arise from that involvement.

Involvement as a partner changes affected community's views

A theme that has emerged throughout all of the extracts from informants, and described in the previous chapter, is that their views, attitudes and understandings have changed as a result of participation. The following extract is a good example of socialisation of 'new' members of the social practice being inducted into shared ways of seeing and doing. As this informant highlights, that is a shared process between the members of the social practice, not unilateral or one sided and is clearly seen as a benefit.

C31 ...I think what we've got is a better understanding of what are the motivators for people who are involved in this and they're different. But they're different between bench scientists and clinicians in relation to development of drugs for example, so it's not surprising that they would be. I think what's happened is, I don't know that our approach has changed, our understanding certainly has and therefore, in a sense because we translate backwards as well as forwards, I think community's views are now slightly different as they have an understanding of the complexities that are there and some of the really complex issues that have to be sorted.

And this next informant verifies that impression. Equally, just as the internal processes of the community can be considered a social practice, the social practice of biomedical research has its own ways of seeing and doing which regulate and educate its members. In essence, bench scientists have been inducted into the social practice of the Australian HIV/AIDS Partnership model and affected community has been

inducted into the social practice of biomedical research for the purposes of the consortium. Importantly, what both extracts highlight is that while the relationship between the parties may not continue beyond the consortium, the knowledge and learning gained from participation continues.

NC11 Oh, they do learn. Certainly they learn as time goes on and they become quite familiar with the read outs and, of course, there's another detailed level of knowledge there that is scientific, biological training type knowledge that's not always easy to impart but certainly learn as things go on and they can... I guess the, sort of, challenge for the basic scientist is to be patient with them and bring them along the process. I think, it's worked pretty well in that, you know, AFAO has often known when to let scientific discussions run their course and not, sort of, drag them out unnecessarily and, but when they need to know, understand something they can ask questions, that has more of a bearing on what they do. So, you know, the potential disadvantage of having them round the table all the time is that you have to explain every single thing, the meetings take forever and it gets a bit frustrating because, you know, it just slows things down and people are busy and have things to do but, so there needs to be a balance between people understanding, you know, the concepts, the broad picture that impacts upon their work and, but letting other things run their course when it probably doesn't have a big bearing on things that they do directly...The sort of critical thing is that it is very person dependent and so, you know, we've had a few different people from AFAO sit around the table at various times and most have been very good. Some have been better than others at that process I guess. And so, you know, it's difficult for them though too I recognise because, you know, they don't want to have the wool pulled over their eyes, you know, they want to know what's going on. So, I mean, that's a hard, you know that's probably true for all, you know, probably aware another process of doing this is the Community Advisory Board approach and I think no matter how

you do it, there is that tension between providing all the scientific knowledge or trying to provide enough that they can make all the decisions that they need to make without getting bogged down in the scientific detail of the whole thing. You know, that's, that requires some give and take on both sides. The scientists have to be patient and the community groups have to be patient as well.

C31 And I think the benefits, having looked at the models that operate elsewhere, are way more beneficial, and on some of those issues where I'm not able to give you the details, where there were issues that for us were very fundamental ones, we were able to say no this cannot proceed until we're satisfied... The position came, the issue arose originally in the decision making part of the consortium. There wasn't a uniform view. It wasn't the community sitting one off. There were a range of views about how the particular hiccup that had arisen ought to be resolved.

The previous informant describes the process of decision making on contentious issues at the consortium. Previously, I indicated there were commercial-in-confidence considerations which prevented me from obtaining all the detail of such deliberations. However, clearly the informant perceives a benefit in the partnership arrangements of the Australian consortium over the less equal Community Advisory Board structure prevalent elsewhere, even going so far as highlighting a threatened veto power prior to proceeding.

Interestingly, the informant explicitly mentions the resistance of some consortium members to community's presence on the consortium on the basis of the potential for breaches of confidential information provided to consortium members. The social history of HIV in Australia would appear to again make a contribution to community's full involvement in the consortium. The reluctance of one consortium member, in particular, was 'sanctioned' by other consortium members used to dealing with affected community around confidential information.

C31 Yep, I don't know whether there's been a DSMB that's been established but I expect again, there'd be a community person that would sit on it because, I mean, that would be quite

uncontroversial that there would be because it's so much of the way in, as the interaction between community and drug companies who are doing clinical trials. And that means that by sitting on the DSMB actually get access to more data than the researchers have got because you actually get to look at unblinded data before a trial's completed. Now, that's just been so much of how we've operated. I think, certainly from talking to a number of people from overseas both in the community sector and in the research sector they're surprised that community was involved in the consortium and some members of the consortium are surprised that community's involved. CSIRO has no history of community involvement and was extremely reluctant at times to have community privy to information that was coming to the consortium. But a view of a large number of other people around the table was that they've seen far more sensitive information and it's not ever been revealed inappropriately so we would have no problem with providing them with that information because they have a track record of being able to use that information confidentially and appropriately.

The previous informant highlights the significant benefits to both AFAO and affected community to being a 'full partner' in the consortium. I have previously indicated that the partnership approach was unremarkable and that is confirmed by this informant. Perhaps this is the most telling explanation of why community representation on the consortium as a full partner is both unique and worthwhile.

It was not only the community informants who perceived benefits of their sitting as a full partner of the consortium. Non-community informants did too. The value of community representatives around the consortium table is expressed by this informant as a 'sliding scale' of effectiveness from inception of the consortium to trialling with participants. They also raise the issue of the proportion of funding that participation warrants.

NC11 Oh well, certainly, certainly it's important to have them at the table. I think that, there are some discussions we have that are

very technical in nature about the vaccines and what antigens are in there and how they work in mice or monkeys or whatever that probably don't have a direct bearing on the community partners but as those things start to move towards a clinical trial they have more and more bearing and, sort of, having them around at the early stage it certainly, kind of, helps that and in many ways it's hard to know when the benefit will be the most and so, it was our view, we should basically have them around all the time. The more difficult decision is not having them there but how much funding pie the community partners get allocated to do their work.

The informant raises the issue of funding allocation again in this extract with a particular emphasis on ensuring the allocated funding is spent wisely.

NC11 The community group has worked very closely with the social researchers in terms of risk behaviour, risk monitoring design. So, that's a little bit harder but, and I think our consortium is pretty unique in that we have the sort of community and social researcher component built into the budget of the whole program but that doesn't mean there are not discussions about you know, well, how much and what's the value of this compared to that and, you know, I guess we're obliged to spend the money wisely and in a, sort of, goal directed manner, but.. So there are, that's, they're the main sort of issues around that.

The informant categorically endorses community presence in the consortium but qualifies that endorsement with a caveat on the extent of the funding pool. Unlike other members of the consortium, where the technology or expertise other members bring to the consortium are quantifiable and measurable, the contribution of the community representatives is less amenable to quantification.

NC11 ...the consensus view is that that's not the case. That we need them on board, you need to spend money on that but it's not a bottomless pit... I mean, we just couldn't have had better support from a community organisation for doing the trial. There was not

bickering, no back biting, no people sort of heaping crap on us and stuff so it's worked very smoothly and that's certainly... It does save you a lot of time and effort later on if you get all that stuff and have to deal with it. People have to spend time on putting out fires and complication all this sort of stuff so we're much better off dealing with it at the start.

Again, this informant clearly establishes the benefits of community involvement from the start of the process as a means of ensuring a smooth process later when trialling occurs. The informant also comments on the behaviour of AFAO and seems surprised there is no 'bickering' or 'back biting'. As I highlighted in chapter 1, there is a history of tension between biomedical scientists and community activists so perhaps this informant expected the same approach from the AFAO representatives.

The next informant raises the notion of a budget allocation as a tension with the scientific members of the consortium. The tension, as reported here, is the perception that the community is competing for funding that otherwise would flow to the scientists. This perception by scientists questions the value of the community's contribution to the consortium. Another interesting interpretation of the extract below is the sense that this informant was somewhat surprised with the community's ability to make a meaningful contribution to problem solving around the consortium table.

NC31 Whenever there is an issue on any of our agenda for any of our meetings, there is an expectation that AFAO are there to contribute to solving problems addressing unforeseen circumstances or whatever else. And the experience has been that's very much what they've done. I think that the inherent tension is that there is a line item in the budget associated with that participation that some of the scientists regard with considerable envy and doubt and a dollar for AFAO is a dollar that I don't get. And that's a friction point.. you know...

The next informant most clearly identifies the tension as an oppositional relationship but expresses the relationship of scientists and community in this context as a symbiotic one. Once again, community involvement is described as invaluable and a risk management approach to things "falling apart" later. Overall, the informant

believes community involvement is critical at the outset for a better process and more effective trial design.

NC41 Absolutely! It's good to have them there and I firmly believe that that we'd really be asking for trouble in terms of the conduct of any program if it doesn't involve a community component, it just won't be anywhere near as effective and you really are running a huge risk of things falling apart unless you have a community component. It's simply, you know, it's the clinician and science perspective versus the community perspective and you really can't have one without the other. So, no, it's been an invaluable relationship. It's been an excellent and been a tremendous group to work with... Yeah, it's, I guess a check and balance all the way through really. You know AFAO is represented at that PMC board level what is a practical... So, you know, they did advise on things like consent forms, its appropriateness. Any materials that we would use to advertise the trial was happening, AFAO put those together on behalf of the consortium and so they, you know, were able to really put a community perspective on the way things were going and the way that we went out to the community, that was largely handled by AFAO. Consultation, the design of the trial, and so on. All those things were really implemented by them. But also there's an internal check because, you know, they sit at implementation and at the Board level. And, you know, they have an equal say at the table so that the program remains appropriate.

The next extract suggests the non-community partners, at least the following informants, were impressed with the way in which the community representatives responded to the provision of complex scientific information. The community participants in the consortium were required to engage with the social practice of biomedical research. As such, and in order to be full participating members of the consortium, affected community members needed to learn and interpret what the scientists were saying. According to this informant, they appear to have achieved that aim.

NC31 Certainly through the granting, sort of, facilitating income stream, there are very formal requirements for community representation and in the US they take the form of Community Advisory Boards. So the community have a separate forum in which they meet and consider and da da da.. And then contribute into a different arena. Whereas in Australia, what we've done is, rather than having a separate Community Advisory Board, the community are part of all of our governance structures by definition. When, we talk about molecule one, da da da da da, unfortunately for some of the community people, that means they have to go through that process. And as difficult as it is for them and as impenetrable as it might be, I think they responded to that challenge enormously well.

Indeed, the next informant suggests the community representatives can synthesise complex scientific concepts and contribute meaningfully to improve the trial design.

NC41 ... I mean, I see them as, I think, as I said, as absolutely critical to the process and so you know, if you're making choices, I think you would always choose to have community at the table just because, at the end of the day, if you're not able to implement your clinical trial because either the community are not behind it or if you've put something into the clinical trial that's, that would be unacceptable to those constituents and there's always a risk of that when you're working in clinical research that you'd never get the trial done. And so, you may have the most magnificently designed program, beautifully made vaccine, and no way of actually doing the work. And that's what community involvement's about, design components, acceptability issues, are critical. And it's not like you're dealing with people who are not capable of handling complex scientific information. There's a very well formed and great contributors on a scientific level as well as on a community level. And understand that there's always a compromise... Yeah.

So I mean, that's something that, you know, did make this unique and I think if the opportunity arose to do it again in the same way, there's not much I would change. It may not be possible to do that in all cases but, you know, I think where it is possible. I think we're a stronger group because of it.

It is hard to imagine a more positive endorsement of community involvement as a full partner than the previous informant's extract. It is clear that they perceived AFAO's involvement as very valuable and worthwhile and critical to the success of the vaccine development enterprise. It is important to remember, however, that those organisations not inducted into the social practice of the Australian HIV/AIDS Partnership did not agree to participate in this research, and may well have been more critical of AFAO's involvement.

Comparisons with the alternative Community Advisory Board model

At the start of this thesis, I describe two alternative methods by which affected community can participate in vaccine trialling. The major focus of this thesis has been the exploration of AFAO's involvement as an equal partner in the consortium. I also described the Community Advisory Board process which is the method of affected community participation encountered in all other parts of the world. The focus in this next section is the difference between those two approaches.

There are significant limitations to Community Advisory Boards, as this informant highlights.

C31 Now, I think, I don't know, but I think that would have played out slightly differently if the question had been flicked across to a community advisory board to say what is your advice to us in relation to this? Where, you know, the community advisory boards when they work well, work extremely well but they work on the basis of a set of personalities who can work together. Where they don't work very well is where the advice is documented and people are told, yes, this is taken account of but in fact it doesn't change anything.

GD So, what I'm hearing you say, is that because of the nature of AFAO's involvement in the consortium and because they're a full partner, the other partners with the different views, had to sit down and work through the issue rather than...

C31 I think what we might have had to do that anyway, even if we weren't there, I can't say that would have turned out differently, had we not been part of the consortium. It may well have been that had we been in a community advisory board, there would have been enough people sitting around that table who had some doubts about what appeared at first to be the majority view of the best way to proceed, that might have changed whether we were there or not. What it did mean, though, was that we were a partner in arriving at that decision, not sitting off to the side, hoping that the arguments that we put as a community advisory board, might be taken into account around the table when the decision was being made. ...The way I think you could get to an answer to that question is to potentially have a look at what's the level of community involvement in clinical trials the drugs area in the US. For example, I'm aware of cases here where community people sitting on advisory committees around drug trials have been the primary instigators of a trial being called off when it got to the DSMB. Now I'm not sure whether clinical trials in the US have community people sitting on DSMBs for example with the capacity to say this trial needs to be stopped.

This informant essentially highlights the limitations on the ability of Community Advisory Boards to affect change in decisions made by another body. The informant uses interesting language in terms of "sitting off to the side, hoping" arguments made by the hypothetical Community Advisory Board made a difference to decisions of the consortium. It is possible, as the previous informant alludes to, that the nature of the affected community's engagement in Australia may have been sufficiently important to the consortium to influence that outcome, but a Community Advisory Board has no direct mechanism to bring about such a result.

The next informant suggests Community Advisory Boards have greater independence in terms of considering information from a fresh perspective. Again, like the previous informant, this informant states that for a Community Advisory Board to change anything, it has to be 'strong willed' and united. Nevertheless, their view is that Community Advisory Boards are predominantly educative rather than decision making bodies, in large part because once protocols and information related to those protocols is provided to it, such protocols have been through the regulatory approval process and consortium members are reluctant to change those once approved given the time and effort involved in gaining the approvals in the first place.

NC11 So, I think, you know, both approach, a CAB is a little more independent if you like and you see things, sort of, fresh but you don't get that same level of interaction. I think probably the critical advantage of the way we've done it is that we can influence things from the word go. A lot of CAB interactions are more educative than the ability to truly change the trial. I mean, you really have to have a very strong willed group of people on a CAB that are united against something that they see as a wrong to change a trial at the CAB... I don't think, I don't really think that advisory's probably the right word. It's more, you know, this is what we're doing, can you take this out to the community and tell people this is what we're doing, not, you know, let's think about doing it this way what do you think about that? Which you have to be much, much earlier in the process. By the time you've got a protocol, you know, going through ethics, going through the regulators, it's not only difficult to oppose.. one of the reasons it's difficult to oppose is because you push it back a long way because you have to go back and do those things. You might delay the trial for 6 – 12 months or something and then people will say to you, well, this might be the vaccine that cures AIDS and you just let X million people get infected because you delayed the trial for a year. You know, that's simplistic but certainly, there are time pressures and so, that's important... It is a tension isn't it? I mean, sure CABs can educate well, they can disseminate, they can

do all that. They have a tough time changing things. You know, they can, sort of, work around the edges, you know, patient payments or, you know, little things, benefits to people in the trial but, you know, the chances of them working on the consent are probably pretty small, the chances of them working on the media campaign are probably pretty small all the sort of things that AFAO did, CABs would be unlikely to...

The previous informant gives a very clear indication that, because AFAO was a partner in the consortium, it had real influence to mould and shape the design of the media campaign and, importantly for this research, the consent process. This is a very strong indication that, at least for this informant, AFAO's participation was meaningful and important. The community informant in the next extract affirms this view.

C21 And that's probably about, we're there, we're not, you know, just, the community involvement isn't just a CAB. It's actually being there. Every decision, the community is there and every decision about our work, the scientists are there as well.

A key difference between the consortium structure adopted in Australia and the Community Advisory Board structure in other parts of the world is described by the next informant which reinforces the views expressed by the previous informants. The informant expresses some surprise in the way the clinicians around the consortium approach their research participants (not wanting the injection to be too big or too painful) and expresses a view that the role AFAO played was to expand those clinician's perception to include a population level rather than an individual level perception. The surprise seems to be in relation to the clinician's concern with their participant's well-being.

NC21 Because I think otherwise, coming in later, it's always, the parameters are all set down and you spend half your life trying to break them or change them or alter them. And I think since they've been there at the beginning, they've actually had a voice in the building and they've actually had a, not huge, but they've had

some impact on the design and, you know, on the ways in which, so called patients or vaccine recipients are positioned. And it's quite interesting because clinicians are very thoughtful about, you know, in some ways more thoughtful than I would be, they worry about how many injections and how big the injections and, you know, they're very careful about, and rightly so, but I mean, to an extent that actually surprised me. I mean, they're more caring than I think, than I think I might be or that I would have thought about being if I'd been in their shoes. So their, but they're very individualistic. I mean, they're dealing with individuals so they're very concerned about each of the participants and their welfare and for their safety. But what the community actually gets the clinicians to think about is, or what AFAO in this case actually get them to think about the population as a whole, you know, about what, how one might deal with the population, how one might improve the understanding of vaccines out there, and the possibility, how one might help recruitment.

There are other avenues for affected community representatives to apply influence to trial conduct decisions as this informant indicates. However, again, this would appear to be highly idiosyncratic to the Australian approach.

The next informant explicitly acknowledges the social practice of the Australian HIV/AIDS Partnership as being a key factor in AFAO's involvement in the consortium.

C22 ...In Australia there wasn't a CAB because there is a long history of collaboration between the community sector and clinical science through the National Centres and AFAO working together and community has always been involved in various working groups within the research centres. So it was a different kind of history and background in Australia that a formal CAB, whether it was, I guess it was a decision not to set up a formal CAB in Australia because there was a, already a structure that had existed and that had been working for a long time about community voice and

community issues being heard within the clinical trial process... It is a bit. I guess the other way of looking at it, I guess, what we see as the benefits of this model. Because it has, even internally at different times in AFAO, it's been discussed of should we even be involved in the consortium or should we have more the Community Advisory Board model or where we are involved, only as advocates of the community. Some benefits to the model that we're in is that we do have full decision making role. So we are involved in, like we have access to all the information, which you should still have if you are a part of the Community Advisory Board or some kind of advisory board, but I think the reality is that we are in a position where we are able to more fully and more equally engage in the debate.

Again, in the previous extract, the informant talks about 'more equally' engaging as a full partner in the consortium. Inherent in what they have said is the different power dynamics at play in being a full partner sitting around the consortium table, able to contribute to decision making, versus as a member of a Community Advisory Board which has an advisory role. As I have stated, they suggest the varying approaches adopted relate to the social history of HIV in Australia and almost imply that the model adopted in Australia for the vaccine trial may not be as successful elsewhere. In the next extract, they go on to raise the issue of tokenism in Community Advisory Board formation in the context of it being set up 'not to work'.

C22 Yeah, and I think that there is a risk of CABs being tokenistic because they can be set up and the structures can be set up where that happens. I mean, CABs can work, but I think that, you know, they can be made to work either.

One advantage of the Community Advisory Board approach is the perceived independence from the decision making body as the next informant explains. They capture the essence of the tension between being involved and being part of the decision making process within the consortium and being, conversely, outside that process and being able to review the process more independently and behave more independently as a result.

NC11 ...but if there's a disadvantage in the, sort of, partnership approach that we took, is that sometimes, I think, sometimes they [AFAO] feel like that they don't have enough independence in viewing things because they're, sort of, part of the process and so that there's a natural tension between wanting to be rigorously viewing things from the outside and being so closely involved that they hear about it all the time, they become, sort of, you know, becomes sort of the doctrine if you like, this is how things are going.

Even though Community Advisory Boards have no formal power, this informant also suggests, as with previous informants, that they have informal influence over the way in which steering committees operate. However, the informant raises the issue of a Community Advisory Board's role as being symbolic, similar to the tokenistic comments earlier. Critically, they believe Community Advisory Boards lack the capacity to engage with the process in order to make a difference, to the extent that they voice opposition to their establishment, not because they were opposed to community engagement with the process, but because advisory boards are engaged so late in the process that its involvement is symbolic rather than meaningful.

NC31 Maybe not explicitly, but I don't think many of the steering committees for programs or projects in the US would be very comfortable or advise doing something that their CABs clearly thought was inappropriate... I don't like the idea of CABs. I think they are because they're advisor is separate. They tend to have the appearance of being almost symbolic rather than substantive. They don't really allow, you know, timely engagement of a perspective that's clearly going to make a difference at some point.

Very interestingly, the informant suggests in the next extract that AFAO is able to replace a hypothetical Community Advisory Board due to its representational nature. Community Advisory Board chairs in other trials do not sit as a full member of the organisational consortium. Indeed, a Community Advisory Board in the Australian trial may have addressed the potential conflict of interest AFAO's

participation as a full member brings. Indeed the framework of a Community Advisory Board is designed to provide independent advice in relation to the trial. AFAO in the context of the consortium, is not independent of the consortium but an integral part of the principal decision making body conducting the trial. Because Community Advisory Boards are independent, even though they have less formalised power, they are able to voice objection both within the consortium and, importantly, outside the consortium. If AFAO, as a consortium member, took part in a decision to conduct the informed consent processes in a certain way, they could not, subsequently, be critical of that approach and remain a consortium partner.

The next informant alludes to a social history in Thailand of Community Advisory Board establishment and participation in vaccine trialling. There is no acknowledgement of the potential conflict of interest inherent in AFAO's two roles by this informant.

C12 ...But they're not a representational organisation so, you know, AFAO I think, can play the role of the Community Advisory Board and replace the Community Advisory Board because we have a role to represent the national community based response in Australia. I mean, in the US, that can't happen as well because there's no agreed upon body in the US that could play the same role. But in Australia, thankfully, I think, AFAO can play that role... there are so many established Community Advisory Board structures in Thailand, that, you know, they like the idea of a Community Advisory Board and they like it as a way, in terms of, getting feedback, getting input from the community.

Chapter Summary

In this chapter, I have explored, using the accounts of the informants, the risks, costs and benefits of AFAO's involvement as a full partner in the consortium. I have explored the internal re-structures required by AFAO and the significant learning required to make meaningful contributions to the discussions around the consortium table. Such learning, however, has enabled AFAO to affect positive changes within the consortium and, most importantly, with the trialling itself. Such a partnership

approach is very different to the Community Advisory Board approach used in other parts of the world and the informants have a clear appreciation of the differences those different models entail and a belief that partnership is better. Importantly, there were risks for AFAO to its covenantal relationship with its members. However, the community informants felt those risks were manageable because of the established social practice of the Australian HIV/AIDS Partnership, and believed the benefits of partnership were important and worth accepting some level of risk.

Conclusions and Recommendations

The conclusions outlined in this chapter relate to both the theoretical and in-practice aspects of the consortium. Both aspects are important in understanding the successes and challenges experienced by AFAO.

I first state my key findings in relation to the consortium as a social practice. Then I evaluate the success of the consortium in terms of the UNAIDS/AVAC core principles for good participatory practice for community involvement in biomedical HIV prevention research. Finally, I compare the partnership model to the Community Advisory Board model and conclude with a series of recommendations.

Consortium as a Social Practice

The consortium, I have argued, is an emergent or fledgling social practice which is the intersection of three, well established, social practices in Australia. The consortium also demonstrates the characteristics of a social practice. I have argued that biomedical research, the affected community and, importantly for this research, the Australian HIV/AIDS Partnership approach all come together and converge in the social practice of the consortium. I make this claim by examining the accounts of the informants in this research against the characteristics of a social practice first espoused by Langford (1991). Those characteristics are:

- * Social practices are constructed by persons existing in a social context who have reciprocal self-awareness of each other's intentions and beliefs;
- * A social practice is directed towards an overall purpose;
- * Social practices have a unique history and tradition which the practitioners are reciprocally aware of sharing
- * Social practices have members who teach and socialise new practitioners into shared ways of seeing and doing;
- * Social practices have an institutional dimension which regulates the behaviour of the practitioners; and
- * The social practice needs to be legitimised by society and recognised as a legitimate practice.

The social practice of the consortium was clearly made up of members who were aware of each other's intentions and beliefs. The accounts from the informants demonstrated that each member had their part to play within the consortium and that each had an equal power and decision making capacity. Although I was unable to

interview some consortium members, they were reported by others as being highly critical of AFAO's involvement. Even though these members singled AFAO out and were critical of the funding flowing to AFAO as a partner in the consortium, it demonstrates that even these reluctant practitioners had an understanding of the other members of the consortium and an appreciation of AFAO's contribution, despite poorly valuing that contribution.

It was clear from the commencement of the consortium's project that the consortium was directed at the overall purpose of developing an efficacious preventative prime-boost HIV vaccine. Indeed, it could be argued that when the social practice of the consortium demonstrated that it could not attain that objective as it set out to do, and the members appreciated that fact, the social practice ceased to exist and was dissolved. At the publication of the interim results, that is exactly what occurred.

The unique history and tradition of the social practice of the consortium is slightly less clear. Given the brief time it was in existence, the casual observer might suggest that it was impossible for it to have a unique history or tradition. What the accounts of the informants demonstrated, however, is that the histories and traditions of the Australian HIV/AIDS Partnership approach and biomedical research, in particular, were a significant influence on most of the consortium members. So much so, that the consortium, by virtue of its practitioners, adopted that unique history and tradition and it was this, perhaps above all others, this that facilitated AFAO becoming a full partner in the vaccine development enterprise in the first place. Indeed it is the confluence of the history and tradition of biomedical research, affected community approaches, social science and the Australian HIV/AIDS Partnership approach which makes the consortium unique. Many of the informants also commented on the uniqueness of this approach.

Importantly, my research theoretically extends the notion of shared ways of seeing and doing within a social practice. What I propose, and what Langford (1991) alludes to but is not explicit about, is that, while there may be some immutable ways of seeing and doing (and I gave the example of statistical analysis), other ways are not so rigid and static. Rather, some ways of seeing and doing in a social practice are dynamic, adapting and changing to the social context. The socialisation aspects are highlighted very strongly within the accounts. Not only were non-community members of the consortium inducted into some of the ways affected community sees

and does things, but AFAO, as the affected community representative on the consortium, was inducted into some of the ways of seeing and doing in biomedical science.

In addition to the international and national research documents which govern the way in which biomedical research is to be conducted, the consortium also operated on a consensus model whereby all partners had to be in agreement for an approach to proceed. This is demonstrable of the institutional dimensions of social practices in which behaviours of the participants are regulated.

Finally, the legitimisation by society may be demonstrated by the significant media attention to the development of an effective HIV/AIDS vaccine over the past 10 years.

Evaluating the consortium using the core principles of good community participation in biomedical HIV prevention trials

Here, I apply the core principles in the UNAIDS/AVAC document *good participatory practice guidelines for biomedical HIV prevention trials* in order to evaluate the performance of the consortium. This is not about determining the consortium's compliance with the guidelines, since they had not come into effect when the consortium began. Rather, the ideas within the guidelines are a useful framework for assessing the success and effectiveness of AFAO's involvement in the consortium. As I show below by examining each of the core principles, the consortium was successful in terms of community involvement, but the autonomy aspects proved most challenging. I will first discuss the areas of success and then discuss the autonomy principle, which proved to be more problematic for AFAO.

Areas of success:

1. Scientific and ethical integrity

Much of the discussion by the informants in this research focussed on both the scientific and ethical integrity of the trialling in Australia and, potentially, in Thailand. Of particular concern for the community and non-community informants was the informed consent and education processes perceived to be AFAO's sphere of responsibility. The informed consent process was comprehensive and dynamic.

Through a variety of methods, research participants' understandings of the trial and their participation within it, was tested and re-tested.

Achieving high ethical standards was by no means straightforward for either AFAO or the consortium more generally. An explicit account was provided by one informant which demonstrated the consortium was required to balance competing ethical principles to achieve that goal. In part, such balancing was necessary to deal with the highly complex scientific basis for the vaccine development and subsequent trialling.

Throughout the course of the vaccine development exercise, the consortium was required to deal with the pace and frustrations associated with those complexities. Indeed, the question of whether to establish an arm of the trial in Thailand subsequent to the interim results from the Sydney arm of the trial illuminated considerations in relation to equipoise. Such considerations are often the obligations of Data Safety and Monitoring Boards, established to ensure the objectives of the research do not come into conflict with the safety of the research participants. Expressed another way, the Data Safety and Monitoring Board ensures that the least possible harm comes to research participants. Extracts quoted in this research demonstrate that Data Safety and Monitoring Boards, rather than only focussing on traditional biomedical markers of harm, should also focus in vaccine trialling (and biomedical prevention trialling more broadly) on changes to participants' protective behaviours.

Also related to the complexity of the research area, the level of efficacy achieved in a particular trial was a matter some community informants had some concern about. This, in part, is a contextual consideration. A poorly efficacious vaccine of around 30 percent may not be suitable to low prevalence countries like Australia but may be highly beneficial to high prevalence areas such as sub-Saharan Africa. Community informants were, hypothetically, grappling with the level of efficacy at which it would be acceptable in Australia and, if they were partners in the vaccine development exercise, how to resolve the potential conflict of interest between their interests as a consortium member and their obligation to advocate on behalf of the affected community with government.

Also of concern to the community informants were the long term effects of participation in vaccine trials. In other words, does participation in a preventative HIV vaccine trial now, which demonstrates limited or no immunogenicity or efficacy, have long term negative effects for the participant should a more efficacious vaccine

be developed in the future? Community informants deliberated on how best to advocate for the affected community in those circumstances.

2. *Respect*

This principle also required some work for the consortium. The accounts I have examined clearly indicated that the community and non-community informants who form part of the social practice of the Australian HIV/AIDS Partnership approach demonstrated mutual respect for each other. The non-community informants in this group respected the values, mores and norms of the affected community and, indeed, viewed affected community involvement as critical and important. The non-community consortium participants who were not part of the Australian HIV/AIDS Partnership approach were reported by my informants to have been critical of, and to have voiced strong opposition to, affected community's involvement. Such minority dissenting voices were counterbalanced by the other participants in the consortium. Respect for the scientific and ethical integrity of the research in order to achieve trial results was also demonstrated by consortium members

3. *Clarity in roles and responsibilities*

The accounts demonstrated that, as a result of AFAO's involvement as a full partner in the consortium and the convergence of three social practices to form another, clarification of the roles AFAO was to play, both internally and within the consortium, required exploration. In a sense, because AFAO was a full partner, some of the role definition necessary was already predetermined by the decision making freedom and constraints inherent in such a role. In defining the roles and responsibilities within the consortium, informants described minor conflict between different individuals but framed such disagreement in terms of the sorts of conflicts had in any relationship and that such conflict was constructive in achieving good outcomes.

As a result of the role AFAO was to play in the consortium and to participate meaningfully as a partner in the process, AFAO's internal advisory structures needed to adjust so that AFAO, and its representatives to the consortium, were able to become more literate in the social practice of biomedical research. As a consequence of being more competent to participate, there was some suggestion that non-

community consortium participants needed to change their way of perceiving their participation in the consortium and change their way of operating as a result.

4. *Towards shared responsibilities*

By virtue of AFAO's partnership in the consortium, there was shared responsibility between the various organisations and institutions in the consortium. The goals, risks and benefits were clearly understood and explored by those partners and, by virtue of the contractual arrangements made with the NIH and with each other, commitments made to each other honoured.

5. *Participatory management*

Similarly with this core principle, because AFAO was a full partner, participatory management was required by all consortium members. Indeed, unlike other participatory models, as a contractually full partner, such a position empowered the AFAO representatives on the consortium to veto aspects of the trial process it did not agree with. The formal power dynamics within the consortium, as a result, were equal and required AFAO's involvement in all aspects of the trial process.

7. *More transparency*

As a full partner in the consortium, the information provided to AFAO was unrestricted. This meant that, unlike other trials, AFAO was required to discuss and make decisions about, all aspects of the trial from vaccine construct to data analysis. This was, in part, as a result of the commercial-in-confidence agreements between the partners which facilitated the necessary level of frank information exchange. This not only allowed information to flow to AFAO, but also allowed information to flow from AFAO to the consortium to facilitate better informed consent processes, trial participant education and communication strategies.

8. *Standard of prevention; and 9. Access to care;*

While these are principles contained within the principal international biomedical research conduct documents, and indeed the National Statement, the emphasis on these core principles in the UNAIDS/AVAC document relate more to resource poor countries than to the Australian context. Australian citizens, who were the participants in the trial, have access to the gold standard of prevention and treatment and care. Such considerations would arise in the context of either a phase

IIb proof of concept trial or a large scale phase III efficacy trial where a potential construct was being trialled. In addition, the trials in Australia occurred in low risk populations who were unlikely to be exposed to HIV. These principles would have been at issue had the Thai arm of the trial are gone ahead.

10. *Building research literacy.*

As I have explained previously, as part of the socialising aspects of AFAO's involvement in the social practice of the consortium, the building of research literacy was a critical aspect for involvement. This has a flow on effect for AFAO in terms of becoming highly research literate and prepared for any future trials

In summary, through retrospectively examining AFAO's participation in the consortium against the ten core principles of the UNAIDS/AVAC document, I demonstrated the consortium was highly concordant with the previous 9 core principles. AFAO's autonomy proved to be the most challenging aspect in relation to these core principles, as I demonstrate below.

The problematic area of autonomy;

The core principle of autonomy was, perhaps, the most difficult aspect for AFAO's involvement. In becoming a partner in the vaccine development enterprise, AFAO's independence decreased. On the one hand, AFAO is tasked with advocating on behalf of the affected community while, on the other, it is required to operate in the best interests of the consortium. I have argued that this represents a potential conflict of interest for AFAO. A conflict of interest essentially means that autonomy is limited. AFAO is not free to act according to its own values and aims, but is constrained by the aims and values of the consortium. This conflict of interest needs to be actively managed. Such management is critical to AFAO's covenantal relationship with its members and with society more broadly. In the next section I will discuss the ways in which conflict of interest may be successfully managed and which are applicable to the potential conflict of interest situation AFAO finds itself in.

How conflict of interest can be successfully managed

As I have suggested in a previous chapter, conflicts of interest can be both personal conflicts and organisational conflicts of interest. This personal/organisational distinction can equally be applied to the ways of managing

such conflicts. Lemmens and Singer (1998: 963-964) argue there are four ways in which conflict of interest can be managed: awareness, disclosure, review and authorisation, and prohibition and avoidance.

Awareness

Lemmens and Singer (1998: 963) suggest the first step in effectively dealing with a conflict of interest situation is awareness that conflict of interest situations are inherent in “every aspect of human affairs, including medicine and science”. So, they say, there is nothing remarkable or inherently unethical in finding oneself in a conflict of interest situation. Levinsky (2002: 760) suggests the heads of research organisations acknowledge that such situations are intrinsic to biomedical research. Problems arise if the situation is not recognised and dealt with which is why awareness is a critical aspect of dealing with such situations. This is true both individually and at an organisational level. Individual awareness is not just critical for oneself, but also ensures awareness of others’ conflicts of interest. In turn, as a result of the internal unity of the social practice, the awareness of others’ conflict of interest enables the organisation/profession/social practice as a whole to be aware that such situations can arise and to be alert to the possibility.

Disclosure

By far the most expeditious way of managing a conflict of interest is to disclose it to authorising bodies (Korn, 2000; Morin, Rakatansky, Riddick et al, 2002). As Lemmens and Singer (1998: 964) say “[a]though trust can be seriously harmed if patients find out about interests that physicians have hidden, trust is likely to be enhanced if patients feel that their physicians are open about it”.

Review and Authorisation

Laws and regulations form another aspect of managing conflicts of interest, from Human Research Ethics Committees authorising research to compliance programs and policies in academic institutions and hospitals (Lemmens and Singer 1998; Morin, Rakatansky, Riddick et al, 2002). The international and national statements on biomedical research are a good example of such guidelines. In such cases, an external body or organisation scrutinises the conduct of researchers. Such scrutiny determines whether the conduct is consistent with the laws, regulations and

rules of the social practice and sanctions behaviour that falls outside those parameters. In terms of sanctions, regulators can punish infractions of the rules by way of fines, restrictions on practice and, ultimately, expulsion from the social practice altogether.

Prohibition and avoidance

In some cases, disclosure and review and authorisation may be insufficient to deal with the seriousness of the conflict of interest. Some medical journals, for example, prohibit articles where a finder's fee for inclusion of participants in research forms part of the financial remuneration of the researcher. In such cases, the incentive to include participants in a trial without adequate informed consent processes is high. In other words, the source, level and type of financial gain to be made by researchers is restricted (Korn ,2000; Lemmens and Singer, 1998).

There are a number of additional ways in which a conflict of interest may be avoided. One could avoid the situation altogether by either voluntarily withdrawing from the situation causing the competing interests to come into conflict or, alternatively, give up one of the competing interests. Using the example of a General Practitioner accepting gifts from a pharmaceutical company for the volume of its drug they prescribe, the medical practitioner could stop practising clinical medicine or they could stop accepting gifts from the pharmaceutical company. Clearly the first option is a serious step for any clinician to take, so the second option would be the preferable position in this example.

Another means of managing conflicts of interest is by structurally placing impediments or barriers or distancing oneself from the situation in order to avoid it. In the current example, a means of restructuring to avoid the conflict may be to have a third party broker with the pharmaceutical company for use of its products. This means of structurally arranging the organisation to remain at arms length from the conflict is the way in which AFAO has sought to deal with its identified conflict.

Application for AFAO

So, I have discussed the nature of conflicts of interest in the context of biomedical research. However, as I have indicated previously, AFAO faces a potential conflict of interest between its obligation to act as an advocate for the affected community it represents and its legal obligation to act in the best interests of the consortium. Its way of dealing with this is limited, but still feasible.

AFAO is the peak national non-government organisation “representing Australia’s community-based response to HIV/AIDS” (AFAO 2004: 01). As a social practice, therefore, AFAO has this as its primary objective. It also has an obligation, both legally and as a member of the social practice of the consortium, to act in the best interests of the consortium of which it is a partner. This potential conflict of interest could arise as an actual conflict of interest when, having approved the protocol for the informed consent process for the trial, a participant who was a member of one of AFAO’s member organisations, complains about the process. AFAO would have taken a decision along with the other consortium members to authorise the informed consent process. It cannot then deal with a complaint about a process it authorised in a way that did not give rise to a reasonable perception of bias.

As I have suggested above, the consortium members, and AFAO as an organisation, already had awareness of the potential conflict of interest. This awareness meant they were acutely aware that it could turn into an actual conflict of interest.

AFAO has not formally disclosed the potential conflict of interest. In reality, there is no effective means of formal disclosure for this type of potential conflict of interest for AFAO. Who would AFAO disclose to? The AFAO membership is already aware of the conflicting roles and have an expectation that the AFAO Board would act in their best interests. The consortium is already aware and its expectation is that AFAO will act in its best interests. And what, exactly, could they disclose even if they could identify someone to disclose it to? Is it reasonable to expect AFAO to disclose the possibility that there *might* be a conflict of interest in this remote circumstance? This would seem to be an unreasonable expectation because disclosing this type of information sets a precedent for disclosing other types of potential information and would quickly become unworkable.

Review and authorisation is the most likely means for AFAO to manage the conflict of interest situations. Fortunately, AFAO is a federation of member organisations. Each member organisation is a distinct incorporated body subject to control by its membership. AFAO, therefore, does not have any direct controlling influence over its member organisations. Indeed, like all membership based organisations, it is the member AIDS Councils and national organisations, which have the controlling influence over the AFAO Board. In addition to the laws, regulations and guidelines inherent in biomedical research of this type, the consortium also has

the additional scrutiny of the NIH as the funder of the contract, with the ability to withdraw funding should infraction of the rules occur. A means of avoiding AFAO's conflict of interest, therefore, would be to establish a complaints mechanism in one of the member organisations which could then advocate on behalf of the trial participant free from the competing obligation to the consortium. Another mechanism that could be established is a Community Advisory Board type structure that could independently examine information and provide advice in relation to potential, perceived or actual conflicts of interest. Finally, an independent trial ombudsman, with all the independence and power of other types of ombudsman, could be established either by the funder (in this case the NIH) or the government of the trial population to examine complaints about the conduct of trials in a manner that is independent, forensic and considered. So, AFAO, the funder or the government of the trial population can manage the conflict of interest by establishing alternative structures to deal with them and, thereby, assist AFAO in maintaining its covenant with its members.

Finally, there is the fourth means of managing conflict of interest which is by prohibition and avoidance. That is, AFAO could have refused to join the consortium or withdraw itself from the consortium. This would seem to be an overreaction by AFAO. The overwhelming view of the informants in this research, with full awareness of the potential conflict of interest faced by AFAO, is that AFAO's involvement as a partner has been highly beneficial and has resulted in positive outcomes for both this trial and future trials of this type in Australia.

What I have shown here is that there are mechanisms by which FAO could enhance the degree of autonomy it has when involved as a partner in the consortium. It can exercise its own autonomy by taking the initiative to set up review and authorisation mechanisms, so that it participates fully in the consortium, knowing that there is an avenue for dealing with the actual or perceived conflict of interest. Nevertheless, by becoming a partner, AFAO inevitably loses some autonomy, because it is bound by consortium decisions. On the other hand, it also gains autonomy, in the sense that it gains more influence over what those consortium decisions are. Overall then, I suggest that it is possible to maintain sufficient autonomy whilst in partnership, but AFAO was not actually directly tested on this matter.

While AFAO's involvement can be seen to be favourably disposed against the UNAIDS/AVAC documents, how does it compare to the advantages and disadvantages of Community Advisory Board structures? This will be the focus of the final section in this chapter.

Benefits of participation and comparison with Community Advisory Boards

In chapter one, I briefly described the differences between the approach adopted by the consortium in Australia and the Community Advisory Board approaches in the United States of America, and indeed, the rest of the world. Having undertaken a more comprehensive examination of AFAO's involvement in the consortium, it would be useful to compare and contrast the two different approaches to community involvement in biomedical HIV prevention trialling.

As I have shown elsewhere in this thesis, AFAO's involvement as a partner in the consortium had significant, positive results on the informed consent and participant education processes because they were involved from the very start of the process and had the capacity to influence, as an equal partner, those processes prior to endorsement by Human Research Ethics Committees or authorising bodies like the Therapeutic Good Administration. AFAO, as a partner, was also able to influence even the way in which the vaccine trial was constructed and the way the trial was intended to proceed by virtue of the equal power structures within the consortium. AFAO's partnership in the consortium came about largely as a result of its involvement in the social practice of the Australian HIV/AIDS Partnership. Indeed, other members of the Australian HIV/AIDS Partnership actively supported AFAO's participation in the consortium and helped defend it from criticisms from other consortium members. However, AFAO's involvement was not free of restriction or issues to be resolved.

As part of the consortium, AFAO representatives, the Board and the Policy Reference Group were required to sign commercial-in-confidence agreements which limited the types of communication it could have with its membership thus interfering with the relationship between the governing body and the membership of the organisation and, indeed, the community at large. AFAO also needed to manage the potential for a conflict of interest in its role as an advocate for the affected community and its role to act in the best interests of the consortium.

Community Advisory Boards, by contrast, tend to receive information in relation to the informed consent processes and community education process later and after approval by authorising bodies like Human Research Ethics Committees or the Therapeutic Goods Administration. This makes it incredibly difficult to fundamentally change these processes. Community Advisory Boards are also not privy to some of the more sensitive information within the consortium because they are not partners in the consortium. There is no social history of community involvement as partners of a type similar to AFAO's history in other parts of the world. The Australian HIV/AIDS Partnership is unique to Australia and AFAO's part in it grew out of gay rights activism. There is a history of community involvement in Community Advisory Boards in other countries but, because other parts of the world have different HIV epidemics, 'community' is a much more difficult group of people to identify or distinguish from the general population.

Although there are significant limitations on the way Community Advisory Boards can *formally* influence biomedical HIV prevention trials, *informally*, there is greater scope. Because AFAO was bound to act in the best interests of the consortium, they were limited in how critical they could be of the way in which the consortium was operating or the trial was proceeding, if they were able to be critical at all. Not so Community Advisory Boards. They have the freedom to be highly critical of trial design, of education processes and of informed consent procedures without the constraints of partnership or confidentiality agreements.

What the previous section demonstrates, in light of my research, is that while AFAO's involvement as a partner in the consortium worked for it, the success was in part due to its involvement in the Australian HIV/AIDS Partnership. This means that successfully introducing affected community into a partnership in a consortium, without the social history to support it, is likely to fail. That is because in other parts of the world, an Australian HIV/AIDS Partnership-like approach is foreign to the shared ways of seeing and doing, there is no shared understanding or history of working together and there is no pre-existing expectation that affected community is central to any response.

The partnership model had constraints that Community Advisory Boards elsewhere do not and had strengths the Community Advisory Board model does not. I suggest that neither is inherently better than the other, therefore, as each has inherent benefits and risks that require negotiating. Which model best suits the participant

community will depend, in large part, on the context of the trialling environment and the history of engagement of the trial community.

What I have achieved in this thesis is to, first, illuminate the nature and complexity of the specific social practice that was the consortium. Secondly, the thesis offers us a way of seeing ethical engagement in clinical research that opens up new possibilities for enhancing the ethicality of practice. Finally, the thesis exemplifies a way of doing ethics that richly augments the philosophical approaches that tend to be taken as largely defining this important area of scholarly inquiry.

Recommendations

I have retrospectively examined AFAO's involvement in a biomedical HIV prevention trial, namely a prime-boost preventative HIV vaccine trial, and made some observations in relation to that involvement. These observations have broader implications for all biomedical HIV prevention approaches, from pre-exposure prophylaxis trials to microbicides trials and, of course, vaccine trials. I conclude by making a number of recommendations to assist in future trials.

1. When community is involved as a partner, structurally separate complaints handling bodies, whether they be within a member organisation, a Community Advisory Board or a trials ombudsman, should be established at the commencement of trials in order to deal with the potential conflicts of interest.
2. Careful consideration should be given by consortia to the best way to incorporate affected community involvement in biomedical HIV prevention trialling, taking into consideration the social history, type of trial and the affected community within which the trial is going to be conducted.
3. Affected communities should give careful consideration to the risks and benefits of participation before deciding on a partnership, Community Advisory Board or other model.
4. Biomedical HIV prevention trial consortia should actively engage affected community in considerations of this type.

5. In future biomedical HIV prevention trials, consortia should utilise the informed consent/education processes developed and adopted for this trial.

9

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