

# **South African stakeholders' perceptions of informed consent in HIV vaccine trials.**

Submitted in partial fulfilment of the requirements of the degree of Masters in Clinical Psychology, in the School of Psychology, University of KwaZulu-Natal, Pietermaritzburg.

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## ABSTRACT

In the history of public health vaccines have proven to be among the most effective disease prevention tools. It is clear that in the fight against HIV that new and powerful preventive technology such as a vaccine is badly needed. Ethically, however the processes of developing a vaccine against HIV have been distinctly different from that of any previous pharmaceutical products. HIV vaccine trials can be ethically complex for a number of reasons. In 2004 the HIV /AIDS Vaccine Ethics Group undertook a research initiative that aimed to collect data from various South African stakeholders of HIV vaccine trials to ascertain what they perceived as the ethical challenges related to HIV vaccine trials. A quantitative content analysis on the data from 31 semi-structured interviews revealed that the ethical issue listed spontaneously by most of the respondents was that of informed consent. Further probing and discussion on informed consent identified a number of sub issues which the respondents thought would pose important challenges to HIV vaccine trials in the South African context.

This study undertook to do a more in-depth qualitative analysis of the data to ascertain whether the challenges and concerns the stakeholders have are consistent with or different to those already identified in the literature and ethical guidelines on informed consent in medical research. What variables may be impacting on the position stakeholders take was also of interest. Results indicated that many concerns relating to the substantive and procedural elements of informed consent were consistent with those debated in the literature. These issues related to first person consent, the voluntariness of participants' consent, practicing cultural sensitivity, dealing with language issues, promoting and assessing understanding of material disclosed, issues around the vulnerability of participants, children and adolescents' capacity to consent and the role of the media. More specific to the South African context, stakeholders were concerned about the legal framework under which the trials take place, the general lack of education and training about HIV vaccine trials, a lack of communication and coordination between stakeholder groups, and the historical influences of apartheid on black South African participants' capacity to consent. The main variables that appeared to impact on the position stakeholders took related to the role the stakeholders play within the trials, the philosophical position underpinning their ethical viewpoints, stakeholders' understanding of vulnerability and capacity to consent, and how they view the universality or relativity of ethical issues.

# CHAPTER ONE

## 1. Introduction:

In the history of public health vaccines have proven to be among the most effective disease prevention tools. The eradication or control of diseases such as small pox, measles and polio, for example, through mass vaccination, is evidence of the efficacy of vaccines (Langan & Collins, 1998). It is clear that in the fight against HIV new and powerful preventive technology such as a vaccine is badly needed (ibid). Numerous vaccine concepts, based on diverse biological pathways, have been developed as part of the collaborative, international attempt to develop an effective HIV vaccine (Lindegger, Milford, Ranchod & Slack, 2006).

Ethically, however the processes of developing an HIV vaccine have been distinctly different from that of any previous pharmaceutical product (Langan & Collins, 1998). A number of reasons have been posited for this. Slack, Lindegger, Vardas, Richter, Strode & Wassenaar (2000) argue that ethical problems associated with HIV vaccine trials relate to the relationship between science and ethics, whereby requests for people to participate in studies with little likelihood of producing meaningful results, are likely to be considered unethical. In addition, they argue that the bioethical principles of autonomy, beneficence and justice tend to be approached as add-ons to scientific procedures rather than intrinsic to them, which is problematic since these ethical principles guide decision making in biomedical research and often need balancing in complex ways. For example, reward for participation may be a legitimate benefit but should not be great enough to constitute undue influence (ibid) which impairs participants' autonomy.

HIV vaccine trials can be ethically complex as they tend to involve partnerships between sponsors drawn from resource rich nations and communities and participants drawn from host nations with limited resources

(Slack, Stobie, Milford, Lindegger, Wassenaar, Strode & IJsselmiuden, 2004) and thus limited power. In addition, most existing vaccine research resides within the private sector whereas most research into an HIV vaccine has taken place (or funded from) within the public sector (Tucker & Mazithulela, 2004). Thus, many more stakeholders are involved and need to be considered.

Lindegger et al. (2006) found that while HIV vaccine trials “share all the characteristics of other clinical trials; they may be viewed as somewhat distinctive because of the highly vulnerable populations required for phase III trials” (p. 716). This vulnerability, they argue, derives from the fact that the populations needed for Phase III trials- populations at high risk of HIV infection- are also commonly characterized by high levels of poverty, relatively low levels of formal education, and poor access to resources.

In 2002 approximately 80 HIV preventative vaccines had been tested world wide (Weidle, Mastro, Grant, Nkengasong & Macharia, 2002) with 24 HIV vaccine trials collectively involving 19 different vaccines, by 2003 (IAVI, 2003). Figures released by IAVI (2008) indicate that this figure increased to as many as 120 trials by 2008. Currently PHASE I - small trials in low-risk populations to test vaccine safety and immunogenicity- HIV vaccine trials are still in progress, with 64 trials still underway in the US, and 27 trials underway in Switzerland, Sweden, the United Kingdom, Peru, Brazil, Thailand, China, Puerto Rico, Haiti, Germany, Russia, Belgium, India, Rwanda, Kenya, and Uganda, collectively. PHASE II - Small trials moving into mid-sized trials in low- and high-risk populations to test vaccine safety and immunogenicity- are currently underway, with 17 in the US, 6 in South Africa, 6 in France, 3 in Brazil and 1 each in Kenya, Uganda, Tanzania, Thailand, Haiti and Jamaica. Eight PHASE III - Large trials in high-risk populations to test vaccine efficacy- reportedly started in Thailand October 2003 and are still in progress.

Weidle et al., have argued for the desperate need for HIV vaccine development in Africa in light of the fact that “although there had been more

than 45 million cumulative HIV infections in Africa by the end of 2001, there have been only two small, phase I, preventive HIV vaccine trials in the continent most severely affected by the epidemic” (p. 2263). Although not comparable to the US there has been some headway in the development and testing of preventative HIV vaccines in Africa. For example, the latest update given by the South African Aids Vaccine Initiative (SAAVI) (2008) reports the completion of 4 PHASE 1 trials and one PHASE 11 trial, with one of the PHASE 11 trials involving 3000 participants having been stopped in October 2007. An additional 2 PHASE 11 trials were started in 2006 and are still underway with an additional PHASE 11 trial still in the planning stage.

In view of the potential ethical challenges related specifically to HIV vaccine trials, and following extensive international consultation, UNAIDS developed and published ethical guidelines for HIV vaccine trials (UNAIDS, 2000, in Lindegger et al., 2006). In South Africa, as part of the South African AIDS Vaccine Initiative (SAAVI), the HIV/AIDS Vaccine Ethics Group (HAVEG) was established to undertake research and training in the bioethics of HIV vaccine trials, and were later commissioned by the Medical Research Council to coordinate the development of ethical guidelines for these trials (Lindegger et al., 2006). These have been published as the Medical Research Council (2003) Guidelines on Ethics for Medical Research: HIV Preventive Vaccine Trials (Book 5) (ibid).

## 1.2. Aims of the Study:

Although the literature speculates some potentially problematic ethical issues related to HIV vaccine trials what the various stakeholders actually involved in the trials believe the existing and potential ethical challenges to be has not yet been addressed. To gain a fuller understanding of what ethical challenges are anticipated and currently being experienced by those implementing existing HIV vaccine trials in South Africa, HAVEG undertook a research initiative with various South African stakeholders to investigate the perceived

ethical challenges in HIV vaccine trials, including informed consent. The study reported in this thesis is a sub-study of the broader HAVEG research, and is focused specifically on informed consent in HIV vaccine trials. The aims of this study are:

1. To explore the perceived ethical challenges around informed consent in HIV vaccine trials among a range of stakeholders;
2. To compare these challenges to issues raised in the literature around informed consent;
3. To explore what the factors might be which influence the stakeholders perceptions of these challenges.

### 1.3. Review of the Literature:

#### 1.3.1. Historical overview of Informed consent:

Informed consent is a widely recognized principle of research ethics (Lindegger et al., 2006). The current practice of requiring informed consent from research participants is relatively new, however (IJsselmuiden & Faden, 1992). The issue of consent has been at the forefront of bio-medical ethics since the Nuremberg trials, which presented horrifying accounts of medical experimentation in concentration camps (Beauchamp & Childress, 1994). The atrocities committed by Nazi “scientists”, an extreme instance of ignoring the value of individual human beings allegedly in the pursuit of knowledge, placed much greater emphasis on a person’s right to accept or refuse participation in biomedical research (IJsselmuiden & Faden, 1992). Although less dramatic, disrespect for the subjects of medical research was common just after the Second World War, reflecting the pervasive paternalistic atmosphere in medical practice at that time (IJsselmuiden & Faden, 1992). The study of immune reactions to live cancer cells injected into mentally retarded subjects and the Tuskegee study of the natural history of untreated syphilis (Faden & Beauchamp, 1986), serve as recent examples of unethical research that stimulated the development of the current theory and practice of informed

consent. Although the Nuremburg Code of 1948 and the Declaration of Helsinki of 1964 both made the consent of subjects a central requirement of ethical research, it was not until the mid 1970s that the practice of requiring informed consent for medical research became conventional in the West (IJsselmuiden & Faden, 1992).

The fundamental justification for requiring consent from human subjects as a matter of public policy was best stated in the Belmont Report of 1978 (IJsselmuiden & Faden, 1992). Since then, multiple ethical guidelines for conducting clinical trials have been developed, including the Declaration of Helsinki (1983), the CIOMS guidelines (Council for International Organizations of Medical Science, 2002), and others. In South Africa, relevant guidelines include the Department of Health's (2004) *Structures, Principles and Processes*, and the Department of Health's (2000) *Good Clinical Practice guidelines* (Lindegger et al., 2006).

### 1.3.2. The Meaning of Informed consent:

There are different notions of informed consent reflected in the literature. Although recent literature on informed consent has begun to employ additional distinctions, often referring to notions such as 'genuine informed consent' or 'authentic informed consent' (Bhutta, 2004, in Lindegger et al., 2006, p. 713), Faden and Beauchamp (1986, in Lindegger et al., 2006) draw a useful distinction between a legal and a moral notion of informed consent. The former refers to formal consent, based on legal rules, in order to indemnify the researcher, whereas, the latter refers to 'shared decision making' (p. 2813). Informed shared decision making has been described as "decisions that are shared by doctor and patient and informed by best evidence, not only about risks and benefits but also patient specific characteristics and values" (Jepson, Hewison, Thompson & Weller, 2005, p. 194). Katz (1984) warns, however, that viewing informed consent as shared

decision making, with informed consent and mutual decision making being seen as synonymous, is too reductionistic.

The legal and moral approaches to informed consent lead to different decisions and guidelines (Lindegger & Richter, 2000). For example, to the question of how much information should be shared with patients “the legal approach, concerned as it is with liability, requires that all technical information be disclosed to patients as part of the process of providing legal indemnity to medical researchers [while] the moral approach is more concerned with facilitating shared decision making, which a burden of excess information might undermine, and is based on the belief that the expert does not know everything and cannot know what is best for each person in a medical trial” (Lindegger & Richter, 2000, p. 314).

Beauchamp and Childress (1994) agree, advocating that informed consent is more than shared decision making and needs to be understood as an ongoing process. This makes sense when viewing informed consent in relation to their conceptualization. In the first sense, informed consent is an autonomous authorization by individuals of a medical intervention or of involvement in research. In this sense “an informed consent occurs if and only if a patient or subject, with substantial understanding and, in substantial absence of control by others, intentionally authorizes a professional to do something” (p. 143). In the second sense, informed consent can be understood in terms of the social rules of consent in institutions that must obtain legally valid consent from patients or research subjects before proceeding with therapeutic procedures or research. In this sense informed consents are not necessarily autonomous acts but refer to institutionally or legally effective authorization, as determined by the prevailing rules. A patient or subject can autonomously authorize an intervention, and so give an informed consent in the first sense, without effectively authorizing that intervention and thus without giving an informed consent in the second sense (ibid).

In defining informed consent Beauchamp and Childress (1994) discuss the conceptualization of informed consent favoured by most literatures. In most instances informed consent is divided into an information component and a consent component. The information component refers to disclosure of information and comprehension of the information disclosed, while the consent component refers to a voluntary decision and agreement to undergo a recommended procedure. Furthermore, five elements are presented as the building blocks for a definition of informed consent. These include: competence, disclosure, understanding, voluntariness, and consent. Accordingly, “one gives an informed consent to an intervention if (and perhaps only if) one is competent to act, receives a thorough disclosure, comprehends the disclosure, acts voluntarily, and consents to the intervention” (p. 144). Due to some reservations that this definition only captures basic notions about informed consent, Beauchamp and Childress (1994), extend their analysis of informed consent to include: 1. Threshold Elements (Preconditions) that include: competence (to understand and decide) and voluntariness (in deciding). 2. Information Elements that include: disclosure (of material information), the recommendation (of a plan), and the understanding of these, and 3. Consent Elements that include: a decision (in favour of a plan) and authorization (of the chosen plan).

The Nuffield Council on Bioethics (2002), make a distinction between the substantive and the procedural aspects of ethical guidelines, the former being concerned with the ethical principle per se, the latter with its practical implementation (cited in Lindegger et al., 2006) These elements reflect what Beauchamp and Childress (1994) refer to as the substantive and procedural rules that specify and guide ethical actions. Substantive rules specify principles by giving them more content. For example, a rule that specifies “the principle of respect for autonomy” (p. 39) is “Make sure you obtain informed consent from all participants before enrolling them into research”, in other words allow them to exercise an autonomous choice. Procedural rules incorporate the rules and procedures, relevant to the society in which the research is taking place (Lindegger et al., 2006), that leads to ethical practice.

Using this conceptualization, informed consent can be understood as a bioethical rule that comprises of both a substantive element, that covers aspects such as competence, and understanding, to specify the bioethical principle of autonomy, and a procedural element, that suggests how to disclose information, assess understanding, ensure voluntariness and help participants make a decision and consent in ways that ensure the practice of autonomy in biomedical research. The remaining section will discuss informed consent and its implications for HIV vaccine trials using this formulation as a way of organizing the data, recognizing that there will be elements of informed consent, for example cultural issues, that fit into both categories.

### 1.3.3. Considerations related to the substantive element of informed consent:

As stated, informed consent is essentially an ethical code of conduct that clarifies ethical responsibilities and offers specific guidelines for ethical behaviour (Beauchamp & Childress, 1994). To fully understand and interpret what constitutes ethical behaviour, however, Pack-Brown and Williams (2003) suggest that there must be an understanding of what an ethical code's underlying assumptions, principles and goals are. The next section discusses the underlying principle of autonomy as well as the moral theories that underscore the substantive element of informed consent.

#### 1.3.3.1. *The principle of autonomy and Informed consent:*

The Belmont report bases the obligation to obtain consent on the ethical principle of respect for persons (IJsselmuiden & Faden, 1992) making the protection of autonomy and the personal dignity of research subjects the focus of the informed consent process. Founded on the philosophical principle of autonomy of persons, informed consent requires that researchers respect the

right of potential trial participants to self-determination, especially with regard to matters pertaining to their own bodies (Beauchamp & Childress, 2001, in Lindegger et al., 2006). Vandeveld (2006) describes respect for autonomy as the chief value of modern, liberal societies, stating that the main forces which have shaped the contemporary debate on autonomy have been put forward by philosophers. Disagreements amongst philosophers regarding autonomy indicates a need for further analysis of the concept (Beauchamp & Childress, 2004). The concept of autonomy, of interest to this study, is used by Beauchamp and Childress (2004) to examine decision making in health care and bio-medical research.

Beauchamp and Childress (2004) distinguish personal autonomy as “personal rule of the self that is free from both controlling interferences by others and from personal limitations that prevent meaningful choice, such as inadequate understanding” (p. 121). Thus an autonomous person freely acts in accordance with a freely chosen plan. By contrast, “a person with diminished autonomy, is in at least some respect controlled by others or incapable of deliberating or acting on the basis of his or her desires and plans” ( p.121). Beauchamp and Childress (2004) point out that although theories of autonomy emphasize different aspects they all agree that two conditions are essential: (1) liberty (independence from controlling forces) and (2) agency (the capacity for intentional action) (ibid).

#### 1.3.3.2. The principle of respect for autonomy:

As Beauchamp and Childress (2004) argue, being autonomous is not the same as being respected as an autonomous agent. At a minimum, to respect an autonomous agent is to acknowledge that person’s right to hold views, to make choices, and to take actions based on personal values and beliefs. Such respect involves more than a respectful attitude, it involves respectful *action* that includes obligations to maintain capacities for autonomous choice in others, while allaying fears and other conditions that disrupt or destroy their

autonomous actions. On this account, respect involves treating persons to enable them to act autonomously, whereas, disrespect for autonomy involves attitudes and actions that ignore, insult, or demean others' autonomy and thus deny a minimal equality to persons.

The question is why is such respect owed to persons? Two philosophers, Immanuel Kant and John Stuart Mill, who have influenced the contemporary debate concerning respect for autonomy (Beauchamp & Childress, 2004) give different, yet supporting, interpretations for respecting autonomy. Kant argued that respect for autonomy emanates from the recognition that all persons have unconditional worth, with each having the capacity to determine his or her own destiny (ibid). For Kant, to violate a person's autonomy is to treat that person merely as a means, in accordance with other's goals, without regard for that person's own goals, which is a fundamental moral violation because autonomous persons are ends in themselves capable of determining their own destinies (ibid).

Mill, on the other hand, was more concerned about the autonomy of persons in shaping their lives, arguing that persons should be allowed to develop according to their personal convictions, as long as they do not interfere with a like expression of freedom by others. In addition, he insists that there is an obligation to persuade others when they have false or ill-considered views (ibid). Whereas Mill's position requires both non-interference with and an active strengthening of autonomous expression, Kant's entails a moral imperative of respectful treatment of persons as ends rather than merely means to an end (ibid). Even though profoundly different, Beauchamp and Childress, (2004) argue they both provide compelling support for respect for autonomy.

#### 1.3.3.3. *Autonomy, authority, and community:*

Some writers have argued that autonomous action is incompatible with the authority of the church, state, or other communities that traditionally legislate people's decisions (Beauchamp & Childress, 2004) since persons who choose to submit to an authority or to be ruled by others necessarily lose their autonomy in doing so. Whereas in some instances autonomy and authority are incompatible, Beauchamp and Childress (2004) argue that no fundamental inconsistency exists, since "individuals can exercise their autonomy in choosing to accept and submit to the authoritative demands of an institution, tradition, or community they view as a legitimate source of direction" (p. 124). Meyers (1989, in Beauchamp & Childress, 2004) questions the model of the independent [autonomous] self being presented as a rational will that is inattentive to communal life, reciprocity and the development of persons over time. He objects to the unrealistic, supreme and overriding value placed on autonomy. Beauchamp and Childress (2004) counter this argument by suggesting that communal life and human relationships actually provide the matrix for the development of the self, a fact that no defensible theory of autonomy denies.

Appeals to authority, often in the form of paternalism, can lead to conflict in medical research. On one hand, autonomy as a principle of non-interference with a right to self-governance, allows every adult to exercise his or her right to determine whether to participate in research, while on the other hand, paternalism, the interference with, limitation of, or usurpation of individual autonomy, usually justified by reasons referring to the welfare or needs of the person (Edwards, Kirchin & Huxtable, 2004) overrides their decision to participate in research. Paternalism, in the context of research, underscores the idea that the research expert knows best, chooses best and does best (ibid) all for the welfare of the research participant. Edwards et al. (2004) argue that it should be left to competent potential research subjects to make judgments about the acceptability of harms and benefits relating to research.

Although the assumption is that paternalism is always unjustified in the research context, Beauchamp and Childress' (2004) definition of paternalism, "the intentional overriding of one person's known preferences or actions by another person, where the person who overrides justifies the action by the goal of benefiting or avoiding harm to the person whose will is overridden" (p. 274), is normatively neutral and does not assume that paternalism is either justified or unjustified. In addition, although the definition assumes an act of beneficence it does not assume whether the beneficence is justified, misplaced or obligatory (Beauchamp & Childress, 2004).

#### 1.3.3.4. Cultural issues pertaining to Informed consent:

Pack-Brown and Williams (2003) argue that understanding and appreciating multicultural ethics requires a "knowledge base built on a historical context of the collective studies of philosophers and philosophical ethics over the years" (p. 35). In addition to consequentialism (discussed later) they propose three other major schools of ethics that also need to be understood when considering ethical behaviour in multicultural ethics. These, as described by Pack-Brown and Williams (2003), include absolutism, relativism, and intentionalism, and will be discussed briefly as follows:

##### 1.3.3.4.1. Absolutism and informed consent:

Absolutism is a school of ethics that upholds the fundamental belief that only one truth about human behaviour exists so that differences in perceiving and understanding behaviour, particularly within a cultural context, are minimized. Ethnocentrism (using one's own culture and worldview as the basis for judging other cultures and worldviews) and subsequent problems are neglected, omitted or discounted when dealing with human behaviour. "When and if the need to evaluate evidence of behaviour emerges, those engaging in the evaluative process apply the same evaluative criteria across cultures in a fixed and unchanging manner ... the same measures, strategies, theories, or

ethical principles related to human behaviour are to be used in the same way, across groups, and without respect for cultural differences” (p. 35). Stakeholders of HIV vaccine trials operating from an absolutist position are likely to apply the same informed consent procedure in the same way in all HIV vaccine trials regardless of the cultural norms, customs, and beliefs individual participants ascribe to.

#### 1.3.3.4.2. *Relativism and informed consent:*

Relativism is a school of ethics that embraces the idea that more than one truth exists in the determination of behaviour so that the reality of different behaviour and perspectives is acknowledged. Those subscribing to this perspective avoid imposing value judgements allowing each cultural context and subsequent behaviour to be addressed in its own right. Pack-Brown and Williams (2003) describe two types of relativism; descriptive relativism and normative relativism. Descriptive relativism is based on the assumption that different people have different moral beliefs which affects how they behave and define problems. From this philosophical position descriptive relativists take no stand on whether beliefs about human behaviour within a particular cultural context are valid or not. Normative relativism, on the other hand, is based on the assumption that each culture’s beliefs are right within that culture. Thus those operating from the normative relativistic school of thought believe that it is impossible to validly judge another culture’s beliefs and attitudes from outside of that culture. “Ultimately, worldview, cultural context and subsequent behaviours are appreciated and recognised in their own right” (p. 36). Thus in HIV vaccine trials those stakeholders holding a normative or a descriptive relativist position may argue that husbands should consent for their wives if it is culturally sanctioned to do so or if his or her moral beliefs allow it, regardless of whether others think it is valid to do so.

#### 1.3.3.4.3. Intentionalism and informed consent:

Intentionalism, often linked with realism, espouses the idea that there is always a mindfulness of and realization that some aspects of reality exist. Persons adhering to the intentionalist school of ethics believe that “the idea of morality is purposive and specific to a person’s intent and/or motives” (p. 36). Those subscribing to Intentionalism are likely to be concerned about the motivation behind their clients’ decisions and behaviour. It is likely, therefore, that the stakeholders of HIV vaccine trials who use an intentionalistic ethical outlook will consider the motivation behind participant’s consent to participate in trials as imperative.

Clearly when different stakeholders of HIV vaccine trials hold different underlying philosophical positions about informed consent conflict may arise at different levels of the informed consent process. While intentionalist are likely to be concerned about what motivates participants to consent, relativists may be more concerned about the cultural norms and personal beliefs regarding who gives consent, while absolutists may insist that the same universal informed consent procedures apply universally.

There is considerable debate in the literature that reflects these philosophical positions. Much of the debate centers on whether ethical principles are universal or relative, since morals are social constructions with ethical standards varying from culture to culture (Slack, Lindegger, Vardas, Richter, Strode & Wassenaar, 2000). Slack et al. (2000), (taking an absolutist’s approach) argue that since ethical standards were propounded to restrain biological-medical research in the first place, where ever it occurs, these principles are specific to the activity and not the setting and thus should be applied worldwide. Other writers, including Mkhize (2006) and Shapiro & Stein (2004), (adopting a relativist position) propose that there must be sensitivity towards local cultural and ethical expectations. Benatar (2004) argues that the place of ethical universalism is at the abstract and conceptual levels, and then there is the need to seek reasoned ways of specifying how

abstract principles are applied at the local level. In doing so he advocates taking the position of reasoned contextual universalism, which allows for the rational application of universal approaches within local contexts. Achieving such middle ground avoids the abstraction that is blind to context while also avoiding the perils of moral relativism.

#### 1.3.3.5. Cultural sensitivity and informed consent:

The notion of cultural sensitivity questions the substantive ethical standard of autonomy in informed consent, particularly in terms of first person consent. Cultural sensitivity in informed consent rests on the claim that the principle of informed consent, founded on the right to personal autonomy and self-determination, is rooted in a particular notion of personhood, synonymous with the individualism of so-called western culture (Lindegger et al., 2006). Such notions of personhood are not universally valid since collectivist notions of personhood are the norm in eastern and African cultural contexts (ibid). Mkhize (2006), for example, argues that “concepts of autonomy based in western ethics often compete with local ethical systems” (p.27) with the result that attempts to implement first-person informed consent have met with problems in societies with a predominantly communitarian conception of self. For example, the threshold elements, information elements and consent elements, suggested by Beauchamp and Childress (2004) may have particular procedural difficulties when applied to a population who hold a communitarian worldview. These difficulties may arise when seeking individual consent in a society that values community decision making, for example. In general these procedural difficulties are likely to have implications for the informed consent process in research in Africa in general (Mkhize, 2006).

#### 1.3.3.6. Moral theories that underscore informed consent:

Moodley (2006) points out that 2000 years of moral debate, starting with the ancient Greeks, have produced secular moral theories that are still widely used and debated today in the context of biomedical practice and research. Three major moral theories that have dominated the debate include virtue ethics, consequentialism and deontology. Virtue ethics is the moral theory that concentrates on the character traits and virtues that persons should possess in order to do good, supporting the view that in order to do good one has to be good (Moodley, 2006). Hence, the good doctor or researcher should possess characteristics or virtues such as compassion, integrity, discernment and trustworthiness. Consequentialism is a theory based on the premise that consequences of actions define their morality so that the right action is the one that produces the greatest happiness for the greatest number of people (ibid). Deontology is a rule based morality that emphasizes a moral duty and moral rules, such as, ‘always be honest with your patient or research participant’ (ibid).

A brief description will follow to orientate the reader to some of the main tenets of these moral theories and how they may impact on informed consent in HIV vaccine trials.

##### 1.3.3.6.1. Virtue Ethics and informed consent:

Virtue ethics is currently one of three major approaches in normative ethics and can be identified by its emphasis on the virtues, or moral character, in contrast to an approach that emphasizes the consequences of actions (consequentialism) or that which emphasizes duties or rules (deontology) (Hursthouse, 2007). Virtue, founded by Plato and more particularly Aristotle, persisted as the dominant approach in Western moral philosophy until the Enlightenment when it took a momentary eclipse (ibid). It re-emerged in the late 1950’s at the increasing dissatisfaction with the prevailing forms of deontology and utilitarianism at the time (ibid). These theories paid little

attention to the virtues themselves, motives and moral character, moral education, moral wisdom or discernment, friendship and family relationships, a deep concept of happiness, the role of emotions in our moral life and the important questions of what sort of person one should be and how one should live (ibid). It is important to realize that virtues such as honesty and generosity are not just a tendency to do what is honest or generous. They are concerned with emotions and emotional reactions, choices, values, desires, perceptions, attitudes, interests, expectations and sensibilities (ibid). Thus to possess a virtue is to be a certain type of person with a certain complex mindset.

In terms of getting informed consent from an HIV vaccine trial participant, a virtuous agent would not hesitate to tell the participant the truth about the real risks of participation, not just because it is part of the informed consent protocol, but because there is real value in truth telling that reflects honesty. Steenivasan (2002) argues that given that virtue is such a multi-track disposition, one must know the agent's reasons for doing something before considering him as a virtuous moral agent. The concept of virtue is the concept of something that makes its possessor good, in that a virtuous person is morally good, excellent or an admirable person who acts and feels rightly as they should (ibid). However, to possess fully such a disposition is to possess full and perfect virtue, which is rare (Athanasoulis, 2000, in Hursthouse, 2007) and an idealistic expectation to have, for example, of stake holders of HIV vaccine trials.

Opponents of virtue ethics commonly assert that someone's compassion might lead them to act wrongly, to tell a lie they should not have told, for example (Steenivasan, 2002). Thus if virtuosity becomes a criteria for choosing stakeholders for trials, one must consider that, in their desire to allow a participant to enter a trial to get access to the benefits of the trial whilst being aware that they do not fully understand the risks of the trial, a virtuous agent's compassion might lead him or her to act wrongly. Thus it would appear that generosity and compassion, despite being virtues, are sometimes faults and

morally good people may be lead by what makes them morally good to act wrongly (Hursthouse, 2007).

#### 1.3.3.6.2. Consequentialism and informed consent:

A moral theory is a form of consequentialism if and only if it assesses acts and/or character traits, practices and institutions solely in terms of the goodness of the consequences (Hooker, 2007). Consequentialists can and do differ widely in terms of specifying the good, with some specifying the good in terms of pleasure, happiness, desire satisfaction, or welfare, while others merely add up each person's share of the Good to achieve the Good's maximization (Alexander & Moore, 2007).

Historically, utilitarianism has been the best known form of consequentialism whereby acts and/or character traits, practices and institutions are assessed in terms of their overall net benefit which is often referred to as wellbeing or welfare (Hooker, 2007). Overall welfare is calculated by counting a benefit or harm to any one individual the same as the same size benefit or harm to any other individual, and then adding all the benefits and harms together to reach an aggregate sum (ibid).

There is considerable dispute among consequentialists regarding what the best account of welfare is, however. Classical utilitarians viewed benefit and harm to be purely a matter of pleasure and pain so that how well a person's life goes depends entirely on his or her pleasure minus pain (Parfit, 1984; Streumer, 2003). Hooker (2007) argues that a criticism often levelled against such a hedonistic approach to what constitutes welfare is that many people care very strongly about things over and beyond their hedonistic instrumental value. For example, many people want to know the truth about various matters even if it does not increase their pleasure.

What is controversial is whether the fulfilment of one's desires constitutes a benefit or harm to that person regardless of how the person feels about it.

Where hedonistic theories argue that only effects on felt satisfaction or felt frustration matter the desire-fulfilment theory of welfare holds that the fulfilment of any desire of the agent constitutes a benefit to the agent, even if the agent never knows that a desire has been fulfilled and even if the agent derives no pleasure from it. Thus “what constitutes a benefit is wider than merely pleasure” (p.3) so that a much broader range of benefits and harms can be included in a utilitarian analysis of overall welfare. How does this apply to research? Using the desire-fulfilment theory of welfare, it can be argued that the practice of obtaining informed consent from all research participants is contingent upon whether such a practice will benefit the overall welfare of the research community involved. Thus in terms of HIV vaccine trials, stakeholders who prescribe to this ethical framework, could argue that if the informed consent process is too arduous, and threatens to delay or prevent the implementation of trials, which are of obvious benefit to the greater good, then it should be omitted or at least modified.

Consequentialism is often criticized for what it seemingly permits or requires in producing greater benefits for others. Consequences alone can thus conceivably justify *any* kind of act, no matter how harmful it is to some (Alexander & Moore, 2007). For example, stakeholders holding a consequentialist viewpoint could argue that community members who fit the prescribed criteria for participation in HIV vaccine trials could be seen as having an obligation to participate in trials for the benefit of society as a whole. To insist on such an obligation, however, the consequentialist would have to prove that HIV vaccines do have overriding benefits to society, a difficult task, considering that the nature of HIV vaccine research is investigative, and the efficacy of vaccines unproven.

#### 1.3.3.6.3. Deontology and informed consent:

The word deontology derives from the Greek words for duty (*deon*) and science of (*logos*) (Alexander & Moore, 2007). In contemporary moral philosophy deontology is a normative theory regarding which choices are

morally required, forbidden or permitted, that falls within the domain of moral theories that guide and assess our choices of what we *ought* to do in contrast to virtue theories that guide and assess what kind of person, in terms of character traits, we should be (ibid). Deontological theories (of which Immanuel Kant is a well known proponent) stand in contrast to consequentialist theories in that they judge the morality of choices by criteria independent of the states of affairs those choices bring about so that no matter how morally good their consequences, some choices are morally forbidden (ibid). For deontologists what makes a choice right is its conformity with a moral norm (ibid). The Right thus has priority over the benefit, and an act that is not in accord with the Right may not be undertaken no matter the benefit that it may produce (ibid).

Alexander and Moore (2007) differentiate between agent-centred, patient-centred and contractarian deontological theories and their different ethical applications. These ethical theoretical arguments are beyond the scope of this thesis and will not be considered at this point. With regards to the doctrine of informed consent, however, a deontological perspective may concern itself with the basic ethico-legal principles put in place to protect the patient's right to dignity by ensuring that the participant's informed preferences are brought into the health care practitioner's plans (Dhai, 2008). Thus those stakeholders holding a deontological viewpoint to the informed consent process in HIV vaccine trials are likely to be particularly concerned more with protecting the substantive element of autonomy and legal procedures put in place to protect it. A valid consent process that includes, for example, disclosure, understanding, capacity and voluntariness (Dhai, 2008) is likely to be of paramount importance.

These ethical theoretical positions may underscore the views stakeholders hold with regards to informed consent and may underlie potential tensions that exist.

#### 1.3.3.7. Issues related to competency to consent to research:

The relevance of a person's mental capacity to the adequacy of his or her consent to research was first formally recognized in the Nuremberg Code and later the Declaration of Helsinki (Appelbaum, Loren & Roth, 1982). The fundamental requirement of informed consent was that every person taking part in research must have legal capacity to give consent (ibid). The standards of competency to consent have been proposed to include four groups of standards by which an individual's capacity to consent can be assessed (ibid). Research participants must demonstrate that they can communicate a choice, have factual understanding of the issues, be able to rationally manipulate the information in the decision-making process, and have an appreciation of the nature of the situation (ibid). Beauchamp and Childress (2004) have described competence in relation to autonomy. Simply put, a person is deemed competent to make a decision to participate in research if he or she has the capacity to understand the material information, make a judgment about that information in light of his or her values, to intend a certain outcome, and to freely communicate his or her wishes to the research investigators.

Many writers have launched cultural and anthropological arguments objecting to this formalistic requirement of legal competency to consent to research. Writers have often appealed to difficulties in communication and comprehension, from differences in language, non-scientific conceptions of health and illness, or from poor education (IJsselmuiden & Faden, 1992) to urge researchers to adapt the information ordinarily used in the process of obtaining informed consent to local concepts of disease and health (Ekunwe & Kessel, 1984).

Implicit in the arguments based on the problems of incompetence, is the view that it is time consuming and difficult to obtain informed consent from subjects in developing countries (IJsselmuiden & Faden, 1992). For instance, commenting on a case study done to ascertain the distribution of hydatid disease, Ekunwe argues that it is permissible for a physician to obtain what is

best described as ‘uninformed consent’ from research subjects who are “among the not so educated members of the population” (p. 23), particularly in most developing countries where the germ theory of disease causation is not yet accepted. Ekunwe states that if the research team “cannot convince them [research subjects] of the true etiology and pathology of the disease [they] should not waste their time” (p.23). He justifies this by claiming that the researcher is informed on the patient’s behalf as he knows that: (1) the procedure is essential to the health care policy decision [to carry out the research] and (2) the risks involved are tiny and no more than the risk of having regular clinical tests. Although this may be true for studies involving minor procedures such as blood tests, IJsselmuiden and Faden (1992) argue it certainly cannot be said of investigations involving much higher risks to participants [such as the potential risk of seroconversion in HIV vaccine trials].

#### 1.3.3.8. Children and Informed consent:

UNAIDS estimates that of the 4.9 million new HIV infections in 2004, 640 000 occurred in children less than 15 years of age (Jaspan, Gray, Robinson, Coovadia & Bekker, 2005). Jaspan et al., (2005) argue that this epidemiological fact makes it clear that both children and adolescents are at the highest risk of HIV infection and to have any hope of successful epidemic control it is imperative that an HIV vaccine target this group. However, involving adolescents in the participation of HIV vaccine trials raises a number of ethical and legal issues (Brindley-Richards, 2006).

There are inconsistencies in the South African law regarding the age at which capacity to consent can be presumed (Brindley-Richards, 2006). The South African Constitution states that no person shall be subjected to experimentation without informed consent and when persons under the age of 18 years are to be involved in research proxy consent from a parent or legal guardian as well as assent from the child must be obtained (Medical Research Council, n.d.). According to the Medical Research Council (n.d.) however,

any person over the age of 14 years is competent to consent without the assistance of a parent or guardian to any medical treatment but not to research. Those who have formulated guidelines and regulations have struggled with how to promote the best interests of children as a group through research whilst protecting the rights and welfare of individual research subjects (Slack & Kruger, 2005). For example, Book 1 of the Medical research Council guidelines (2001) has more restrictive provisions on research involving research with children than other South African guidelines that, Slack and Kruger argue, rest on a number of conceptually confusing provisions such as the classification of research as ‘therapeutic’ or ‘non therapeutic’ (p. 269).

HIV vaccine trials require informed consent at a number of different stages. The first stage consists of screening candidates for eligibility to participate involving an assessment of the individual’s risk-taking behaviour and their ability to give consent (Medical Research Council, n.d.). Although one thinks of respect for autonomy as applying only to adults the National Commission for the Protection of Human Subjects in Biomedical Research recognises that individuals do not suddenly develop the capacity to make their own decisions at the age of 18 years but rather their decision making capacity develops over time, with many children being able to make their own decisions before they reach the legal age of adulthood (American Academy of Paediatrics Committee on bioethics, 1995, in Wendler & Shah, 2003). The implication is that the threshold for consent should be fixed at the age when (most) children become capable of making their own research decisions.

Wendler and Shah (2003) argue that the threshold for children to consent to research should be fixed at the age of 14 years of age and that a dissent requirement should be adopted for all children in the context of non-beneficial research. However, most commentaries regard the assent requirement (defined as positive agreement) as an important protection for children (Kodish, 2003) as it is not clear which children are capable of consent (Wendler & Shah, 2003).

In the US, federal regulations only specify that when determining which children are capable of consent one should take into account the children's ages, maturity and psychological state (Wendler & Shah, 2003). The question is which aspects of children's age, maturity and psychological state should investigators take into account when determining whether they are able to consent (Brindley-Richards, 2006)? Is the ability to communicate a decision sufficient or must children have full understanding of the purpose of the research, its risks and the alternatives? Or should investigators only rely on a general age threshold, and if so, which one (Wendler & Shah, 2003)?

Wendler and Shah (2003) suggest that in order to determine which children are capable of consent it may be helpful to identify the rationale behind the assent requirement. They point out that the National Commission for the Protection of Human Subjects in Biomedical Research (1977) states that the consideration of children's assent to non beneficial research begins with the respect for subject's autonomy, which implies that "individuals who can understand and shape their lives should be allowed to decide whether to enrol in research based on their own conception of a flourishing life" (Wendler & Shah, 2003, p.2).

Berg (2001, in Wendler & Shah, 2003) argues that to make an autonomous decision as to whether to enrol in research, potential subjects must be able to understand the study in question and their own medical and personal situations, and make a voluntary decision to participate on this basis. In addition, Wendler and Shah (2003) propose that potential subjects must appreciate how the elements of informed consent pertain to their own circumstances. This involves not only an understanding that a study poses certain risks or injury but an appreciation of how this risk is relevant to their circumstances. Wendler and Shah (2003) argue that the most abstract element of informed consent is the purpose of research. As non-beneficial research is intended to develop generalizable knowledge that might help others, the age at which children understand and appreciate these more abstract elements of informed consent provides an approximation of the age at which they can make their own research decisions. However, as Wendler and Shah (2003)

point out, understanding and appreciating the purpose of non-beneficial research does not require that the potential subjects are motivated to help others. An individual can understand fully that a study is intended to help others but not care to help them in that way.

To demonstrate this, Wendler and Shah (2003) suggest one looks at it from the perspective of incapacity. Children who do not understand the concept of altruism cannot decide for themselves whether helping others by enrolling in non-beneficial research would further their conception of a flourishing life. They cannot decide whether the moral reasons for helping outweigh the risks of the research. Therefore the autonomy rationale suggests the consent threshold should be fixed when most children develop the concept of altruism.

Ausubel (1977) have proposed that because adolescents' thinking is more flexible and abstract than younger children, they can accommodate a variety of complicating factors in deciding moral issues. However, Mussen, Conger, Kagan and Huston (1990) argue that given the complexity of modern society, in which numerous factors have to be weighed up against each other, many adolescents struggle to be consistent in applying their moral principles. Further, adolescence is often characterised by conflict, mainly with parents, about moral issues, attributed to the way in which they seek certainty about their identity. Bester (1992, in Gouws, Kruger & Burger, 2000) argues that age itself cannot cause a change in moral judgements, but rather it is a change in age accompanied by a change in cognitive, affective and social development that affects moral development. Factors influencing adolescent moral development include parental warmth and trust, the frequency and intensity of parent-adolescent interactions, the type of discipline adolescents receive, peer group influence, mass-media exposure, schooling and cultural factors within their community.

#### 1.3.3.9. Notions of personhood and informed consent:

IJsselmuiden and Faden (1992) argue that the anthropological literature on Africa is often represented as indicating that it is “typical of African culture

that the person perceives him or herself as an extension of the family and as an intermediary between ancestors and future generations rather than an individual person in his or her own right” (p.831) and, that in terms of social structures, that authority is located in the leader of a village or tribe and in the head of the household who is usually a man. Responses to these observations argue that insistence on first-person informed consent in group oriented cultures is a form of medical ethical imperialism that is morally unacceptable (Barry, 1982; Taylor, 1979; Willett, Kilama & Kihamia, 1979).

Lindegger et al. (2006) point out that behavioural researchers in this area caution against the risk of assuming cultural homogeneity, that is, “the assumption that every person of a particular ethnic, religious, or language group or living in a circumscribed geographic region shares the cultural beliefs, values, and identity of that group” (p.722). IJsselmuiden and Faden (1992) have also argued that there is no single African culture, with more than 900 different contemporary or historical ethnic and cultural groups having been described in Africa (Price, 1989).

Spiro (2000, in Lindegger et al., 2006), based on a review of the anthropological research on cultural variations in self-construction, argues that an important distinction needs to be drawn between manifestations of personhood at a group or collective level and individual experiences of personhood. He warns that much of the research providing apparent evidence for differences in notions of selfhood between westerners and non-westerners is drawn from expressions of personhood seen in symbols, beliefs, and values of groups of people at a collective level which may not necessarily exist at the level of individual experience of selfhood. Gasa’s (1999) research on indigenous understandings of informed consent in rural KwaZulu-Natal, for example, found that some African women were strongly in favour of individual consent for participation in clinical trials, despite their membership of a cultural group with strong collective and relational values around personhood.

Although studies of cross-cultural comparisons in construction of self (Lindegger, 2002; Hart & Lindegger, 2002), found “evidence of differences in self-construction, with more individual constructs of self in English-speaking white participants and more collective constructs in isiZulu-speaking black participants” (p. 722), their studies have also revealed marked intra-group and even intra-individual variation in notions of self, as a function of the contexts of time and space. These and other studies challenge the assumption that Western and non-Western cultures are clearly dichotomized in their notions of personhood, and suggest it would be very risky to assume the irrelevance of informed consent, especially first-person consent, in some communities (Lindegger et al., 2006).

#### 1.3.4. Considerations related to the procedural element of informed consent:

##### 1.3.4.1. Procedures involved in informed consent:

Lindegger and Richter (2000) highlight point 12 of the most recent prepublication version of the UNAIDS guidelines for HIV vaccine research, which states that “Independent and informed consent based on complete, accurate and appropriately conveyed and understood information should be obtained from each individual while being screened for eligibility for participation in an HIV preventative vaccine trial and before she or he is enrolled in the trial. Efforts should be taken to ensure throughout the trial that participants continue to understand and to participate freely as the trial progresses. Informed consent, with pre and post test counseling, should also be obtained for any testing for HIV status conducted before, during and after the research” (p. 313).

In addition “A process of consultation between community representatives, researchers, sponsor(s) and regulatory bodies should be used to design an effective informed consent strategy and process. Issues such as illiteracy, language, and cultural barriers, as well as diminished personal autonomy

should be addressed in this consultative process” (p. 313). “Three guidance points on informed consent are also included in the Medical Research Council (2003) guidelines. Guidance Point 12 requires ongoing informed consent for each stage of participation in the research. Guidance Point 13 requires that special measures be taken for people who might have limited ability to provide informed consent. Guidance Point 15 requires ongoing monitoring of the informed consent process” (Lindegger et al., 2006, p. 716).

With regards to what particular information participants will need to be provided with the CIOMS guidelines (cited in Lindegger & Richter, 2000) prescribe that prospective clients must be informed:

1. that they have been selected for participation because they are at high risk of HIV infection;
2. that they will receive advice and access to means to reduce their risk (such as condoms), although some of the participants in the trial may nonetheless become infected as a result of their high risk status;
3. that only some of the participants will receive a vaccine, while others will receive a placebo;
4. that the effectiveness of the vaccine to be tested in preventing HIV infection or AIDS disease is not known;
5. that only some of the specific risks of physical, social and psychological harm are currently known or anticipated – such as testing HIV positive as a result of the vaccine and being labelled as being HIV positive, with possible discrimination, by communities as a result, and;
6. of the nature and duration of the care and treatment that is available to them, should they become infected with HIV during the trial.

As Lindegger and Richter (2000) argue, informed consent is a complex and some what idealised process and that these formalistic requirements are, in many ways, almost impossible to meet, “a reality that necessitates a careful analysis of the aims of informed consent as an ethical rather than formalistic condition” (p. 313). Alexander and Moore (2007), on the other hand, argue that just because the application of ethical practice (procedural elements) may

be difficult to achieve does not mean that the ethical principle (substantive element) needs to be revised but rather that those instituting procedures should try harder to apply the principle. In other words, the substantive element of Informed consent should not be held hostage, to the procedural difficulties researchers may face in its implementation.

The main issues addressed in the literature regarding the difficulties of implementing informed consent in HIV vaccines trials concern the confrontation between culture and ethics, ensuring voluntary participation, evaluating the competence of participants and whether children can consent, assessing participant understanding, how and what information to disclose, and confronting legal issues. The next section discusses these contentious issues.

#### 1.3.4.2. *The practice of cultural sensitivity in informed consent:*

Lindegger et al. (2006) point out that one of the most widely debated aspects of informed consent centers on the practice of cultural sensitivity in informed consent. Although cultural sensitivity is a substantive issue in informed consent the implementation of culturally sensitive informed consent has procedural implications. Bayer (2000) suggests that there are three possible ways of understanding cultural sensitivity: semantic, instrumental, and principled. First, semantic understanding refers to the use of appropriate and understandable language, when providing participants with information about trial participation. Second, instrumental meaning refers to understanding how social and cultural context might affect participation in a trial, as, for example, in obtaining the permission of traditional leaders to commence a trial (Moodley, 2002). Third, the principled meaning refers to the notion that research ethics should not challenge or undermine cultural norms.

Suggestions have been made to modify informed consent requirements to suit the cultural context wherein trials take place. IJsselmuiden and Faden (1992) propose that to modify informed consent requirements the complex

motivation behind decisions to conduct research in developing countries must be taken into account. Some reasons for carrying out studies in Africa are questionable, they argue, and include factors such as lower costs; lower risks of litigation; less stringent ethical review; the availability of populations prepared to cooperate with almost any study that appears to be curative in nature; anticipated underreporting of side effects because of lower consumer awareness, the desire for personal advancement and, the desire to create new markets for pharmaceutical agents and other products. The existence of such an array of reasons to carry out research in Africa that are “generally antithetical to the interests of research subjects” (p.833) provides justification for being suspicious of any suggestions to replace or modify the requirements for first-person informed consent.

Some writers have suggested that in addition to, or even instead of, first-person informed consent researchers should obtain consent on behalf of otherwise competent adults from a trusted village leader (Cash, 2006; Moodley, 2002). In addition to Bayer’s (2002) argument that in principle this would violate the substantive element of informed consent, IJsselmuiden and Faden (1992) propose a number of practical reasons why this may not be feasible. They propose that besides the dwindling numbers of such persons, as a result of urbanization and development, there are serious problems in identifying who they are and in assessing whether or not they are genuinely trusted by the community. With reference to consent given by the heads of households on behalf of women, for example, migrant labour often takes the male heads of households away to urban areas for the greater part of the year whilst at the same time women’s educational status and the number of households headed by women are increasing, particularly as a result of the AIDS epidemic (ibid).

Furthermore there is increasing demand for the end of discriminatory practices against women challenging the justification of asking heads of households for consent on behalf of competent adults, a practice that would be morally incomprehensible in the West. In addition, this is “certainly out of step with

the movement of many African countries toward structural changes to enhance the emancipation of women” (p. 831) most exemplified by the Woman’s League of the African National Congress in South Africa (Ijsselmuiden and Faden, 1992).

Ijsselmuiden and Faden (1992) argue that appeals to cultural sensitivity are no substitute for careful moral analysis, and that there are no convincing arguments for a general policy of dispensing with, or substantially modifying, the researcher’s obligation to obtain first-person informed consent in biomedical research in Africa. They substantiate their view by claiming that those who defend such a policy have relied on limited and often dated anthropological literature that does not reflect the rapid cultural changes brought about by colonialism and independence, warfare, and urbanization, together with their tendency to confuse appeals to problems of competence and communication as well as their exaggerated sense of the role of biomedical research in solving Africa’s pressing health problems.

What is clear is that there is a need for great caution in making broad claims about the non-applicability of informed consent (including first-person consent) in various cultural contexts (Lindegger et al., 2006). However, the Medical Research Council (2003) and UNAIDS (2000) suggest that informed consent procedures should be implemented in a manner that respects cultural norms, such as inviting participants to involve important others in the consent process, and asking permission of legitimate leaders to enter a community.

#### 1.3.4.3. Issues regarding the voluntariness of informed consent:

Lindegger and Richter (2000) highlight a number of contentious issues in informed consent that need consideration when designing HIV vaccine trials. They argue that one of the several issues that can potentially confuse informed consent as an expression of individual autonomy is that of social desirability. Their research has demonstrated the tendency for volunteers in trials to

behave and respond according to what they surmise to be socially acceptable norms for the situation. This includes trying to create a favourable impression to win the favour of researchers, and /or, fearing reprisals for giving an unfavourable impression, particularly when researchers are viewed by volunteers as being in a powerful position. Further more participants' decisions may be influenced by the amount and types of rewards offered for their participation. An issue that remains controversial is the issue of what type of incentive and how much incentive to offer participants to partake in HIV vaccine trials. It is generally accepted that if incentives are too great they may act as undue inducements enticing participants to take part in order to get the benefit.

#### 1.3.4.4. Information Disclosure:

Information is a prerequisite for active involvement in decision making about research participation (Forde & Vandvik, 2005). According to the Declaration of Helsinki, patients who take part in clinical trials must be “adequately informed about the trial’s aims, methods, anticipated benefits and potential hazards of the study and any discomfort it may entail” (Recommendation 9, p.38). Despite this Forde and Vandvik (2005) argue that issues relating to patient information and communication have generally been given low priority. Lindegger et al., (2006), however, argue that most ethical codes provide specific guidance on what information must be disclosed to potential participants. In addition to those suggested above they include information regarding the right to withdraw. However, they also argue that, “if this information is to enable potential participants to make meaningful personal decisions, it needs to be relevant to their personal interests and circumstances, and provided in a way that makes sense to them” (p. 719).

There has been much controversy in the literature about information disclosure to research participants (Lindegger & Richter, 2000; Harper, 2007; Moodley, 2002). Two aspects, concerning the quantity and content of information given, have been prominent in this debate.

First, is the question of how much information should be provided to potential trial participants? Faden and Beauchamp (1986) make a distinction between legal and ethical versions of informed consent. To satisfy the legal requirement for informed consent all information required by ethical codes should be disclosed. However, as Lindegger et al. (2006) argue, the provision of excess or inappropriate information (especially technical) may unnecessarily complicate decision making, burden the participants, or increase their anxiety, which may not facilitate a good decision-making process and therefore may not be informed consent in the full ethical sense. This may especially be the case where there is a lack of appropriate language for scientific terms in certain indigenous languages (Moodley, 2002). Lindegger and Van Loon's (2004) recent study that involved intensive interviews with clinical trial researchers and staff about informed consent revealed that potential participants often find long forms difficult to understand. "Even though forms are translated into local languages, interviewees reported that forms should be written in 'street language' to improve understanding" (p. 720). In addition, it was found that trial stakeholders often find themselves in a double-bind situation regarding information disclosure, when community-based groups request full information disclosure in the interests of transparency and trust-building, but, on the other hand, are concerned that excess information will impede decision making.

Second, is the question of who should decide on what information to provide, and who should provide the information? Lindegger et al. (2006) suggest that, whereas, researchers may believe they are well placed to decide what information to give, based on their technical expertise, community advisory boards might also claim that they are better placed as advocates for the community's interests. Veatch (1995, in Lindegger et al., 2006) has recommended the principle of 'value-pairing' in deciding who should best provide this information. "This principle suggests that people who share the core cultural, social, religious, and other values might be best placed to decide what information should be provided, and to transmit it" (p. 720). However, it

is possible that in small communities those who share similar values may be known to participants, threatening confidentiality (Lindegger et al., 2006). In addition, Lindegger and Van Loon (2004) found that trial counselors obtaining informed consent often feel a heavy burden of ensuring understanding by participants.

The role of the media in disseminating information about HIV /AIDS has been well documented. In relation to informed consent Hanefeld (in Hanefeld, Coates & Kruger, 2005) describes the media's role as information provision about modes of transmission, prevention, treatment and care. The potential of the media to influence behaviour, effect social change, challenge sexual norms and attitudes and influence policy (ibid) has also been highlighted. Cullinan (2001) has brought to focus a number of media violations in the reporting of HIV/AIDS, however. The most troubling violation pertains to the violation of the privacy of ordinary people living with HIV. Guidelines set out for media reporting on HIV/AIDS include, amongst many, avoiding sensational reporting, avoiding stereotyping and discrimination and using sensitive, non-discriminatory, simple and understandable language (Swanepoel, Fourie & Froneman, 2005).

The minimum standard of what participants of HIV vaccine trials should be informed of, and what they should understand, is described by Lindegger and Richter (2000) to include: the rationale for the study (such as the reason for developing an HIV vaccine), technical issues (of the nature of the products), technical consequences (possible side effects), unknown outcomes (that there is no guarantee that HIV vaccines will offer any protection against HIV infection), methodological issues (placebo or randomization), practical aspects involved in personal participation (e.g., the kinds of procedures and tests that participants will have to undergo), the costs and benefits of participation in the study (e.g., the reduced benefits from future vaccines or access to treatment), and the personal implications of participation in the study (e.g., discovery of one's HIV status and the psychosocial effect of this knowledge).

#### 1.3.4.5. Promoting and assessing understanding:

Ferguson (2002) argues that a patient's consent to participate in a clinical trial can only be regarded as morally acceptable if he or she is competent and a genuine volunteer. Not only does this imply that potential participants be provided with adequate information on which to make a decision, but later requirements of informed consent insisted that they must also be able to understand the information. With regards to understanding of disclosed information Lindegger et al. (2006) suggest two ways in which behavioural issues become important. First, in finding what the most appropriate way of improving understanding is, even though most vaccine sites have elaborate preparatory processes for potential participants, mainly in the form of vaccine discussion groups. Second, what is the best way to 'test' understanding? To determine whether subjects have understood the information presented to them, Kessel (in Ekunwe & Kessel, 1984) suggests that the best alternative is to provide an opportunity for subjects to ask questions even though they may have difficulty in framing them. This may require the researcher to develop a setting in which subjects are encouraged to explore the nature of the study and its potential risks and benefits and gives the researcher an opportunity to determine the meaning that the subject gives to disease, such as HIV/AIDS for example, and his or her own understanding of the risks and benefits to be derived from the study.

Ferguson (2002) argues that self reports on understanding may not be reliable. Although the results from his study found that in general patients felt that they were given appropriate amounts of information and reported a reasonable level of understanding these findings are not synonymous with a finding that patients are capable of assimilating the information they are given. "Patients may feel they have a reasonable grasp of a concept, but if this were to be tested it might not in fact be correct" (Ferguson, 2002, p.48).

Lindegger et al. (2006) point out that it has become common practice for HIV vaccine trial sites to assess understanding over and above self-reported

understanding, which may be heavily influenced by social desirability processes (Lindegger & Richter, 2000, in Lindegger et al., 2006). Even though the most common way to test understanding at sites appears to be forced-choice or multiple-choice checklists of key concepts (Lindegger et al., 2006) which are very cost-effective, they may be measures of short-term recall of technical information rather than measures of personal understanding (Lindegger & Richter, 2000). It is possible that, despite adequate checklist scores, participants may not have understood trial information in terms of the personal implications (Lindegger et al., 2006). Flory and Emanuel (2004) argue that repeated use of checklists may measure well-learned responses that do not reflect real understanding, and suggest that these binary (right/wrong) approaches may run the risk of cultural insensitivity.

Several studies have found that the information provided to patients is too technical for the lay person to understand, or is pitched at a reading age that is too advanced for many participants (Ferguson, 2002). Ingelfinger (1972) has argued that it would be impractical and probably unethical for investigators to present endless lists of all contingencies to research participants. Priestley, Campbell and Valentine (1992 in Ferguson, 2002) compared the readability of 50 consent forms for clinical trials with ten top British daily newspapers using the Gunning Fog and Flesch-Kincaid indices. They found that the consent forms were significantly more difficult to read than newspaper editorials. Whilst Ferguson (2002) cites several studies that have subjected information leaflets to scrutiny (see Grossman, Piantadosi & Covahey, 1994; Meade & Howser, 1992; Tarnowsky, Allen & Mayhall, 1990), with some studies asking potential trial participants to assess their information requirements in respect of hypothetical trials (see Corbett, Oldham & Lilford, 1996), only a few studies have asked patients who are actually participating in actual trials to assess the adequacy of the information they received about the trial.

Results from a study done on Aborigines suggest that a one-off presentation of informed consent materials, even if designed specifically for Aboriginal people, is unlikely to produce the level of “informed consent” that is legally

and ethically required by current guidelines for participants in research (Russell, Carapetis, Liddle, Edwards, Ruff & Devitt, 2005). In comparable indigenous populations Russell et al. (2005) point out that it has been argued that morality and ethics are community rather than individual issues. “Our experience supports this view, and also that the current process of promoting individual autonomy over collective or consensual decision making may not reflect the ways in which decisions are made in some cultures” (p. 492 ).

#### 1.3.4.6. Legal Issues and Informed consent:

Legally regulated informed consent has become the main modality for achieving patient autonomy within medical ethics and research (Harper, 2007). Human rights questions have been raised most particularly in the context of HIV/AIDS, where affected people suffer extensive stigma and discrimination (Slack, et al., 2000). Thus promoting human rights protects the inherent dignity of persons affected by HIV/AIDS (ibid). Since much HIV vaccine development work will take place in under resourced communities where people are at high risk of HIV infection, human rights implications for participants and communities need careful consideration (ibid). Slack et al. (2000) cite a number of physiological and psycho-social risks of participation in HIV vaccine trials that may impact participants, accentuating why informed consent is such a critical issue for HIV vaccine Trials vaccine trials. The fact that participants may be exposed to such severe potential risks, some of which are still unknown, justifies the need for further research into the process of informed consent and its implementation in HIV vaccine Trials vaccine trials.

##### 1.3.4.6.1. The South African Constitution and informed consent:

In an attempt to protect research participants from being coerced into participation in HIV vaccine trials, which poses considerable potential risk to participants, Dhai (2008) points out that section 12 of the Bill of Rights, of the South African Constitution on freedom and security of persons, affirms that all individuals have the right to bodily and psychological integrity, ensuring

the right to security and control over their body. Dhai (2008) argues that although all patients and research subjects have the right to free choice and informed consent and refusal in the health care context every right has a corresponding responsibility. An important aspect of the informed consent process would be the need to highlight the importance of patients honouring their obligatory responsibilities as being part of the health practitioner-patient or researcher-participant relationship.

#### 1.3.4.7. Ethical guidelines on informed consent:

A number of ethical guidelines have been produced both internationally and locally for the conduct of health research on human subjects. Section 72(6) of the National Health Act empowered the National Health Research Ethics Council (NHREC) to set up ethical guidelines to govern all health research in South Africa (Strode, Slack & Mushariwa, 2005). Other guidelines issued by the South African Medical Research Council, adapted from the UNAIDS (2000) *Ethical considerations in HIV Preventive Vaccine Research*, include the *Guidelines on Ethics for Medical Research. HIV Preventive Vaccine Research* (ibid). In addition, the Medicine Control Council's HIV Vaccine Clinical Trials Group is also developing draft HIV/AIDS vaccine trial guidelines that include recommendations regarding the conduct of HIV vaccine trials.

In common with most ethical guidelines for research the National Committee for Ethics in Social Research in Health (NCESSRH) (2003) guidelines stipulate a number of requirements for informed consent. Amongst others these guidelines require that consent for participation in research is voluntary and informed, be given both verbally and in writing, that participants are furnished with written information giving adequate details of the research in a manner and language that the participants know and understand and demonstrate an adequate amount of comprehension of this information, that participants are given anonymity and confidentiality, that they know they have the right not to participate and the right to withdraw from the research, that

consent is an on going process and that participants are given adequate protection from discriminatory practices. In addition where permission is obtained from community gatekeepers this consent must not be substituted for the need to take separate and full informed consent from participants.

What challenges stakeholders anticipate in implementing these guidelines in the South African context is of interest to this study.

#### 1.3.5. Conclusion:

Different notions of informed consent have been reflected in the literature. Whereas some refer to formal consent based on legal rules, others, taking a moral approach, refer to informed consent as a process of shared decision making. These approaches are based on different assumptions and have different practical and theoretical implications for informed consent. To help ameliorate some of these problems, additional conceptualizations of informed consent have been offered. The Nuffield Council on Bioethics (2002) distinction between the substantive and the procedural aspects of informed consent has been used in this thesis as a framework to highlight issues debated in the literature on informed consent.

Issues related to the substantive element of informed consent include those relating to the underlying assumptions, principles and goals of informed consent. While some authors have argued that since informed consent was founded on the philosophical principle of autonomy of persons requiring researchers to respect the right of potential trial participants to self-determination, other writers have argued that autonomous action is often incompatible with authority structures that traditionally legislate people's decisions. Although philosophers give different, yet supporting, interpretations for respecting autonomy, Meyers (1989) has objected to the supreme and overriding value placed on autonomy arguing that the independent [autonomous] self is presented as a rational will inattentive to communal life.

In this regard issues concerning the universality and relativity of informed consent, particularly in terms of first person consent, in multi-cultural context have been widely debated. Writers have argued that cultural sensitivity in informed consent rests on a principle rooted in particular notions of personhood that are not universally valid in all cultural contexts. Many writers are concerned about the practical implications of westernized individualized notions of informed consent on participants from predominantly nonwestern collectivist societies. Where some writers have suggested researchers obtain proxy consent from trusted village leaders (Cash, 2006; Moodley, 2002), for example, a number of practical and substantial reasons why this may not be feasible have been proposed (IJsselmuiden & Faden, 1992; Bayer, 2002).

Two fundamental substantive requirements of informed consent are that participants have the capacity to give autonomous consent and to do so voluntarily. Concerns about the participants from vulnerable sectors of society in South Africa and their capacity to consent to HIV vaccine trials have been raised (Ekunwe & Kessel, 1984; Ferguson, 2002; Lindegger et al., 2006). The question of whether children are competent enough to consent to HIV vaccine trials, and at what age, has been an area of considerable debate. What research incentives should be offered to participants and what effects inducements will have on the voluntariness of participants' consent has been raised in the literature as a pertinent issue that affects both the substantive element and the procedural elements of informed consent.

The main procedural elements addressed in the literature, regarding the implementation of informed consent in HIV vaccines trials, centre around unresolved debates about how much information to provide trial participants, who should decide on what information to provide, what information to include in consent materials, issues concerning language, promoting and assessing participant understanding, and how to manage the interface between the law, culture and informed consent.

When disclosing information, suggestions have been made that to satisfy the legal requirement for informed consent all information required by ethical codes should be disclosed. However, the provision of excess or inappropriate information has been argued to unnecessarily complicate decision making. As to who should provide the information, suggestions have been made to include community representatives as educators. Debates concerning the type of information given to participants centre on the issues of scientific versus lay language. This links to issues around participant understanding. What is the quality of participants' understanding particularly in terms of language differences and understanding complicated informed consent forms? Numerous studies have evaluated informed consent forms (see Grossman, Piantadosi & Covahey, 1994; Lindegger & Van Loon 2004; Meade & Howser, 1992; Tarnowsky, Allen & Mayhall, 1990) and their effects on participants' understanding. Assessing participant understanding of information about trials is an area of considerable debate. Although many suggestions have been made as to how participants understanding should be assessed there is an equal amount of disagreement about the validity of these assessment procedures (see Corbett, Oldham & Lilford, 1996; Ekunwe & Kessel, 1984; Lindegger et al., 2006; Lindegger & Richter 2000; Ferguson, 2002; Flory & Emanuel, 2004).

Finally, since promoting human rights protects the inherent dignity of persons affected by HIV/AIDS (Slack et al., 2000) it is not surprising that laws have made provision for the protection of subjects who enter trials. The issue of how the legal requirements of informed consent conflict with cultural demands on participants have been a topic of debate (Dhai, 2008). What becomes clear is the complexity of implementing an informed consent process that takes into account both the procedural and substantive elements in a multicultural, multilingual, developing country.

Despite widespread acceptance of informed consent as an ethical prerequisite for health research, this literature review has identified many of the controversies around informed consent, some of them substantial and others

procedural. Informed consent has been carefully implemented in HIV vaccine trials internationally. However, there have been concerns about the effectiveness of the informed consent process. This study seeks to begin an exploration of these issues by asking stakeholders what their concerns are regarding informed consent in HIV vaccine trials in the South African context.

# CHAPTER TWO

## 2. Methodology:

The literature has identified a number of contentious issues in informed consent in biomedical research. These issues relate to both the substantive and procedural aspects of informed consent. Whilst the literature has identified some problematic areas of informed consent that may be of relevance to HIV vaccine trials, this remains speculative. The aim of this study has been to examine the areas of concern that various stakeholders involved in HIV vaccine trials in South Africa have about informed consent. Are their concerns consistent with those issues raised in the literature, and do they raise additional concerns about informed consent that have not yet been raised in the literature? Examining what might be informing the positions stakeholders have on informed consent is also of interest to this study.

### 2.1. Research design:

This study was part of a broader study undertaken by the HIV/AIDS Vaccine Ethics Group, to examine ethical concerns about HIV vaccine trials in South Africa. This was an exploratory, qualitative study of data obtained from a sample of stakeholders in South African HIV vaccine trials. This thesis focuses only on the informed consent part of this study.

### 2.2. The sample:

Key stakeholder groups were identified and selected because of their involvement in HIV vaccine trials in South Africa. These key stakeholders included:

- Community advisory boards/groups (CABs) at HIV vaccine trials sites.
- Trial site staff/Investigators, including the Principal Investigators, Medical Officers, and vaccine educators.
- Media personal that had reported on HIV vaccine trials.
- Civil society, including human rights, gender and child groups representatives.
- Government representatives.
- Research ethics committee members (RECs) who had reviewed HIV vaccine trial protocols.
- Sponsors of HIV vaccine trials.

Key respondents (e.g. chairs and Principal Investigators) from the selected sample groups were purposively sampled. Some of the respondents were selected using snowball sampling technique, for example, in cases where key respondents suggested that they knew of other more relevant persons to contact. The number of respondents eventually interviewed depended on the number in each group who agreed to be interviewed, or until the ethical issues identified in the interviews became redundant. Because the sample was a convenience sample that relied on the availability of respondents from each stakeholder group there was inconsistency in the number of respondents making up each group. The breakdown of respondents making up the final research sample (n = 31) was as follows:

CABs	n = 5
Site staff	n = 7
Media	n = 6
Civil society	n = 5
Government	n = 2
RECs	n = 3
Sponsors	n = 3

Note: For the purposes of clarity, throughout this thesis, the terms respondent and representative refer to the stakeholders that were interviewed in the study whilst the term participant refers to the HIV vaccine trial participants that are referred to by the respondents.

### 2.2.1. Sampling procedure used:

Potential respondents were contacted telephonically or via email. An information leaflet describing the research, along with an invitation to participate was then sent to each potential respondent. If the respondent agreed, an appointment was made for the respondent to partake in a semi structured interview at a venue convenient to the respondent. At the scheduled interview the proposed research was described in detail. Respondents were then asked to give their consent to participate if they were still willing after which the interviews were recorded and extensive notes were taken.

### 2.3. Data Collection:

In qualitative research the semi-structured interview is often used as a guide that can be adapted to suit a particular situation (Babbie & Mouton, 2001). Semi-structured interviews allow for open ended questions that allow respondents to communicate their experiences or opinions about an issue in their own words, without any restrictions (Terre Blanche & Durrheim, 2002). In the larger study, of which this study is a part, the interviewers used a semi structured interview schedule. Each interview with the respondents was conducted in their language of choice and started with the respondent being asked to spontaneously list, in order of perceived importance, those ethical issues that they thought were a challenge in HIV vaccine trials. During the process of probing for more detail about the spontaneously listed issues other ethical issues came up which respondents were probed to talk more about.

In addition, all respondents were asked to discuss three pre-identified issues; Informed consent, the use of children in HIV vaccine trials and the standard of care to be offered to participants of HIV vaccine trials. For Informed consent the interviewers were instructed to simply raise the issue and prompt discussion. All 31 interviews were transcribed and translated into English where necessary. This study focuses only on that part of the interview dealing with informed consent.

#### 2.4. Data Analysis:

##### 2.4.1. Theoretical underpinning of the qualitative data analysis used:

This study was informed by a grounded theoretical approach. Popularised by Glaser and Strauss, Grounded theory is an analytical strategy used in qualitative research that stresses the “building of a theory from the ground up brick by brick so to speak. The bricks being the concepts that we ground as we proceed through the analysis process” (Babbie and Mouton, 2001, p. 642). According to Strauss and Corbin (1990) a grounded theory is one that is inductively derived from the study of the phenomenon it represents, in that theory is discovered, developed and provisionally verified through systematic data collection and analysis of data.

Grounded theory holds as a basic tenet that qualitative researchers do not set out to test hypotheses to add to an already existing body of knowledge, but rather it allows the researcher to study a relatively unknown social phenomenon (Babbie and Mouton, 2001) such as, in the case of this study, the problems facing the informed consent process in HIV vaccine trials. Thus the data collection, analysis and theory stand in reciprocal relationship with each other. One does not begin with a theory then prove it but rather one begins with an area of study and what is relevant to that area is allowed to emerge.

#### 2.4.2. Procedure used in developing data driven themes and codes:

Strauss and Corbin (1990) identify two main processes to a grounded theory analysis, namely coding procedures and adjunctive procedures. Coding procedures include open coding, axial coding and selective coding. Open coding, the creation of certain categories pertaining to certain segments of the data text, was the method used in coding the data for this study. Thematic analysis was used to help the researcher organize the data into different categories to increase accuracy in understanding, and interpret the data (Boyatsis, 1998). Towards this goal, doing a thematic analysis on the data would allow the researcher to identify patterns in the respondent's responses which could be used to develop themes and codes. As Boyatsis (1998) argues a good code that captures the qualitative depth of a manifestation can be used to analyse, interpret and present the research.

As suggested by Boyatsis (1998), themes and codes were developed from the data. Whereas a theme is a pattern found in the information that at the minimum describes and organises possible observations or at the maximum interprets aspects of the phenomenon, a code is a label or definition of what the theme concerns. Codes and themes were generated after reading through each respondent's responses several times to enable the researcher to get a good sense of the material. Rather than imposing a framework on responses, the researcher allowed the codes to emerge as they occurred in the data (Weber, 1985, in Boyatsis, 1998). A sample of interviews was independently coded by two raters to generate a coding schedule in order to check the accuracy and consistency of the coding. This was done to assess for inter-rater reliability of the coding. Discrepancies were then discussed in detail and an updated schedule produced with any additional themes added. The remainder of the transcripts were then recoded using the pre-established list of codes and themes around major components of informed consent in Nvivo 2000 by the researcher.

## 2.5. Ethics:

### 2.5.1. Ethics approval:

Ethical approval was granted by two local research ethics committees for the original study.

### 2.5.2. Ethical considerations:

Before deciding about participation, the study was fully explained to potential participants and written material about the study was made available. Written informed consent was obtained from each of the participants.

Of concern to the researchers were the possibilities that respondents may develop some negative sentiments in response to any perceived shortcomings of their capacity, anxiety about the possibility of social scrutiny and anxiety over the possibility that their responses may be divulged to the public which could create negative impressions of the organization the role player represents. Respondents may have raised expectations regarding potential training or capacity building as a result of the study findings. Individual respondents may be uncomfortable providing information on behalf of a certain stakeholder group and thus may require higher authority to do so. Respondents who may have been past or who are present HIV vaccine trial participants may perceive this research as being part of the HIV vaccine trial and that enrolment or withdrawal from one may affect their involvement in the other.

### 2.5.3. Minimization of potential risks:

To minimize these potential risks the following efforts were made: 1) To reassure respondents that the interview was not an evaluation of their personal or group's capacity, but rather that the aim was to identify the challenges of

HIV vaccine trials perceived by stakeholders. 2) To inform respondents of the proposed use of and dissemination of the data collected as well as issues of confidentiality. 3) To outline the potential limit of confidentiality to various stakeholder groups that because there is only one regulatory authority, limited ethics committees, CABs and other target groups, it is possible that individual respondent's responses may be identifiable in a report of the findings, for example, through rich text quotes. In this regard every attempt has been made to summarise the data so as to make respondents as unidentifiable as possible. 4) To interview key role players, each of whom were assured of their right to participate or withdraw from the study at any time and, 5) To inform the respondents about the potential benefits of research participation, including the opportunity to facilitate the development of appropriate interventions for role players of HIV vaccine trials, such as capacity building programmes or interventions.

# CHAPTER THREE

## 3. Research Results:

### 3.1. Description of emerging themes and codes:

On examination of the data the following main themes around Informed consent emerged. These included themes related to both the substantive requirement and the procedural elements of informed consent, which will be discussed respectively.

Themes related to the substantive element include:

- ❖ The capacity of participants to consent
- ❖ Challenges around child and adolescent consent
- ❖ Decisions about participation

Themes related to the substantive element include:

- ❖ Voluntariness of informed consent
- ❖ Understanding
- ❖ Communication
- ❖ Information disclosure
- ❖ The regulation of informed consent
- ❖ The impact of context on the informed consent process
- ❖ Challenges around informed consent

#### 3.1.1. Participants' capacity to consent:

A number of concerns were raised by respondents about the capacity of participants in the South African context to consent to HIV vaccine trials. Respondents were concerned about the degree of vulnerability of certain

sectors in society that might impact on their decision making. The issue of gender and power emerged. Respondents questioned the capacity of many women to consent to HIV vaccine research in South Africa. This respondent believed that:

“There are significant I think, gender implications underpinning women's participation as well, as an issue, as an ethical challenge. I think the gender in its form is particularly mindful of the challenges that women face as a reality that women experience and I think it's within that context that we have to view women's participation in the trials. Firstly, about the extent to which you can give informed consent to participate in the trial, and if she does, what is the substance and the spirit of that consent?” (Civ Soc)

On the other hand, women and children's vulnerability to the Human Immunodeficiency Virus was perceived as enough reason to include them in HIV vaccine trials regardless of their real capacity to make autonomous decisions.

“I do work among women and children and I've seen that a lot of children have become very vulnerable to HIV and Aids, and hence, I think they should be included in vaccine trials and it's clearly evident that they're not at the moment .... it's apparent that children are excluded from engaging into any scientific research because they cannot give proxy consent. In order to submit yourself to scientific research, you have to give consent on your own and in this situation, children cannot give consent because they're minors so hence, it would seem that in terms of our legislation, they will not form part of any scientific research” (Civ Soc).

In addition, some respondents were concerned that in South Africa individuals subjected to poor socio-economic factors are generally ignorant of their rights and therefore lack the capacity to make informed choices to consent to trials.

“I think, because South Africa has got vulnerable groups, really, people don’t really know their rights. They are really critical for South Africa. Particularly, Africa also because, because you know there are different, different eh things that drive people to participate. And most of them are the socio-economic issues, really. I suspect that in America people know their rights, most of them, they know their rights, they make a choice really, not to participate, or to participate” (Gov).

### 3.1.2. Challenges around child and adolescent consent:

The issue of child and adolescent consent emerged from the data as one of the most important issues of informed consent for all the respondents. This theme addresses perceptions of the perceived capacity of children to give consent, as well as the risks and benefits around child participation. The age at which children should be able to consent to participation in HIV vaccine trials emerged as a contentious issue amongst respondents. Although the new South African Children’s Act clearly sets the age at which children can consent to non-beneficial research as eighteen years, a number of respondents raised this as problematic considering the urgency of finding an HIV vaccine suitable for use on children. The scientific need for children to participate right from the start was evident in the following comment.

“I think there are four phases I think children should start participating in the first phase because if they do not begin in phase one then how are we going to determine the safety and immunogenicity of the vaccine in children” (Civ Soc).

Adolescent decision-making capacity was expressed as one of the main issues surrounding the inclusion of children and adolescents in HIV vaccine trials. Respondents viewed the reluctance of parents to allow children to participate in the trials as stemming mainly from their inability to see the need for children to participate, the uncertainty of whether the vaccine would work and their objection to their children being exposed to perceived offensive sexual language.

“I suppose the very first thing is that you have to talk about sex to a child, which some people may even object to” and “if you're talking bringing words like penis into the interview, is this going to upset people?” (Med).

Respondents speculated that conflict may develop between unwilling parents and adolescents who want to participate in the trials. Furthermore, conflict related to disclosure of an adolescent's sexual activities was likely to interfere with the decision making process. A respondent speculated that:

“[I]t is highly unlikely for a parent to give consent once they know that their daughters are sexually active. They probably, probably going to get an absolute fit or the daughter wont get parental consent because she is scared of disclosing to her mother that she is sexually active” (REC).

One of the challenges facing the informed consent process related to children's understanding of the material disclosed. Respondents expressed the need for appropriate information disclosure strategies that would address the issues of using language more suitable to their level of understanding. Respondents argued that the evaluation of children's understanding of HIV vaccine research in Africa is incomparable to that of children in the West, however. On one hand, some respondents perceived children and adolescents as a vulnerable group who needed to be protected, while other respondents

argued that adolescents in Africa are not as vulnerable as people suspect, giving the impression that in general there was no real danger in the recruiting adolescents into the trials. Some respondents went as far as to use the different social demands that African children are exposed to as justification for re-evaluating them as more competent and capable of consenting to HIV vaccine trials than children in the west. A respondent explained:

“[T]his research is different from past research. We are re-evaluating the risk-benefit ratio in our context. We operate in a different social context, where our children are not as sheltered as children in the west. They come from vulnerable backgrounds where they sometimes need to grow up fast and be self-sufficient” (Civ Soc).

Despite this perceived invulnerability of African children, a number of different opinions emerged around who should consent to children and adolescents participation in HIV vaccine trials. One respondent was adamant that:

“The decision/choice should be given to the community. If the community says no, children should not participate” (CAB).

Others argued that in many South African cultures it is customary for parents to make decisions and take responsibility for their children, which ought to include their children’s participation in HIV vaccine trials:

“In our culture a child is under parents and they make decisions for him/her because once something goes wrong the parents will be responsible to correct it ... As a parent you weigh advantages against disadvantages before giving your child permission no matter how old the child is”, and “you don’t want to get any old Tom, Dick and Harry to sign

your child, you want to get a legal, a legal guardian, and if there is none, then you don't involve the children" (CAB).

Not all respondents agreed with parental consent, however, advocating the child as the decision-maker. Some argued that consenting to participate in HIV vaccine trials is no different to consenting to having an HIV test. There were also some unexpected issues raised. For example, parents could exploit their children for their own personal gains, for example.

"[B]ecause children can't give consent themselves ...so that means they're dependent on their parents...and I don't know how you can ensure that the parents are not using this to for their own personal gains or needs versus that of the child..." (Civ Soc).

"But then going back to the fact that these are, well helpless children, we, the mothers, could be drunkards, could be so desperate...I mean they could want this children to be involved in research just because they are looking at getting paid and not caring about the consequences to the child's life at all..." (CAB).

"...It may be easier for a parent to accept an incentives if they're not putting themselves in the risk but rather their child" (CAB).

### 3.1.3. Decisions about participation:

How decisions to participate in HIV vaccine trials should be made, and who should make them emerged as a theme. Even though the substantive requirement of informed consent requires individual autonomous decision making some respondents argued that two levels of decision making that

includes both the community and individuals was more appropriate in the South African context, where collective decision making may be viewed as part of most collective cultural practices. Using the community as gate keepers for access to individuals was seen as essential. Respondents suggested using community representatives to scrutinise proposed research in the area to protect individuals and facilitate the decision making process:

“[T]his will enable us, the community members, to discuss the research and see if it is harmful or not to the community based on our different cultural practices and beliefs. To review the questionnaire, and see if it raises hopes to the potential participants or not. The community should be informed from the start about the proposed research” (CAB).

A contradictory suggestion was also made, however, questioning whether community members were really as powerless or vulnerable as claimed. Respondents advocated making use of an existing participant base of more empowered individuals, perceived to be better able to make and take responsibility for their own decisions regarding the research. Interestingly literacy was perceived as the main criteria of empowerment and thus the ability to protect one’s rights.

“[I]f you have got a participant base that is a little bit more literate, more empowered, those are the type of participants that can protect their own rights” (Sponsor).

Concerns were raised about the potential consequences of not getting community consent since without it some participants would be unduly ostracized. For example a respondent warned:

“If in the opinion of the community says ‘no children should not participate’ then they should not, meaning; the children would go back to the community and find it difficult to

mingle with it if they participated without the community's approval, but if it says, yes, it does not matter what the law says" (CAB).

#### 3.1.4. The voluntariness of informed consent:

With voluntariness being a major component of the substantive requirement of informed consent, respondents were concerned about offering incentives to participate in HIV vaccine trials. The influence of incentives could undermine the voluntariness of participation. If incentives were too great they could act as undue inducements particularly in the context of poverty. Respondents argued that incentives can also hamper understanding:

"[L]ike I mentioned about the school children doing it for money, you know, that perhaps, you know, sometimes people don't even look at the issues, you know, they might be interested in what they are going to get out of the trial in terms of money" (REC).

Some respondents were ambivalent about how and whether offering incentives would effect participants' decisions to participate, however:

"I mean the issue of remuneration, and incentives for participating in research. You know, sometimes, the money itself distorts the whole purpose of the research. At the same time, the money itself encourages, you know, people to. So I, really I don't think I have an answer to this one, really [Laughing]" (Gov).

### 3.1.5. Understanding of the material disclosed:

The issue of understanding of trial related information was identified as an issue in informed consent. Given the complexity of HIV and vaccine trials, some respondents thought that understanding needed to begin at the level of the broader community as a prerequisite to the individual informed consent. This should begin with broad HIV/AIDS education. Better community level understanding of HIV/AIDS and vaccine trials would facilitate community buy-in, and it was important to understand and respect the community perspectives from which research participants were selected. One particular reason advanced for beginning with broad HIV/AIDS education would be to dispel false beliefs and myths some participants may have about HIV/AIDS, which may affect understanding of HIV vaccine trials, such as believing that if they get a vaccine then they will be safe from HIV vaccine Trials, potentially increasing their levels of risk taking behaviour, as well as the false belief that it is HIV infected people who participate in trials. This was illustrated beautifully by saying;

“It [understanding] is especially critical when you are dealing with HIV because it is a field where there is a lot of gobbly goop and misinformation and pseudo science ok? And there is, it is very easy to presume that an HIV vaccine is an act of in fact infecting people with HIV” (CAB).

However, broad HIV/AIDS education could be potentially complicated by the growing AIDS fatigue around HIV/AIDS information in SA. There was some concern that this may affect the desire to participate in the research.

The need for participants to understand the personal implications of participating in HIV vaccine trials and not just the general risks and benefits was viewed as an essential component of informed consent. For example, participants would need to be aware of the risk of stigmatization when seen at the HIV vaccine trial sites by members of the community, particularly in the

South African rural communities who are presumed to be less educated. Respondents felt that participants of HIV vaccine trials would need an understanding of the risk of stigmatization against trial participants from the community, insurers and others.

“[F]or instance, if you had to test, if you were a young person, okay, but if you want to take life insurance and you have your HIV test done okay you will have your certificate from the trial that you have participated in this trial but still the insurance company is going to say but you could have got HIV since then” (REC).

A number of challenges were raised concerning participant understanding of the information. Challenges to understanding included various cognitive and educational issues such as illiteracy, limited formal education, difficulty in understanding scientific concepts and the lack of scientific concepts in indigenous languages. It was even suggested that educators themselves often do not always understand the information.

There was inconsistency in whether the exclusion criteria for informed consent are discriminatory toward certain participants and therefore unethical. For example, the requirement that participants have a certain level of literacy would unnecessarily exclude participants who have the capacity to understand trial related information in another medium.

“Again you’ve illiteracy issue going on here and so there is discrimination there too because they are demanding literacy, they are demanding English speaking and everything and so therefore they kind of excluding a lot of people who has a potential to understand and to benefit” (REC).

This argument was not shared by other respondents, however, who argued that the exclusion criteria for informed consent was appropriate for the illiterate as it

would serve to protect them from coercive practices by researchers. A respondent explained:

“[M]y attention was drawn to it by the participants who come in and say now what if I couldn’t I couldn’t speak and I couldn’t read or write, my parents haven’t sent me to any school and empower me and the way you saying I could read a paper and sign it you know and what would you do? Would you just take me because I’m 20 years old? I’m young and I’m HIV negative you know” (Site Staff).

Illiteracy was seen to complicate participant understanding, even though some argued that illiteracy does not imply stupidity. Participants with lower education levels were seen as being more vulnerable to exploitation affecting the voluntariness of the consent given. Being well educated was seen to guarantee understanding because of the difficulty of many of the concepts. As a research ethics committee representative pointed out:

“Eh, I can’t understand them and I have a PhD and I am an () Scientist and I can’t understand them ... And I can show you the evidence but I do not think that they, it is realistic for them to understand all these concepts, okay” (Gov).

Assessing whether participants really understand the information required for them to give informed consent was seen as a likely challenge, with a special concern about how understanding would be assessed. A Research ethics committee representative elaborated on the inadequacy of assessment practices in one of the HIV vaccine trials:

“[T]he counsellor made some brief attempt to try and check comprehension using yes/no question. We came in afterwards and did the narrative thing and where she had signed on and said yes I understand everything and I mustn’t

get pregnant and all those things. When we asked her she said eh I am signing on to this trial because my boyfriend sleeps around and ehm because I am HIV positive now eh and I need to enter” (REC).

Respondents suggested that assessing understanding would need to be an ongoing process, which required different methods for different communities. A suggestion put forward was that assessing understanding could take place through feedback, where participants are asked to repeat the information given to them back to the educator.

Various participants expressed concern about the consequences of lack of understanding of HIV vaccine trials by participants and community members, such as increased fear and distrust resulting in increased attrition from the trials, participants having false expectations or unrealistic hopes, and not realizing that they have the freedom to withdraw from trials at any stage. A respondent argued that:

“[W]hat is important for me is that they understand that they are under no obligation to complete the contract with us, you know they can terminate the contract at any time and um they will not be shamed or shouted at or prejudiced or anything like that” (Site Staff).

With informed consent being a legal requirement, some respondents were concerned that a lack of understanding by participants may lead to legal retaliation against the trial site by participants claiming that they were not told about certain aspects of the research. Respondents offered various suggestions as to how best to facilitate understanding. These suggestions varied from using key people in the work place as educators, being aware of possible power differentials that may exist between the research educators and potential participants and regularly reminding participants about various aspects of trials. Some mentioned that responsibility for facilitating and

assessing understanding rests mainly on the principal investigators. Although the research investigators were not expected to actually assess participant understanding themselves they were expected to ensure that there are enough vaccine educators and trial staff to do so.

#### 3.1.6. Communication:

Given that understanding is a crucial element of informed consent respondents emphasized the importance of communication in facilitating understanding. Good communication was seen as the key to informing participants about different aspects of the trials. Stakeholders' understanding how best to communicate with people was seen as an essential moral requirement of informed consent, as was expressed in the following.

“I think the moral imperative is first to understand as best we can, how to communicate with people and make a very, very careful and sincere effort to communicate with them, and to exclude them if it is clear to us that they can't get it”  
(Sponsor).

Respondents described communication and transparency as making up the two main pillars of informed consent with communication being seen as having the power to allay fears about the risks of participating in the trials, for example.

“I think there was very little fear on the part of the volunteers because they had had very clear communication and they were kind of ready for hearing something you know a little bit, they understood that it was a little bit risky, but they were comfortable having taken that risk” (Site Staff).

Concerns were raised about white researchers in general not being sensitive to the needs of black community's understanding of research, resulting in participants not being given the chance to communicate their non understanding of information given.

“As I said, these things (research) are very difficult and sometimes people who are conducting the research are white people and they think we understand research as they do. And most often they miss the point that we should be given that opportunity to say I do not understand” (CAB).

In order for participants to ‘buy into’ and trust what they were being told about the trials it was suggested that clear and transparent communication would need to happen between the researchers and community leaders. Communication at this level could facilitate understanding and ameliorate potential problems between principal investigators and trial participants.

“[T]he relationship between the principal investigator and the participants is problematic. It's usually mediated by a host of other individuals whose training is not necessarily uniform, whose background is not necessarily uniform, whose notions are not necessarily uniform and whose language, though maybe the language of the participants in the study, may not necessarily be. So I think there are layers of communication breakdown, which are horrific” (REC)

To facilitate understanding respondents expressed the need for communication to be a two way process between the principal investigators, other stakeholders involved, and the trial participants. In addition, respondents felt that reciprocal communication between different trial sites in the country would help stake holders identify and find solutions to problems experienced in the informed consent process.

### 3.1.7. Information disclosure:

Respondents were concerned about how, what, and how much information should be disclosed to participants. Information disclosure to, and education of participants emerged as one of the main themes concerning informed consent. This theme incorporated concerns about how information should be given to research participants as well as the potential dangers and challenges that may be involved when doing so.

Respondents felt that with transparent and clear information, participants would be able to make informed rather than coerced decisions to participate.

“I think also that with transparency people can then make better decisions...you know, If I know all the possible or known facts then I can make a better informed decision.”

(Site staff)

Stakeholders agreed that information would need to be disclosed at all levels to ensure uniformity of information given to participants across different stakeholder groups, as was expressed in the following:

“Ja ... So you actually tackle it at all these levels (I: Ok) at the same time and obviously you need to make sure that they all get the same information so that at the end of the day they they’ll hear the same thing from three different groups of people, not everyone had their own story about it” (Site Staff).

Although the substantive requirement of informed consent hinges on individual autonomy respondents raised the issue of broad community education about HIV vaccine trials as a prelude to individual education. In this regard using key players in the community to disseminate trial related information to participants was suggested, due to the availability of a number

of groups in communities that could be used to facilitate this process. The media particularly was perceived as having an important role in disseminating trial related information to communities. Some respondents questioned how accurately information was being portrayed in the media, however. It was apparent that tension existed between media houses wanting to sensationalize media stories about the trials and journalists wanting to report the facts about the trials. Dealing with the tension between giving accurate information and producing interesting stories that would sell newspapers was difficult for journalists. This was expressed by a media representative who said:

“I feel torn between, I feel the dilemma between being part of what I feel is an advocacy struggle ... One of my strengths and real interests is building a bridge between what I can establish with credibility is the correct, ethical and scientific way forward with emphasis on the scientific, that’s my stuff, and then using my skills to educate but at the same time I also have to try and tell the story” (Med).

The question of what and how much information to disclose to participants to constitute legitimate informed consent emerged as a dilemma. One begins to see in the data quite clear inconsistencies around what and how much information respondents thought should be disclosed. On the one hand, there was the perception that researchers cannot be trusted, thus motivating the need to give participants all trial relevant information, for example:

“[A]ll the knowledge, all the information that’s available (I: Ja) and as information becomes available that should be transmitted or communicated with your participants or whoever you are involved in so that they know what is happening” (CAB).

And yet, there was concern about the overloading of information. Respondents argued that discussing hypothetical risks to participants which

may not be relevant provides excess information that distracts the participant from the vital information needed for informed consent:

“[T]he kind of example of putting a hypothetical risk that is very um developed country centric and trying to explain it to somebody, and I think you just distract their attention and ... they’ll spend so much time trying to figure that example out that they won’t be able to focus on the things that have relevance to them” (Sponsor).

On the other hand, other respondents argued that one should disclose information only relevant to participants’ specific needs, for example:

“So it has to be specific to that person, the education can’t just be generic. You can’t just say well you know, there’s ...there’s all education for all the people ...it has to be specific to, you know the type of person that’s coming forward” (Site Staff).

A possible explanation for this inconsistency became apparent in the various types and levels of suspicion that emerged, whereby respondents would question the validity of the informed consent process. Some respondents warned that with knowledge comes power as was demonstrated historically in the South African context of Apartheid where knowledge was withheld from the public leaving the public vulnerable to coercion.

“I think that we need to realize that information is power, or knowledge is power and with that knowledge you can begin to influence people ... there was knowledge that wasn’t uh used to inform people properly so that’s why communication is so important and I mean we come from a history where uh certain things were kept from the public” (Med).

Some respondents claimed that information about certain aspects of the trials was being withheld from participants to the extent that participants themselves became suspicious enough to want to withdraw from the trial. There was fear that communities were being exploited by the researchers who did not explain the facts about the research to community members in a way that would allow them to make adequately informed decisions about research taking place in their community. The suspicion was that researchers almost bullied their way into the communities who were then told what would happen, for example:

“ [W]hat sometimes happen is that, let us say, there is a study that is to happen in the community, so just like they come and tell us, but or explain, but not explain that in a way that a person would understand, but just to tell us that this is what is going to happen” (CAB).

An additional concern was raised where the FDA legal requirements of giving participants *all* the trial relevant information conflicted with various stakeholders’ experiences that a large proportion of the South African population do not understand all the legal jargon. An exasperated respondent asked:

“I mean have you seen those consents? I mean you fall asleep on page three!” (Site Staff).

These concerns reflect the procedural difficulties experienced when importing ethical concepts such as informed consent from developed countries and trying to apply them to different contexts. Respondents suggested that to ameliorate this problem procedural adjustments would need to be made during information disclosure to facilitate understanding.

“What we need to probably have is a very brief patient information leaflet and modified informed consent that is applicable to the south, the region that unpacks the main

informed consent. And then once people understand that one, you then go ... through the, the really complicated informed consent, so that you basically start with something simple, that a bit more complicated and then go through the kind of FDA required informed consent” (Site Staff).

Using the right strategy to educate or disclose information to participants was seen as important. Some respondents argued that it was not necessarily the layout of information on the informed consent forms that need to be challenged but rather the way in which the information is articulated and disclosed to participants. Some participants argued that a multi-level education strategy needed to be set up. For example:

“I think um I guess the easy answer is that you have to have a good education strategy that is um culturally appropriate and preferably in ...the potential participant’s home language um and that’s an ongoing thing, so its not all the information in one session but that there are repeated opportunities to get concepts across and for people to ask questions and then again once they enrol its an ongoing process that they, that you keep giving them information, reinforcing concepts” (Site Staff).

While another respondent suggested simplifying difficult scientific jargon into terms that participants would understand:

“[W]e have got to make it so easy and speak about soldiers that protect people from infection. Because when you even before you mention phagocytes and microphate macrophage you see, it is far fetched from people, so people must first understand when you speak about those that they patrol the phygosite/hagocyte and those that will withhold the infection the microphatmacrophage, you see? You have got to

elucidate the scientific jargon, because if you just go jargon and you will be speaking microphageshatism that is very difficult to understand” (Gov).

Not all respondents thought that the informed consent forms should go unchallenged, however. Some respondents argued that the informed consent forms were too lengthy, too legalistic and included irrelevant information. In addition, the layout of the forms as well as the language used was not easily understood by participants. Respondents indicated that attempts to address these problems were being investigated, however.

“Part of our research has been modifying the form using pictogram changing the order of the form, putting important things up, first checking comprehension and those kind of things” (REC).

Other challenges pertaining to the disclosure of information also emerged. Concerns were raised regarding whether participants who speak a different language to the language being used by the educators disseminating the information, would have sufficient understanding to be truly informed about the trials. The need to communicate in English as well as the local language of the community from which participants would be drawn was viewed as essential.

“One of our standard operating procedures is that informed consent has to be in a local language. I mean patient information leaflets, videos anything that you get or if you are putting up posters in that community is all got to be in a local language” (Site Staff).

Related to the issue of language concerns were raised about the use of translators in disseminating information. Respondents argued that translators would need to consider the vernacular of the language spoken by different

cultural groups. The difficulty of translating scientific jargon into a language where such concepts do not exist was also raised. Some respondents suggested simplifying complicated scientific jargon before translating the information into other languages as a possible solution.

#### 3.1.8. The regulation of informed consent:

Respondents raised questions regarding what laws or regulations should be in place to regulate informed consent. Again, conflict was evident between those respondents who believed informed consent should be regulated and those who thought it shouldn't. Some respondents were suspicious that trial sponsors from wealthier, developed countries, who were under pressure to recruit large numbers of participants, would be tempted to cut procedural corners when obtaining informed consent from participants in developing countries they perceived to be less educated. These respondents argued that informed consent needs to be strictly monitored with tight regulation that may necessitate legislation. One respondent went as far as to suggest that the media could play an important policing role in giving participants a forum in which to complain if they felt their consent was not legitimate.

“[P]olicing monitoring role, you know if the vaccine trials are not working or if someone feels exploited, they should feel that they could come to the media and say that this is how I felt, this is why my education ...I didn't think that they, ....I didn't consent properly” (Med).

Not all respondents agreed that informed consent should be so tightly regulated. Some respondents were worried that excessive regulation would stop trials from taking place. Over regulation was predicted to create potential conflict between those stakeholders who were under pressure from the community to comply with certain cultural practices and following prescribed regulations set out by law.

### 3.1.9. The impact of context on the Informed consent process:

Respondents raised the issue of the impact of context on informed consent. Factors such as poverty, power relationships and other vulnerabilities were seen to affect the capacity of participants to make informed decisions. Some argued that there are many communities in South Africa who may be easily manipulated into participating in trials because of their perceived vulnerability.

“[Y]ou can go into many of our population, of our black population, with a lesser education ... but sometimes you know, it’s easier to persuade people with a lower education level, um, ok when you are coming into a trial” (Site Staff).

It was argued that there is an historical context of African people respecting “white authority” in South Africa. The implication was that African participants who still continue to view the HIV vaccine researchers as in a position of authority may not feel they can refuse to participate in trials.

“It is important that in most cases, most people will have an investigator who happens to be white and they happen to be Africans, and coming from this disenfranchised type of history where we come from, most participants are still under that belief that the investigator knows it all, and theirs is just to sign the informed consent” (Sponsor).

Some sectors of South Africa’s population were viewed as never having been allowed to make their own research decisions. An interesting contradiction emerged when, in one breath, a respondent complained about how hierarchical decision making, historically the norm in the mining industry, violates the voluntary decision making of miners by forcing them to participate.

“[T]hey still experience research as something being decided by the mining um, or mine management and they kind of forced to take part whether they want or not” (Site Staff).

And, in the next breath, he or she indicated how the miners had become so accustomed to having the mine management handle their affairs that they actually preferred to have decisions made for them.

“[I]n the past they probably relied on these people to handle all their matters whether it was finances, working conditions or, um ... and that’s just a culture that came from all of that, now they are depending on, or still in this system of everybody else having to make decisions for them” (Site Staff).

In addition, miners were also seen to be influenced by their co-workers, hinting at a preferred collective decision making process.

“So and unfortunately you know a lot to these men, don’t feel they are in a position where they can actually voice their own opinions and make their own decisions of ... it’s not only by the mining um structure but also their, their co-workers” (Site Staff).

#### 3.1.10. Challenges around Informed consent:

The need to get informed consent for a variety of procedures was seen as an administrative challenge since different separate informed consent procedures would need to be done at various times during the trial. One person speculated that:

“maybe five years down the line where we are putting needles into them and we have to get consent for that, which

is gonna be separate and we might have to get consent for blood testing and counselling but not necessarily for questioning interviews” (REC).

Some respondents argued that the substantive requirement of individual consent may be challenged by cultural expectations. In cases where there may be cultural differences in decision-making that demands collective or shared decision making, for example, the procedural elements of informed consent may need to be adjusted for the South African context.

“Although the Constitution gives all rights, there is a need to consider this issue because of cultural practices. It may be advisable to involve both partners in seeking prior consent. I don’t know how this would work but it would depend on the cultural group. If both partners agree, it may be easier” (Civ Soc).

Trying to “sell” the trial to participants versus obtaining genuine Informed consent from them was a concern expressed by some respondents. The tension between encouraging participants to join a trial, in order to recruit large numbers of participants needed for stage three trials, and ensuring that they are adequately prepared to make an informed choice was raised by a respondent who suggested:

“We really have got to weigh the pressure of recruitment of a large number of people against truly enrolling truly informed people” (Site Staff).

## 3.2. Findings by stakeholder group:

### 3.2.1. Civil society:

The Civil Society group tend to see themselves as caretakers of society. It was important to civil society representatives that both participants and communities have a good understanding of trials and the personal and community implications of them. Thus it was not surprising that they felt that participants and, especially, communities should be fully engaged in decisions around participation. As one respondent stated:

“Civil Society must engage the process, absolutely. You know, what and that's round what is the product? What does it mean for people participating in the trial? What does it mean for community? You know what I mean? Who are making the decisions around the trials and to what extent can community be involved in the decision making processes? So literally at every level and in every aspect, community should be central” (Civ Soc).

Context related issues perceived as affecting participants' autonomy, such as, poverty, lack of education, lack of social power and specific vulnerable groups such as rural women and children were main concerns for Civil Society representatives. For example a Civil Society representative asks:

“How do you do a trial that involves poor people, or people who are not very well educated? While another Civil Society representative suggested “There are definitely South African specific issues in terms of our social situation and epidemiological issues. While there are generic ethical norms and standards, we need to take context into account”.

Information disclosure to the public about HIV vaccine trials was also an important issue for civil society representatives, for example:

“The results of these things are important. It should be more publicly disseminated. Information should be accessible to all. It should be made more public” (Med).

### 3.2.2. Community Advisory Boards:

For the Community Advisory Board Representatives the issue of communication was of prime concern. A Community Advisory Board Representative proposed that communication needed to be:

“properly set up, I prefer starting with the CAB itself then moving to a trial site to the site, and then also to have communicated with, with what is happening at other CABs (I: Ok) within our country and then to extend that into Africa” (CAB).

Most Community Advisory Board Representatives expressed the importance of setting up community advisory groups to facilitate community involvement from before the trials start as a means of empowering the community in preparation for HIV vaccine trials and thus by implication aiding the Informed consent process. A Community Advisory Board Representative said:

“The people who are involved in the vaccine have made a very good step to say that we should form a CAG before a trial itself starts. It empowers the community to know exactly what is happening around us...I can say that community members need to be involved and should be given a chance

to voice their concerns even before everything else starts (CAB).

The importance of educating the Community Advisory Board Representatives first was seen as crucial since the role of Community Advisory Board Representatives is seen as primarily to:

“[L]ink researchers and the community. Meaning if there is a planned research these people should be the ones to disseminate information to the community and hear their concerns and refer them back to the researchers. These are the spokespeople on behalf of the community... As a matter of fact even before we go and educate the community down out there, the very people who are going to be educating the community need to be educated too” (CAB).

Even though the perceived function of Community Advisory Board members is as spokespeople on behalf of the community, a Community Advisory Board Representative ironically worries that miners may feel pressured *by the researchers* into recruiting for HIV vaccine trials, stating:

“We were worried that maybe miners were chosen just because they are miners and they would easily agree to participate in the research just because researchers said they should” (CAB).

### 3.2.3. Site staff:

How context impacts on the informed consent process was an important issue for site staff representatives. When speaking about the plight of mine workers a site staff representative pointed out that:

“The whole history of um the mines it’s one of, you know they work at the mine and they, they kind of they’re controlled by the mining bodies... a lot of decisions were made for them in the past by either their um labour representatives or the mining representatives and that now actually poses problems for us because um, they still experience research as something being decided by the mining um, or mine management and they kind of forced to take part whether they want or not”. What happens when you do informed consent on an individual level? Do people say no, even if the whole group of them think that they want to take part? (Site Staff)

The issue of undue inducements that offers incentives to participate in trials was also seen as problematic, as it may affect the voluntariness of participants’ consent. Of particular concern was the offering of financial rewards to participants from socio-economically vulnerable populations, as a site staff representative said:

“[F]inancially if there any anything that is a financial gain to them they’ll probably participate just to do, just to get the money and not because they want to ... or understand the study. Um, I think that makes both communities vulnerable. In the general community you get a very high level of unemployment” (Site Staff).

A second site staff representative highlights this issue when suggesting that when offering incentives researchers:

“[N]eed to be very careful um, you know, how you structure it because um, well for our mining community for example they if if you want to give them money for transport costs or something like that that is going to be an incentive to them to

do it, to get the cash because they have free transport (I: Oh, ok) provided by the mines (I: Ok) where in the general community you don't have that. Um, and if you want to give them something, you know, something like food or something you know for the mining community would be better to use – a better incentive to use than you know, giving them money for transport costs where the general community would definitely use that money for transport because that is the only way they can get to, to the research site and back home” (Site Staff).

An example of how undue inducements can affect the voluntariness of participants consent was realised when participants continued to come back for the monetary rewards offered in other clinical trials they had participated in:

“[W]hen we did a lot of clinical trials for them. And they pay participants an amount per visit every time they pitch up and, you'll find people coming for you know their visits and then after the study is finished you know they would come back still on a monthly or two weekly basis and say “Now ok, where's my money?” (I: Oh dear) So we realised well ok, that is a bit of a problem because they are only coming to get the money and nothing else” (Site Staff).

The issue of who makes decisions to participate in the trials, the community versus individuals, was also of concern to site staff representatives. A site staff representative emphatically stated that:

“You don't speak to the Induna to give consent for the whole community, every person should be asked for consent” (Site Staff).

#### 3.2.4. The Media:

Understanding the personal impact of consenting to trials was one of three main concerns voiced by the media representatives. A media representative was concerned about participants' ignorance of how media articles can potentially stigmatize them if their identity was inadvertently mentioned. The suggestion was that during information disclosure this possibility should be discussed with participants in order for them to make informed decisions.

“I’m very aware of it because I work in HIV, and do lots of HIV stories, and I know that anytime someone is identified with anything to do with HIV or AIDS, it can have repercussions: it can be negative, they can be positive, but people must be very aware of what they, um, are getting into. And I think journalists are very casual about it: where they’ll use peoples’ names and identities without thinking about it”  
(Med).

The important role that the media plays in educating the public about HIV vaccine trials was acknowledged. Education of the public through the media was seen as an important information disclosure tool in the informed consent process to prepare participants. Media representatives raised the issue of AIDS fatigue within the media and the general population. Aids fatigue was seen to be problematic in that it may affect coverage on HIV vaccine trials by the media and the motivation of individuals to read information about the trials. For example, a media representative pointed this out in the following:

“[B]ut the downside of it is that there is a high increasing amount of AIDS fatigue, which I have, I pick up a lot even at the level of my newsroom you know, um they have just had enough, you know. It’s like how many more times can you write about like AIDS ...Then there’s a high level of AIDS fatigue amongst our readers. You know, we’ve had a survey

were we found that anything on AIDS on the front page, when I write a story on the front page, our circulation drops” (Med).

The issue of lay versus scientific knowledge about HIV vaccine trials was a concern of some media representatives who questioned whether ‘true’ informed consent could ever be achievable if participants did not understand the information given to them. For example a media representative proposed:

“I think that it is incredibly important with all research to ensure that you have true informed consent. Um, however I think often what happens isn’t true informed consent. And I think that to a degree, true informed consent is never really possible. Because the person who is required to be the subject doesn’t have the same scientific knowledge that the scientist has...” (Med).

The authenticity of the informed consent process in terms of whether recruiting participants for HIV vaccine trials is a voluntary or coercive process was also questioned by media representatives as was expressed in the following quote:

”Um, I think the most important one would be about participation, about the whole process of getting volunteers. I would imagine, is a, is a (dice) between needing to be somewhat persuasive because you want volunteers, and at the same time needing to be actually sure that it is informed consent. And you need to ensure that um, ja that no-one has been forced into it and that they understand the dangers and the implications of participating in research” (Med).

However, offering incentives to participants in HIV vaccine trials was not seen as necessarily coercive. A media representative admitted:

“Ja, it’s an incentive, I don’t think it’s a coercive thing. It should be an incentive for people to sign up, but hopefully if they’re signing up for a vaccine trial, they’re very well informed and they’re not going to put themselves at high risk, anyway: even though I know that’s not true (laughs). I think it’s a fair incentive!” (Med).

### 3.2.5. Government:

The disclosure of information to and the education of participants, as well as their understanding of the information given, were identified as important issues that impact on informed consent by government representatives. This was demonstrated by the following statements made by a government representative:

“This issue is so critical you gonna have to make sure that you reach people from where they are, and there are so many people who are illiterate in the country ( ) English does not mean a thing to them, and those are the people who in fact are mostly at risk for HIV infection and if we do not reach them then we will miss the bigger population ... You have to use the language that people will understand and the way the messages, should be context specific, culturally sensitive so that they can contextualise, they can understand the construct, how they construct the messages to be meaning what they intended to mean” (Gov).

Government representatives were also concerned about the issue of children and their capacity to consent to participation in HIV vaccine trials. Children were also seen as vulnerable to exploitation and thus the need to monitor the Informed consent process was seen as vital, as is seen in the following quote by a government representative:

“The issue of consent, I have already raised it. So I think that one should be monitored really very well. To say who, who, who consents, for the child, because you see if there are incentives, and then there is an agreement that children are going to participate, and then the child is not staying with the biological parents, for example, and stays with a.....grandmother or so, if that grandmother is coerced or is of the opinion that, you know, she needs the money, she might, she might consent for the child to be part of the of the. So we need to balance that issue to say, who should really consent for the child?” (Gov)

Having suggested that the consent process should be carefully monitored, however, the same government representative also suggested that the Informed consent process does not necessarily need to be strictly regulated when he or she suggested:

“You know in terms, I think in terms of ethics, you can regulate up to a certain extent, really. You can’t just regulate totally. I think we will use the guidelines as a reference really. I don’t think there is anything that you can change, unless, from the outcomes, of the trials, something drastic is really endangering the people, we will need to look at the guidelines, but I think for now, the guidelines really form a framework, in terms of how we should conduct a, the trials” (Gov).

#### 3.2.6. Sponsors:

The sponsor representatives raised the issue of the complexity of informed consent forms and how these would need to be revised. For example a sponsor representative explained:

“Well we had an interesting discussion about this in which, internally, we were talking about the complexity of consent forms, and one of my colleagues asked me, well who is it that makes you make these so complicated? We were agreeing that they are too complex” (Sponsor).

All the sponsor representatives raised the issue of communication between different stakeholders involved in HIV vaccine trials and the community. The difficulty in reaching consensus between them about how to proceed with the ethical requirements of the trials was expressed by a sponsor representative, for example:

“You know there is a lot of players, WHO, all the way down from WHO to the people at the community level to the press, uh, who come in with different levels of beliefs and information, so trying to get all those people to agree on how to proceed is difficult ... I think that it’s a good thing to have open discussion with a lot of different players, sometimes you just have to be patient with people who have their own concerns and let them work through it themselves. But I do think that discussing as opposed to just filing written documents or whatever is sometimes very helpful” (Sponsor).

### 3.2.7. Research Ethics Committee

Most of the Research Ethics Committee representatives expressed an awareness of their responsibility towards the safety of participants in research. This was expressed by one of the Research Ethics Committee representatives who asked:

“You know, we are going to be using vulnerable people and you know how are we going to make sure that these vulnerable people are not exploited” (REC).

Participants’ lack of knowledge to adequately protect themselves, and thus give fully autonomous consent, was identified as problematic for the informed consent process. For example, a Research Ethics Committee representative stated:

“Because of a responsibility that eh one holds in ethic issues, that science evades ethics. One the most important things is the safety of the patients particularly in population where they don’t have knowledge ability to protect themselves” (REC).

How well informed they could be in regards to the unknown risks and the safety of participants of an HIV vaccine was also identified as an issue, as was expressed by a Research Ethics Committee representative in the following:

“[Y]ou see of all these things interconnects because the informed consent relates to our adolescents and our children, illiteracy and the understanding of the whole concept of the HIV/AIDS virus, you know the particular population being studied have so much myths and difficulties with the concepts and coming into vaccine trials you must be coming into something that is gonna kill you. So informed consent means that they know really what they are coming into and that they have a right to decide. And it concerns me because we don’t really know what the risks are to explain to people” (REC).

Despite concern about the unknown risks of an HIV vaccine, however, some Research Ethics Committee representatives were critical about how the legal

distinctions made between therapeutic and non therapeutic research restricts children's participation in HIV vaccine trials, for example:

“[W]e gonna have legal, statutory requirement of the National Health Act and capacity to consent (I: under legal), ehm, ministerial authority, I mean the concepts, the concepts of therapeutic and non therapeutic, invasive and non invasive to that whole quagmire (laughter) ... but then the whole problem relates to legality whether it is therapeutic or it is not therapeutic ... the statutory criteria may be too restrictive and that bureaucracy may hamper progress in research” (REC).

The regulation of informed consent was of concern to half of the Research Ethics Committee representatives. This was expressed in the following example:

“Process, I am thinking that informed consent when eventually it is done how do you confirm misinformed consent, how to monitor it, uhm, do we go outside and get somebody who is completely independent to come and witness the signature ...because the guidelines say we should have an independent witness and I don't think that we've been having an independent witness in this group” (REC).

Linked to the monitoring of the Informed consent process was ensuring that participants understood what they were actually consenting to. Research Ethics Committee representatives felt that part of their task should include checking to see how researchers planned to check understanding by participants when submitting research proposals, as suggested by a Research Ethics Committee representative:

“Maybe that, you know, when we look at protocols we must make sure that there is a testing of informed consent you

know. I think to me that is very important eh that once you obtained informed consent you cant really just take that at face value ad that you need to go a step further and test to see if this is really informed consent. And you know ask questionnaire that your participants have to answer if they really know, you know, the truth about what the vaccine is going to do” (REC).

One of the problems identified related to the perceived incapacity of Research Ethics Committees to monitor the informed consent process:

“Ja, research ethics committees just don’t have enough capacity [to do audits, checking that procedure is followed]” (REC).

Of particular concern to Research Ethics Committee representatives was how power dynamics created between wealthy researchers, driven by remuneration incentives to run trials, and participants from low socio-economic areas will affect the informed consent process. The issue of undue inducements was of particular concern in this regard.

“That remuneration issue for me is currently a power issue. There is such a lot of money floating around, uhm, for investigators who are interested in doing this kind of research” (REC).

As with the sponsor representatives, the issue of communication between the principal investigators and participants was seen as problematic by the Research Ethics Committee representatives. This is clearly seen in the statement made by a Research Ethics Committee representative who believed that:

“[T]he relationship between the principal investigator and the participants is problematic. Its usually mediated by a host of other individuals whose training is not necessarily uniform, whose background is not necessarily uniform, whose notions are not necessarily uniform and whose language, though maybe the language of the participants in the study may not necessarily be. So, I think there are layers of communication breakdown, which are horrific, to be honest and I have got evidence for that” (REC).

# CHAPTER FOUR

## 4. Discussion:

The aims of this study were to explore the perceived ethical challenges around informed consent in HIV vaccine trials among a range of stakeholders, to compare these challenges to issues raised in ethical guidelines around informed consent, and to explore what the factors might be which influence the stakeholders perceptions of these challenges. This being a qualitative analysis necessitates a discussion of the results of these aims using a more narrative approach. In keeping with the general format of this thesis the first two aims are discussed in relation to those challenges identified by participants in the data under the substantive and procedural elements of informed consent whilst the third aim is discussed separately.

### 4.1. Substantive issues raised by stakeholders

#### 4.1.1. *The issue of first person consent:*

The question of who should consent to participation in HIV vaccine trials has been raised in the literature. These concerns go to the heart of the substantive requirement of autonomous decision making by research participants. Writers have questioned the insistence on autonomous agency by participants in non Western countries (Mkhize, 2006), in cultural settings where cultural norms may demand community and/or patriarchal decision making practices where the man is perceived to be the ultimate decision maker for the family. Some writers (Cash 2006; Diallo et al., 2005; Moodley, 2006) have suggested that in developing countries, with a predominant community orientation, first person consent to research should be replaced by community consent, usually sort from traditional leaders. This trend was not apparent in this data set, however. Consistent with Ijsselmuiden and Faden's (1992) views that first person

consent should not be replaced by or accompanied by village leaders or heads of households some respondents were quite adamant that consent from the Induna (tribal leader) should not replace individual consent. Although respondents were concerned about community involvement in decisions made at the procedural level of informed consent they did not argue for the replacement of first person consent by community based consent. Respondents argued rather, for clear and transparent communication between the researchers and community leaders as a way of facilitating understanding to ameliorate potential problems between principal investigators and trial participants.

#### 4.1.2. Participants' capacity to consent:

The demand for transparency in the informed consent process appeared to stem from what appeared to be a pervasive lack of trust by respondents of the motives of researchers. Two possible reasons for the level of suspicion displayed by respondents appeared to be connected to the legacy of apartheid and to the perceived over utilization of communities for research purposes. Whereas the over utilization of communities for research in developing countries by developed countries has been documented (Ekunwe & Kessel, 1984; Slack, et al., 2004), research into the effects of apartheid on the decision making capacity of black participants to take part in HIV vaccine trials is lacking.

The possible influence of apartheid on black participants' decision making capacity became apparent by the perception of some respondents that mine workers, for example, were vulnerable in the face of perceived powerful white researchers as, historically, decisions were always made for them. This argument was not shared by all of the respondents, however. A few respondents argued that mine workers may be so used to having decisions made for them that they preferred it, not from a lack of perceived capacity to be autonomous, but more because they were comfortable with the status quo. In addition it was acknowledged that mine workers in general preferred to

take time to engage in dialogue with their friends before arriving at a decision to participate in trials. This is consistent with Russell et al's. (2005) findings that non westernized participants may require time and the opportunity to think about and discuss information with other trusted individuals, before reaching a decision.

The ambivalence demonstrated by respondents about the perceived incapacity of mine workers, and by extension many other black workers in South Africa, asks fundamental questions regarding the theory and practice of informed consent in this country. Firstly, is autonomous agency really valued universally, or is the complacency to leave decision making to others purely a result of the historical influence of apartheid policies? Secondly, what effect will the answers to these questions have on the procedural elements of informed consent in the South African research context? To begin to answer these questions a potential area for investigation would be to ascertain the actual perceptions mine workers have in South Africa of their decision making capacity and their preferred decision making practices to participate in HIV vaccine research.

Respondents raised specific issues regarding South African participants' capacity to consent. In many instances the perceived vulnerability of participants in certain sectors of society was equated with incapacity to consent to trials. This "vulnerability discourse" appears to have been used in a number of problematic ways by some respondents. First, vulnerability is used to justify why women and children, as a result of their perceived vulnerability to contract the Human Immunodeficiency Virus, should be included in trials and therefore be allowed to give their own consent to do so. Second, respondents argued that vulnerable individuals, such as rural women, need careful monitoring and mediation before giving their own consent. Third, a respondent mounts a slippery slope argument that sees the informed consent process as potentially leading to vulnerability and fourth, the low socio-economic status of many individuals in South Africa was argued to render them incapable of knowing their rights and thus incapable of making an

autonomous decision to participate in HIV vaccine trials. The question is how are these seemingly rational arguments problematic to the notion of informed consent?

The first argument suggests that if the research is likely to benefit a group of people particularly vulnerable to the disease being researched then this group of people should automatically be enrolled in the research on the grounds of their perceived vulnerability rather than their actual capacity to consent. Using this argument when enrolling children into trials, for example, the principle of autonomous agency may be trumped by the principle of beneficence. Although Beauchamp and Childress (1994) acknowledge that there are certain instances where one biomedical principle can trump another, these need careful consideration and balancing. For instance, one needs to consider that children's lack of understanding, and therefore, autonomy is what makes them vulnerable to exploitation as research subjects which is part of the reason why they are legally excluded from participating in non therapeutic trials. The question of what age South African children are likely to understand and appreciate the risks and benefits about the research to classify them as autonomous agents able to consent to trials continues to be debated in the literature (Bester, 1992; Gouws, Kruger & Burger, 2000; Wendler & Shah, 2003).

In the second argument respondents questioned the capacity of women to consent to HIV vaccine Trials on the basis of the challenges that they face as African rural women. The implication of this argument is that women vulnerable to the challenges of a rural existence are incapable of thinking for themselves and thus need mediation in their decision making capacity. Whilst it is essential that researchers need a good understanding of all aspects of the community from which they intend to recruit participants (Ekunwe & Kessel, 1984), which may require a good grounding on gender empowerment and its interface with HIV, care must be taken that researchers do not undermine women's real capacity and therefore their status to make their own decisions by only recognising the capacity of men. This is more likely to happen if researchers assume that vulnerability equates to non-autonomy and therefore the inability of vulnerable

participants to make decisions for themselves. Using Beauchamp and Childress's (2004) understanding that "a person with diminished autonomy is in at least some respect controlled by others or incapable of deliberating or acting on the basis of his or her desires and plans" (p. 121) may help stakeholders in their assessment of whether African rural women do have diminished autonomy or whether it is a matter of others not respecting their autonomy.

In the third argument the vulnerability discourse was used to highlight a potential conflict between respecting the substantive right to autonomy versus respecting the demands of the cultural context in which trials take place. Respondents argued that some cultural normative beliefs and practices may clash with the demands of first person consent making certain women vulnerable to being marginalized or harmed in other ways by their communities if the cultural rules are not adhered to. This argument takes the form of a slippery slope argument which is essentially saying "If we respect the participant's right to autonomy it can lead to dire consequences, we assume, and thus we should rather do as others demand". Edwards et al. (2004) would argue that applying such faulty logic may act as a smoke screen for paternalism. But, what if women were at risk of harm for consenting to trials individually? In such cases, if individual participants are made aware of such potential risks during information disclosure, they can be given the opportunity to decide for themselves whether this represents a personal risk to them and outweighs the benefit of participation. Ultimately the decision to participate still lies with the participant and her status and autonomy to make her own research decisions is respected and preserved.

The fourth argument uses the vulnerability discourse to support the view that, unique to Africa, is the problem of poverty and the tendency of researchers to take advantage of poor people perceived as not knowing their rights. Evident in this way of thinking is the assumption that vulnerability, caused by socio-economic factors in this instance, renders individuals ignorant of their rights and, by implication, incapable of making autonomous choices. Not only is this deduction erroneous, as according to literature the capacity to be

autonomous depends on competence to understand and decide, make decisions voluntarily and authorise one's consent (Appelbaum et al., 1982; Beauchamp & Childress, 1994; Ferguson, 2002; Lindegger & Richter, 2000), it is insulting.

The above arguments are not meant to imply that there are no legitimate problems experienced in the context of vulnerability and informed consent. In fact, on the procedural level, issues pertaining to vulnerable persons and implementing informed consent processes that are not coercive or exploitative was of great concern to respondents. How stakeholders use and understand potential participants' vulnerability, however, needs to be considered to avoid (a) unnecessary exclusion of some participants from HIV vaccine trials; (b) allowing inclusion of non-autonomous participants, such as children, into HIV vaccine trials, and (c) employing unethical informed consent practices that violate individuals' autonomy. In addition, more research needs to be done to ascertain the actual competence of participants to consent to research from vulnerable sectors of society in South Africa.

#### 4.1.3. Children's capacity to consent to HIV vaccine trials:

The Legal framework under which the trials take place in South Africa has been argued to pose a challenge with regards to who gives consent for children to consent to HIV vaccine trial participation. Respondents' concerns regarding children's capacity to consent was consistent with arguments raised in the literature. As Strode, Slack, Grant and Mushriwa (2005) have argued, the National health Act and Children's Bill of Rights require that children assent to research participation together with their parent's formal consent when the child is capable of understanding. The difficulty lies in the lack of guidelines or suitable testing instruments to help stakeholders determine when children have the capacity to understand the research.

With regards to children, other arguments raised by respondents included the argument that African children are not comparable to children from the west

and thus should not have the same evaluative criteria applied to them when considering their capacity to consent to HIV vaccine trials. This argument is similar to those posed by Swartz, Kagee, Kafaar, Smit, Bhana, Gray, Lesch, Lindegger, Milford, Richter, Seedat, Skhosana and Stein (2005). Problematic with this line of argument is that self sufficiency or childhood resilience may not equate to meeting the criteria for making informed decisions regarding participation in trials. For instance, a 13 year old adolescent who heads a household, as so many aids orphans in Africa do, may not have the understanding necessary to give informed consent to trials despite his or her level of self sufficiency.

In a study focusing on the how those working with South African children evaluate the readiness of adolescents for selection into HIV vaccine trials Brindley-Richards (2006) recommended that when evaluating the maturity of adolescents to participate in trials a range of factors would need to be considered. These included psychosocial factors, the adolescent's cognitive development, self concept, level of motivation, the quality of their relationships with their parents and other adults, how effectively they deal with peer group influence, how resilient they are and their ability to regulate their emotions. In addition, the adolescents' talents and abilities, future orientation, personality, cultural upbringing, moral and religious development, age, risk taking tendencies, the gender of the adolescent, their level of education and their ability to take the future into account, were also seen as contributing factors. Suitable instruments to ascertain the readiness of South African adolescents to independently consent to HIV vaccine trials still need to be developed however.

#### 4.1.4. The voluntariness of participants consent:

The substantive requirement of autonomy in consenting to research requires that consent is given voluntarily by participants (Beauchamp & Childress, 1994; Berg, 2001). Respondents were concerned about what effect

inducements would have on participant's voluntariness to participate in HIV vaccine trials particularly in light of pervasive poverty. Due to a lack of empirical studies on the concept of and complexities of voluntariness (Barsdorf & Wassenaar, 2005) in the informed consent process, however, limited clarity has been provided as to what actually constitutes voluntary consent to research and what types of ethical transgressions are likely to undermine voluntariness (Pace & Emanuel, 2005). Research needs to be done on how various types of research rewards influence low socio economic participants decisions to participate in HIV vaccine trials in the South African context.

#### 4.2. Procedural concerns raised by stakeholders:

Demographically South Africa is a multicultural society with a diverse range of cultural beliefs and practices that impact on the procedural elements of informed consent. A number of concerns were raised by respondents about the implementation of informed consent in HIV vaccine trials. These concerns were consistent with many of the procedural concerns covered in the literature.

Despite the fact that Forde and Vandvik (2005) argue that issues relating to patient information and communication are generally given low priority, the data from this study did not reflect this. Consistent with UNAIDS guidelines for HIV vaccine research, a process of consultation between community representatives, researchers, sponsor(s) and regulatory bodies, was seen as essential by the respondents.

With understanding or comprehension being a central issue in informed consent, together with the social, political, cultural and linguistic differences of the South African population as compared to those of the west, it is not surprising that it was raised as an issue of real concern for all the stakeholders. Issues relating to information disclosure, communication and participants' understanding of the information given them, were primary concerns

consistent with those concerns reflected in the literature. Beauchamp and Childress (2001) and Lindegger and Richter (2000), for example, have argued that participant's understanding of the information disclosed to them is a key issue in Informed consent.

#### 4.2.1. Participant understanding:

With there being eleven official languages in South Africa the issue of participants understanding the material given to them, particularly if delivered in a language that is not their first language, was of concern to respondents. In this regard issues relating to the translation of information from one language to another were of most concern. In addition to the common concerns reflected in the literature, that some languages do not have words to describe certain scientific jargon (Moodley, 2002; Gasa, 1999), affecting what Bayer (2000) refers to as semantic understanding, respondents argued that certain questions could lose their true meaning when translated, yielding answers that may not accurately reflect the participants real understanding of the information. Linked to this was the problem of using translators from different areas who do not share the same vernacular of the language used in the area from which participants came. This was consistent with concerns raised in the literature (Moodley, 2002).

Respondents were divided about how much information to include on consent forms, as well as participants understanding of them. Concerns that participants may not understand complicated and lengthy informed consent forms were consistent with Epstein and Lasagna's (1969) findings. When deciding on how much information to give participants respondents gave mixed messages, reflecting the ambivalence in the literature. While some respondents argued that participants should be given all trial relevant information, not necessarily to satisfy the minimum standard of what participants of HIV vaccine trials should understand, as highlighted by Lindegger and Richter (2000), but to ensure that participants received the information they needed in case the motivations of researchers could not be

trusted, other respondents were in agreement with Iselinger (1972) and Lindegger et al. (2006) that discussing irrelevant hypothetical risks to participants provides excess information that may distract the participant from the information needed for informed consent.

While there should be some mindfulness of the suspicions some stakeholders have of researchers' motives, due in part to the effects of apartheid and over utilization of black populations for research, Lindegger et al. (2006) warn that while providing participants with all the information about trials may satisfy the legal requirements of disclosure of information the ethical condition of understanding in order to make decisions in one's own best interest may not be satisfied because of the volume of information participants need to understand.

Linked to the understanding of the material disclosed to participants was the issue of what assessment procedures should be used to assess participant's understanding. The literature cites a number of questions regarding the different methods used to assess participant's understanding. Lindegger and Bull (2002), for example, question the use of formal tests of knowledge to assess participant understanding "in research conducted in less formally educated, culturally diverse or developing country contexts" (p. 4). Further complicating the issue is that understanding is an elusive concept and it is not easy to evaluate the nature and level of understanding that individuals have of a concept, event or process (Lindegger & Richter, 2000). Whereas it may be relatively easy to evaluate the adequacy of the information disclosed to participants "it is far more difficult to assess whether and how the information and its implications are truly understood" (p.315). The danger of using relatively easy formal assessment practices was elucidated in this data set where a respondent found the practice of using yes/no questioning, in one of the HIV vaccine trials, to check participants' comprehension to be completely inadequate.

While respondents agreed that assessing understanding must be done on an on going process, they suggested using different methods of assessment for different communities, such as using a feedback mechanism where participants are asked to repeat the information given to them back to the educator. The implication was that assessing understanding needs to be more context specific to accommodate cultural differences in understanding. These views fit well with those expressed by Lindegger et al. (2006). Exactly what these community specific variables are that require participants' understanding to be assessed differently is unclear and is an area of research that may require further investigation.

The general lack of education and training of stakeholder groups expected to educate the community about trials was of concern to respondents. If information disclosure about the trials is to be part of the responsibility taken on by Community Advisory Board members, for example, then clearly they themselves need to be well informed about what and how much information is required for participants to consent. Poor understanding of the knowledge educators must impart to the community potentially results in misinformation about trials affecting the quality of informed consent. Exactly how knowledgeable stakeholders need to be to produce adequately informed participants is unclear and needs further investigation.

Providing this training to Community Advisory Board members in addition to the stakeholders already directly involved in educating the community poses extra financial challenges to trial sites with existing poor resources. An existing lack of communication and coordination within and between stakeholder groups in the provision of this training was of concern to respondents. What type and amount of information to include and who should provide this training needs to be clarified.

#### 4.2.2. Information disclosure:

The role the media can play in disseminating information about HIV vaccine trials to enhance community awareness was acknowledged by respondents who expressed concern about the poor media coverage about trials. A number of challengers were highlighted by the media representatives in disseminating information about the trials. Challenges pertaining to HIV vaccine trials/ AIDS fatigue, the tension between sensationalizing HIV vaccine related stories to sell newspapers as against reporting the facts, and reporting difficult scientific information about HIV vaccines in a way that the public will understand, was consistent with those highlighted in the literature (Hanefeld, Coates & Kruger, 2005; Cullinan, 2001; Swanepoel, Fourie & Froneman, 2005).

In addition, some respondents portrayed the media as callous and cold. This was despite evidence in the data that showed a degree of compassion and virtuosity in some media representative's ethical decision making capacity when reporting on HIV vaccine trials. This reflects Swanepoel, Fourie and Froneman's (2005) concerns regarding the negative impression created by the press when reporting on HIV/AIDS and HIV vaccine trials. The negative perception some stakeholders have of the media may prevent the development of the symbiotic relationship needed between the press and the stakeholders, however, to enhance trial related information dissemination to the public.

Evident in the data was respondents' apparent lack of knowledge about, use of, or access to the ethical guidelines set out for HIV vaccine trials. The lack of knowledge and subsequent use of the ethical guidelines by stakeholders may have a negative impact on the application of the informed consent process at the levels of both pre-trial education and information disclosure to participants. If stakeholders do not know the legal and ethical requirements of the informed consent process how can they ensure that participants meet the requirements of what they should understand as set out in the informed

consent protocols? Further more, on a procedural level, lack of consensus between stakeholder groups on how to implement the informed consent process is likely to affect uniformity across HIV vaccine trials in the country. Exactly how much knowledge South African stakeholders of HIV vaccine trials have of these guidelines and or the reasons why they are not utilized needs further investigation.

This section has attempted to discuss respondents concerns in relation to theoretical arguments portrayed in the literature and the implications they may have for both ethical theory and the practice of informed consent. A number of concerns about informed consent similar to those reflected in the literature were highlighted. These concerns were discussed in relation to both the substantive and procedural elements of informed consent. Substantive concerns related mainly to the issue of first person consent, participant's capacity to consent and whether participants consent voluntarily.

Of particular interest was the way in which respondents tended to use what I have referred to as "vulnerability discourse" in potentially problematic ways. First, vulnerability was used to justify why women and children, as a result of their perceived vulnerability to contract the Human Immunodeficiency Virus, should be included in trials and therefore be allowed to give their own consent to do so. Second, respondents argued that vulnerable individuals, such as rural women, need careful monitoring and mediation before giving their own consent. Third, a respondent argued that the informed consent process itself potentially leads to vulnerability and fourth, the low socio-economic status of many individuals in South Africa was argued to render them incapable of knowing their rights and thus incapable of making an autonomous decision to participate in HIV vaccine trials. Procedural concerns related to information disclosure, participants' understanding of information disclosed, including how to assess their understanding, issues around cultural sensitivity, and the regulation of informed consent. In addition, some issues emerged as being specific to the South African context, such as the impact of apartheid on

participants' perceived capacity to consent to trials, and its impact on stakeholders' perceptions of informed consent in HIV vaccine trials.

#### 4.3. The variables impacting on the positions taken by stakeholders:

The third aim of this study was to explore what the factors might be which influence the stakeholders' perceptions of these challenges. A number of possible factors which appeared to underlie the positions stakeholders appeared to take will be discussed next.

##### 4.3.1. *The role of stakeholders*

As mentioned, part of the aims of this study was to determine what variables impact on the position stakeholders take on the issue of informed consent. In addition to how stakeholders use vulnerability discourse (discussed earlier), other variables appeared to be related to the role of different stakeholders in trials, the philosophical position underpinning their ethical viewpoints, and respondents' views about the universality or relativity of ethical issues in research.

It would appear that the roles stakeholders have within the trials impacts on the position they take with regards to Informed consent. From the data it became apparent that Community Advisory Board members see themselves as mediators between the researchers and the community. This was consistent with Moodley's (2002) views on the importance of using advisors from the communities to represent communities in research. Whilst they acknowledged their educative role there appeared to be an underlying paternalistic sense of responsibility felt by Community Advisory Board representatives to make certain decisions on behalf of the community. With their main concerns centered on issues of community and participant exploitation by researchers they may fall into the trap of underestimating the true capacity of community members to make their own individual decisions to consent to trials. In fact,

some respondents questioned the validity of using Community Advisory Boards as mediators of community decisions to participate in research, showing scepticism about their competence and representativeness of the community. Their concerns reflect the concerns raised by IJsselmuiden and Faden (1992) who question the identification of community representatives genuinely trusted by communities. Some investigation needs to be done into Community Advisory Board members' levels of competence, to what degree they do represent the community's views regarding HIV vaccine trials in South Africa and what their actual responsibilities are.

The Civil Society representatives appeared to perceive their responsibility as operating on a broader macro level. They see themselves more in terms of being protectors of society so they were much more concerned about the vulnerable groups in society and their capacity to consent. Their perceived role as protectors of society impacted on the way they view informed consent in that they were more likely to advocate a need for structure and continuous monitoring of the process of informed consent. Interestingly the representatives of this group were more familiar with existing ethical guidelines than most other groups were.

With the Site Staff having direct contact with participants at trial sites they face the practical task of ensuring that the informed consent process is carried out competently and ethically, according to protocol. Their role pertains to implementation which requires a good foundational knowledge of the ethical guidelines that need to be adhered to as well as an understanding of the issues identified in the literature around cultural sensitivity (Bayer, 2000; Lindegger et al., 2006; Moodley, 2002). When site staff are faced with the complexities of applying standardised informed consent protocols to all participants who vary considerably in their notions of personhood (IJsselmuiden & Faden, 1992; Mkhize, 2006) cultural understanding and cultural norms, it may explain some of their ambivalence around informed consent.

The trial staffs' abilities to identify and resolve problems encountered at trial sites better than other stakeholders was acknowledged. The perception of most stakeholders was that site staff knows the community, the language and the culture of participants and is therefore better able to manage the procedural expectations of informed consent. Whether this perception is correct is an area needing further investigation. What is evident is that if researchers are to gain perspective about the practical complexities of implementing complex informed consent procedures, so that ongoing improvement can occur continued communication between stakeholder groups is essential.

The monitoring of ethical standards related to informed consent was perceived to be the responsibility of Government. This monitoring process was perceived as the main role of Research Ethics Committees. There were concerns that the over regulation of informed consent, however, could hamper trials if context related problems in informed consent procedures are not allowed to be amended to suit the context. There appeared to be a lack of consensus between stakeholder groups about whether informed consent should be regulated.

Although the media's role was viewed as mainly educative, the potential of the media to serve an additional regulatory role that challenges stakeholders to run trials in accordance with protocol was recognised. In relation to informed consent the media's policing role was advocated for the purpose of giving participants a forum in which to complain if they felt their consent was not legitimate. The ability and or preferences of South African participants to make use of such a forum is a topic for investigation.

The main role of the trial sponsors is to provide the resources needed to conduct the trials. Not surprisingly they expressed concern about the slow pace of trials. A fear was that if trial sponsors take what they perceive to be trivial matters about informed consent to the ethics committee involved this would delay trials. Pushing trials to go ahead at a pace that does not fully address all the potential ethical issues pertaining to informed consent,

however, may not be within the best interests of participants, stakeholders or the trial sponsors. Infringements of legal ethical guidelines may stop trials permanently and in effect, not only waste valuable resources, but seriously delay finding a solution to HIV/AIDS in the form of an HIV vaccine. How significant the procedural concerns stakeholders have regarding informed consent need to be to warrant the research ethics committee's involvement needs consideration.

#### 4.3.2. The philosophical ethical positions adopted:

Stakeholders' ethical viewpoints on informed consent revealed different philosophical positions, which may affect the way they view the implementation of informed consent. Both the government and the Community Advisory Board representatives appeared to take a more paternalistic ethical approach that aims to protect communities. The impact of functioning from a paternalistic ethical framework on the informed consent process, however, has the potential to violate the substantive requirement of autonomous agency by participants if decisions are made for competent individuals to consent or dissent to trials on their behalf.

Civil society representatives appeared to advocate that all HIV vaccine trials in South Africa follow strict protocols when obtaining consent from participants. This was mainly to protect individuals from being used as a means to researcher's ends. This deontological ethical stance (Moodley, 2006) may explain why stakeholders from the civil society group generally expect universal ethical norms and standards to be applied to all participants engaging in the informed consent process, together with strict monitoring of this process, as a way of guaranteeing protection of all participants regardless of their inherent differences.

Site staff representatives appeared to take a descriptive relativist ethical stance to the process of informed consent in that there was recognition that "different people have different moral beliefs which affects how they behave and define

problems” (Pack-Brown & Williams, 2003, p. 36). This philosophical ethical framework may be influenced by the role site staff have in implementing the informed consent process. Taking into consideration the different cultural and moral perspectives participants may have (Pack-Brown & Williams, 2003) site staff may be particularly concerned about the relational impact individualized consent practices may have on family structures and the wider collective community (Mkhize, 2006) which in turn may impact on, and be impacted by, the procedural demands made by the informed consent process.

Some Media representatives appeared to be concerned about the consequences of trial participation and the consequences of the way journalists potentially violate participants’ confidentiality in their representation of HIV vaccine trials in the media. Their concern related to the possibility that participants’ consent was not truly informed if they were not made aware of these possible violations to their confidentiality and the consequences that may result. These media representative’s concerns appear to reflect a deontological ethical framework that is concerned about participants’ individual rights. Their deontological ethical stance may explain the tension they experience when reporting facts about HIV vaccine trials since it conflicts with the utilitarian outlook of media houses who want sensationalised stories about trials to sell newspapers. This tension felt by reporters highlights the tension between deontological and utilitarian approaches to ethics mentioned in the literature (Alexander & Moore, 2007; Hooker, 2007).

The concern about the slow pace of trials by trial sponsor representatives was a good demonstration of utilitarian concern as it highlights the tension between proceeding cautiously, according to the rules (Deontology), which holds back trials, and completing trials as quickly as possible to arrive at a solution, which potentially could save millions of lives (Utilitarianism). A utilitarian ethical outlook by trial sponsors may create pressure on other stakeholders to proceed with trials without full consideration of the ethical and practical dilemmas inherent in informed consent in trials of this magnitude. Stakeholders may find it difficult to negotiate the tension between the

deontological need to protect participants' rights to fully informed consent and the utilitarian need to proceed with trials as quickly as possible.

The Research Ethics Committee representatives indicated a number of different ethical positions that may inform their views on informed consent in HIV vaccine trials. A possible virtue ethical understanding of informed consent was evident in the expectations some Research Ethics Committee representatives had that stakeholders should be honest and virtuous. Others showed a possible consequential ethical concern about whether the costs of participation in trials outweigh the benefits for participants and whether they understand the personal implications of these costs. In addition, others demonstrated an intentionalist ethical framework concerning the motivations behind why participants consent to trials as well as the motivations of principal investigators who run HIV vaccine trials. The variety of philosophical and ethical positions held by Research Ethics Committee members may be reflective of their primary task to discern whether there are any ethical transgressions in the research protocols they evaluate that may violate the informed consent process.

In summary, both the government and the Community Advisory Board representatives appeared to operate from a concerned paternalistic ethical framework. The Civil Society representatives appeared to demonstrate a deontological ethical position. Media representatives appeared to be concerned about the consequences of trial participation as a result of the way journalists represent HIV vaccine trials in the media. Their consequentialist viewpoint reflects a deontological concern about participant's rights and highlighted the tension journalists feel when having to negotiate the utilitarian ethical stance used by some media houses to justify selling newspapers. Trial sponsor representatives, on the other hand, appeared to demonstrate a utilitarian concern in trying to move HIV vaccine trials along at a much faster pace. The Research Ethics Committee representatives indicated a range of different ethical positions that included consequentialism and intentionalism and a virtue ethical understanding towards informed consent, whilst Site staff

representatives appeared to take a descriptive relativist ethical stance that gives cognisance to the different views held by participants.

The implication of stakeholders' viewing informed consent from these different philosophical and ethical theoretical perspectives is that tension may exist between stakeholders when making decisions. The tension between different ethical theoretical perspectives was implicitly evident in some responses made by the respondents. The tension between deontological ethics and utilitarianism, for example, appeared to cause conflict between stakeholders when making decisions as to whether to protect individual rights or the public good. On a procedural level, where, for example, an absolutist and/ or deontologist may expect rigid adherence to legal protocols for informed consent, descriptive and normative relativists and utilitarians may insist on more flexible procedures that are more accommodating to the cultural beliefs and norms presented by participants and perceived overall societal benefits. This tension may also cause ambivalence within individuals who may be uncertain about their ethical perspectives. Furthermore when different members within a Research Ethics Committee hold different views about the informed consent process it may hamper the speed at which research protocols are agreed upon which in turn may cause some of the delays that concern and frustrate other stakeholders.

#### 4.3.3. The Universality versus relativity of informed consent:

Respondents views about the universality or relativity of ethical issues may impact on the position Stakeholders take with regards to informed consent. When considering the issue of universality versus relativity of ethical theory and practice in research Pack-Brown and Williams (2003) suggest that it is always pertinent to ask how Western/monocultural and multicultural perspectives are similar and different. When reviewing these perspectives in terms of the informed consent process in HIV vaccine trials, a Western/monoculture approach, based on mainstream American values and beliefs, is likely to place value on individualism and autonomous agency as

well as the legal protection of individual participants and researchers. From a multicultural approach, there is likely to be more focus on the importance of “subjective relationships that focus more on people than on progress, more emphasis on sharing and cooperation for the good of all those involved and more emphasis on community needs than on individual needs, all of which contribute to the underlying social and spiritual importance of harmony and balance” (ibid, p. 194). From these two perspectives, the monocultural approach is likely to insist on first person consent rather than proxy or community based consent advocated by a multicultural approach.

Using Pack-Brown and Williams’ (2003) dichotomised approach, stakeholders who follow a monocultural perspective to ethical research are likely to maintain that ethical principles like informed consent are universal and therefore the same protocols should be practiced where ever the research is taking place. Those ascribing to a multicultural approach, on the other hand, are likely to argue that the informed consent process should be adapted to the unique context relevant to the population being researched.

Furthermore the perceived universality or relativity of ethical challenges in HIV vaccine trials by the respondents is likely to be informed by the philosophical and ethical theoretical positions they hold. Those with a deontological perspective, for example, are likely to view informed consent as universally applicable, since it hinges on the principle of autonomy, whereas those ascribing to a utilitarian ethic are likely to view informed consent practices as relative to whether it benefits the particular context.

All the respondents of this study were asked whether they thought the ethical issues they identified were universal or unique to South Africa. The responses given by most of the respondents within all the groups were not consistent with Pack-Brown and Williams (2003) expectations that researchers would see monocultural versus multicultural perspectives in such a dichotomous way. What became evident was the tendency for respondents to accommodate both perspectives in one viewpoint. This broad approach that attempts to

accommodate both a universal and relativist conceptualization to informed consent is more consistent with what Benetar, (2004) refers to as taking a reasoned contextual universal approach to informed consent.

Taking a reasoned contextual universal approach to informed consent may be based in part on an awareness stakeholders may have of the different notions of personhood that exist in the multicultural society present in South Africa. Using such a broad approach is likely to inform consent that takes into account the different arguments regarding, for example, notions of personhood described in the literature (Lindegger, 2002; Hart & Lindegger, 2002; Mkhize, 2006; Ijsselmuiden & Faden, 1992; Christakis, 1988; Barry, 1982; Taylor, 1979; Willett, Kilama & Kihamia, 1979; Shapiro & Stein, 2004; Gasa, 1999) as well as the demand that the Medical Research Council (2003) and UNAIDS (2000) guidelines have placed on researchers to implement informed consent procedures in a manner that respects cultural norms.

# CHAPTER FIVE

## 5.1. Limitations of the study:

The main limitation of this study was the small sample size. Some previous studies exploring perceptions of ethical concerns in HIV vaccine trials have used larger samples and closed ended questionnaires. However, in this study it was explicitly decided that it would be preferable to conduct an indepth study with a small sample of stakeholders. Further, the unavailability of some members making up stakeholder groups, for example only two government and three research ethics committee and only one trial sponsor representative, makes this an even more limited sample. Clearly there can be no widespread generalization of the findings of this study. However, the findings do raise a number of critical issues as far as the implementation of informed consent in HIV vaccine trials is concerned.

There were also some practical limitations of the study. Although, as Kvale (1996) suggests, the interviewing process offers the researcher an opportunity to begin the emersion process whilst collecting the data, words and phrases inaudible on the taping were difficult to decipher. Thus some meaning may have been lost in the analysis.

## 5.2. Conclusion:

This study formed part of a larger study done by the HIV /AIDS Vaccine Ethics Group which aimed to provide information to aid the South African Aids Vaccine Initiative's objective of investigating the ethics of HIV vaccine trials. The three main aims of this study were to explore stakeholders perceptions of ethical challenges around informed consent in HIV vaccine

trials, and to explore what the factors might be that influence the stakeholders perceptions of these challenges.

According to debates raised in the literature on informed consent in medical research, a number of contentious issues were expected to be raised by stakeholders partaking in HIV vaccine trials. These issues related to substantive elements such as the autonomous capacity of participants to give first person consent, challenges around child and adolescent consent, and the voluntariness of participants' consent, and procedural elements such as participant understanding, communication, information disclosure, the regulation of informed consent, and the impact of context on the informed consent process. Would South African stakeholders' anticipate additional challenges to informed consent in HIV vaccine trials in the South African context? In light of Lindegger et al's. (2006) argument that the populations needed for Phase III trials are populations at high risk of HIV infection and are also commonly characterised by high levels of poverty, relatively low levels of formal education, and poor access to resources, would South African stakeholders' concerns differ from those already raised in the West? Since many of these debates remain hypothetical, it was considered important to ask South African stakeholders involved in HIV vaccine trials what their concerns were.

On examination of the findings, the main concerns around informed consent expressed by the stakeholders were consistent with issues already identified and debated in the literature. When considering the capacity of participants in the South African context, stakeholders debated whether vulnerable participants could be considered fully autonomous and thus able to give first person consent or whether proxy or community consent should be sort; whether the capacity of South African children, perceived as more resilient and mature because of the difficulties they are exposed to, should be evaluated using the same criteria as those used on western children; and whether vulnerable participants would be even more vulnerable to the influence of inducements for participation because of their poor socio economic status. On

a procedural level, stakeholders were concerned about the challenges they faced when trying to implement informed consent according to what was required by ethical guidelines. Stakeholders had the same concerns identified in the literature pertaining to information disclosure and the education of participants, ameliorating language barriers, disclosing information in a way that participants could understand, assessing participant understanding, facilitating community involvement from before the trials starts as a means of empowering the community in preparation for HIV vaccine trials, reducing possible stigmatization of participants, enhancing the relationship between researchers and participants through communication and dealing with issues related to cultural norms and practices that may clash with legal requirements.

Stakeholders raised some additional issues not reflected in the literature. The perception was that socio-economic issues in Africa are qualitatively different from those in the West, rendering African participants more vulnerable and therefore in need of more protection during the informed consent process. Of particular concern was how power dynamics will affect the informed consent process particularly with regards to communication between the principal investigators and the participants. The perceived power of the community was also interesting. In some instances, not only was the community perceived as more powerful than the law in terms of who should consent for children, but the community was seen to have the power to stigmatize participants known to be involved in trials. And yet at the same time stakeholders were concerned about the voluntariness of participants consent. The emphasis put onto community by stakeholders may be a reflection of the communitarian worldview of many traditional African people. The level of suspicion raised about the motives of researchers was not surprising considering South Africa's history of apartheid and the tendency of developed countries to take advantage of research populations in developing countries. What was surprising however, was the extent of stakeholders' levels of suspicion. Stakeholders were concerned that parents would exploit their own children, putting their needs in front of their children's needs, by forcing them to participate in HIV vaccine trials for financial gain.

Identifying the variables that may impact on the position stakeholders take on the issue of informed consent was also part of the aims of this study. Factors such as the role the respondents play within the trials, the philosophical position underpinning their ethical viewpoints, the way in which respondents use the vulnerability discourse, and their views about the universality or relativity of ethical issues was speculated to impact on the position they take with regards to informed consent. The impact of these variables on the implementation and theory of informed consent together with opportunities for additional research in the field was considered and these will be addressed next.

### 5.3. Recommendations:

The perceptions stakeholders in this study expressed about the vulnerability of South Africans is potentially problematic for recruitment of participants into HIV vaccine trials and the informed consent process. If potential participants are perceived of as vulnerable and are incorrectly deemed to be non-autonomous agents, they may either be excluded from participation unnecessarily or have their autonomy usurped by proxy consent. Assessment procedures assessing participants' real capacity to consent, to prevent unfair discriminatory practices that override personal autonomy or exclude people from participation in HIV vaccine trials, need to be researched and formulated. Of particular importance is the development of suitable testing instruments to ascertain the readiness of South African adolescents to independently consent to HIV vaccine trials.

Research into the effects of apartheid on the decision making capacity of black participants to take part in HIV vaccine trials is lacking. Investigation into the actual perceptions of mine workers on their decision making capacity, and their preferred decision making practices, may begin to answer the

question of the extent to which apartheid policies have impacted on black South African research subjects decision making.

As highlighted by Pace and Emanuel (2005) limited clarity has been provided on what actually constitutes voluntary consent to research and what types of ethical transgressions are likely to undermine voluntariness. Additional research in the context of HIV vaccine trials in South Africa regarding what constitutes undue-inducements, for example, and how various types of research rewards influence low socio economic participants decisions to participate could be of assistance.

The potential value of having representatives of communities to assist the informed consent process in HIV vaccine trials cannot be overstated. However, considering the concerns some respondents had regarding Community Advisory Board member's representativeness of their community, their actual knowledge base of HIV vaccine trials, and their ability to adequately disseminate such information to potential participants, investigation into these factors as well as defining what their actual responsibilities are needs to be done to improve and capitalize on this valuable resource.

Similarly, stakeholders believed that the staff working at different HIV vaccine trial sites know the community, the language and the culture of the research participants and are therefore better able to manage the procedural expectations of informed consent. Whether this perception is correct is an area needing further investigation.

Negotiating the demands imposed by the interface between multi-cultural beliefs and practices and the often westernised legal requirements set out in guidelines, is concerning to the stakeholders of this study. More research that clarifies these procedural concerns for South African stakeholders needs to be done.

The slow pace of HIV vaccine trials was a concern to stakeholders for various reasons. A fear expressed was that if trial sponsors take what they perceive to be trivial matters about informed consent to the ethics committee involved it would delay trials even further. How significant the procedural concerns related to informed consent, in the South African context, need to be to warrant the research ethics committee's involvement is an area that needs clarification.

The adequacy of training given to Stakeholders to provide the information necessary for informed consent was questioned. Exactly how knowledgeable stakeholders need to be to produce adequately informed participants is unclear and needs further investigation. In addition, what type and amount of information to include and who should provide this training needs to be clarified.

In relation to information disclosure investigations into the impact of complicated and lengthy informed consent forms on participants in the South African context may be of value when considering how much and what type of information to include on informed consent forms.

Using the media as an additional regulatory body that provides participants with a forum in which to complain if they feel their consent to participate in HIV vaccine trials has been violated was suggested. The ability and or preferences of South African participants to make use of such a forum, however, is a topic for investigation.

Although the Medical Research Council requires that international human rights laws/norms and standards should be considered, some respondents argued that there is no elaboration of what these are. Respondents indicated that international norms and standards must be expanded to the South African situation. Research that addresses what these norms and standards are is likely to give stakeholders more clarification on how to apply them. Benatar, (2004) suggests researchers take a reasoned contextual universal approach when

considering when and how it is morally appropriate to take local contexts into consideration in applying universal ethical principles. Researchers should consider whether local cultural values inflict harms that could and should be avoided (or are harmless) and whether (or not) they infringe on human rights or abrogate respect for human dignity.

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