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INFORMED CONSENT IN RESEARCH IN DEVELOPING COUNTRIES: IS THERE SOME UNFINISHED BUSINESS?

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A report submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree MScMed Bioethics and Health Law

Johannesburg November 2009

DECLARATION

I, Norma Mabel Tsotsi declare that this report is my work and has not been submitted or incorporated in another dissertation or thesis for any other degree.

N. M. Tsotsi
4th November 2009

DEDICATION

To the women in my life

Mary Nongauza, my aunt for your advice during this project

Nongauza ancestors: Nontsikelelo my mother; Ursula, my aunt; Jemima-grand mother

Thank you all for being my guiding light and

To my husband – Zola and my children Mlungisi and Thandiwe Tsotsi

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PREFACE

The application of informed consent in research in developing countries continues to be a topical and complex issue. The debate concerning informed consent has become even more relevant in light of the groundswell of international collaborative research that is conducted in developing countries. The discussion centres on the uncertainties of the application of informed consent in developing countries based on the normative criteria set out in international codes and regulations. Although the ethical and legal basis of obtaining valid informed consent is incontestable, contextual differences between developed and developing countries is a key problem. For example, it is debated if the tenets of 'Western' research ethics, mainly in the application of a written informed consent model can truly be applied in the African context.

The question is whether the participants of research when conducted in developing countries actually are "informed" in the consent process. There are perceptions that the protective instruments that guide researchers on how to obtain informed consent from research participants are not robust and sensitive enough for developing countries needs. In literature, some have questioned the relevance of its purist application in the context of developing countries as 'overly paternalistic'. Others have argued from the view point that the Eurocentric approach recommended in obtaining informed consent in developing countries has the potential to undermine cultural norms and traditions. In the latter argument, concerns are raised about the principle of respect for persons / 'autonomy' and its applicability in so-called communitarian

societies. To overcome some unique hurdles, there are voices that call for tailor-made processes for obtaining informed consent to suit the prevailing context, suggesting therefore that there should be some variance in its application. The importance of the issue of informed consent becomes critical as much international collaborative research takes place in Africa where health services are often inadequate and research is perceived by participants as a means of ameliorating some of their suffering.

Given the philosophical and the 'universal' ethical foundations at the heart of the international regulations and codes on the issue of informed consent, there is a need to further explore the foundation of these perceptions as they raise various ethical issues which need to be discussed.

The question concerned in this research report is "is there unfinished business not addressed in the process of obtaining informed consent in developing countries?"

In order to answer this question, it is necessary to look at some of the requisites for the application of informed consent principles. I will examine whether the content of the commonly cited ethical codes and regulations (originally initiated in developed countries) are sufficiently broad enough to explain the aims of obtaining informed consent, the steps to be taken in obtaining informed consent and the structures necessary for its facilitation. In addition I will examine whether the *intent* of the codes and regulations take cognizance of socio-cultural variations. In other words, is the environment sufficiently conducive to apply the concept and are the guidelines flexible enough to deal with "unusual

circumstances". In consideration of the latter, I consider the question of the adequacy of structures to ensure the essence of respect for persons is not lost in dealing with "unusual circumstances". I contend that if the answer is in the affirmative it is only then can it be said that the principles of informed consent are being adequately addressed and meet the moral, ethical, and legal obligations of research activities.

CHAPTER DIVISIONS

Chapter One gives an overview of informed consent as a concept and outlines its importance in research. The literature review in this chapter is meant to describe the diverse views pertaining to informed consent. The end of the chapter describes the aims and objectives of this paper and briefly justifies why the topic merits further discussion.

Chapter Two explains the Ethical and Legal Frameworks for analysis of the concept of informed consent and explores the extent the various declarations, codes, guidelines and some regulations pertinent to the obtaining of informed consent in research

Chapter Three focuses on South Africa and will give a description of Legal and Ethical documents supporting informed consent for good Research Activities.

Chapter Four provides some ethical, legal and cultural commentary on Informed Consent in Research.

Chapter Five highlights the “unfinished business” in informed consent and Recommendations for its further development.

The conclusion will suggest how we might try to overcome some of the obstacles and enhance the obtaining of informed consent in an ethical manner in research but at the same time avoid dogmatism in its application.

CHAPTER 1: The Importance of Informed Consent In Research

This chapter will analyse the concept of informed consent and its importance in research. The literature review highlights the contentious areas of informed consent in research. The end of the chapter will describe the aims and objectives of this paper and briefly justify why the topic merits further discussion.

INTRODUCTION

Research is important and is vital for the advancement of medicine. The ethical basis of medical research is to discover interventions which have the actual or potential ability to save lives, and improve peoples' well being. These interventions can be at prophylactic, diagnostic, or therapeutic levels. Research may be conducted on patient volunteers or healthy participants. Patients can be based within or outside hospital settings. Crucial to the endeavour of health research is the realisation that although volunteers could get benefits in various ways, in general, the majority may not qualitatively and quantitatively benefit from research results. Although, sound scientific research methods and working to maintain the best interest of the research participants' welfare are crucial, they are not sufficient to render the research ethical if respect for persons / autonomy and informed consent are ignored. The two critical reasons why informed consent (IC) should be obtained from research participants prior to and during the research process is to ensure that participants' rights and welfare are protected as well as and to ensure that they can make autonomous decisions about whether or not to participate in research.

Informed consent (IC) has been a misnomer in the research community for a long time. It appears that in many instances participation was acquired through overt paternalism, deception and coercion by researchers. The extent of transgressions in research in relatively modern times is best demonstrated by Nazi doctors during the Holocaust (Beauchamp & Childress, 1989:142-143). The *Nuremberg Code* (1947) was the first document, which was participant – centred. It did so by clearly articulating the supremacy of research participants and the importance of obtaining consent from them. At the same time it clearly spelled out the elements needed to fulfil the conditions of obtaining consent. In unequivocal terms it also addressed the moral and legal responsibilities that researchers have towards to research participants. The Nuremberg Code to an extent, therefore, cemented the bridge between the ethical basis of doing research and the legal requirements. The legal tone of the Code reflects the role played by judges in crafting it.

Following the War Crimes Tribunals after World War II, the idea of obtaining "consent" from subjects / participants in medical research was first conceived. Later, when research activities became more common, consent was reconceptualised as "informed consent". The goal was to seek solutions for the protection of individuals from unethical researchers through application of the ethical mechanisms involved in ensuring 'consent' was truly 'informed'.

It is not surprising therefore that the protection of individual rights and welfare are the principal reason why the concept of informed consent in health research in developed countries received considerable attention. Because their governmental systems reflected the idea of individual autonomy and rights,

particularly in the context of the USA, the literature from at least the 1960's shows much discussion concerning the meaning, scope, role and application of informed consent (ibid).

The four basic principles of biomedical ethics, respect for persons / autonomy, non-maleficence, beneficence and justice extend to research ethics. In the history of research ethics, philosophers, lawyers, social scientists and belatedly the research fraternity argued for the promulgation of the principle of autonomy and respect for persons as a cornerstone of informed consent as opposed to exclusively relying on the principle of beneficence (Wear, 1993:111-112).The principle of beneficence was first used as the means by which some assurance was given that the safety of participants in research was monitored (ibid). The principle of beneficence (to do good - actively promote the good of others) if inappropriately applied can result in paternalism and even worse coercion. Because history has revealed that great breaches of research ethics in the guise of beneficence occurred in developed countries (e.g. Tuskegee Syphilis study, Willowbrook) some may argue this gave impetus for further investigation of the issue of IC. This did occur in developed countries and later spread globally where other voices were raised concerning the applicability of IC in different cultural contexts.

An Overview of Issues Pertaining to Informed Consent in Developed and Developing Countries

The application of the principles grounding informed consent in both developed and developing countries is not straight forward, in fact, it is complex. In part, this is due to the interpretation of informed consent from the legal and ethical perspectives whose intent and justification differs resulting in a complication of the 'universality' of its application. The legal perspective is principally driven by rules for the purpose of seeking legal redress. Whereas the ethical perspective looks at the ways in which a mutually beneficial moral relationship between the researcher and the-would-be-participant can be realized. In addition, there is a difference between legal and ethical justifications. The former is to prove negligence and the latter to encourage collaboration decision making (Fadel & Beauchamp, 1986). Beyond these considerations Parker asserts that IC plays a preventive role as it gives a warning of potential areas of ethical concern and helps with strategies aimed at mitigating their occurrences (Parker, 1995:520-523).

It is important to note that the IC process does not occur in isolation but is influenced by the context in which it applied. The context is composed of any factors such as the preponderance of vulnerable groups, educational levels, un/employment levels and types, poverty, and poor if any healthcare structures. Moreover, research is often conducted in countries where gender inequality is a norm, and where communal consent (at least supposedly) trumps individual consent. The context is further compounded by institutional constraints such as,

poor or inadequate health care management as well as insufficient resources (financial and human). Moreover, the legacy of colonialism is still pervasive, and many still accept authority without questions (Dhai, 2005:595-597). Conditions such as these could have a direct impact on obtaining informed consent from participants.

Although individual informed consent is a universal requirement in research, studies have shown that this is not as universally applied as required in both the developed and developing countries. Infringements have occurred at various levels of obtaining IC ranging from: involuntary participation in research, sketchy understanding of intent of the research by the participants, poor imparting of risks and to an extent exaggeration of benefits that may occur, and finally, insufficient information imparted to the participants to make decisions thus negating rational informed choices.

Literature review – background

'Consent' in the Oxford dictionary means *inter alia* "approval" agreement, "seal of approval". This definition does not clarify whether there is a condition attached to approval e.g. if disclosure of all information is necessary. But informed consent is normative in that "any consent is informed if it satisfies the operative rules governing the practice" (Fadel & Beauchamp, 1986:30-33) Informed consent assumes that the consent is given provided that adequate and relevant information is given to the participant prior to the intervention. The information should include risks that might occur. Informed consent requires that

a person is competent or has the capacity to give consent. Concerning capacity, Dworkin[a] (1988:104-108) says … *capacity refers to the ability to reflect one's motivational structure*.

So the idea of capacity, so defined, calls for the potential participant to have the ability to think about why he or she is or is not interested in research participation. The reliance on the researcher to disclosure relevant information which will feed into the potential participant's final decision then becomes a vital ethical directive. Moreover, a demonstrable understanding of the information by the participant is necessary to the assurance of IC. According to Emanuel (2005),

> … *understanding is not what the researcher thinks is important, but what is important, is for participants to decide whether a study fits with their values and beliefs and to decide whether the risks are worthwhile …*

He (ibid) also identified studies that show that the more educated a participant is, the more they are likely to have higher scores concerning understanding information. Although this is not surprising, it has bearing on the fact that poor people in developing countries may lack basic education and therefore may score low in understanding what has been said to them – even if presented in their home languages. This concern was echoed in a study from Ghana that revealed that participants were deficient in understanding some aspects of the

research and this was revealed as attributable to lack of education (Hill et al , 2008: 48-53).

Four broad themes which may be used to assess a participant's competence are outlined in an article by Levine (2003:197-201). He suggests:

- That the participant has the ability to make a reasonable choice when given alternatives to choose from which to choose.

- That the participant understands the basic tenets of the information about the research.

- That the participant has the capacity to make a rational choice and;

- That the participant understands the overall implications of being involved a research project.

As shown above, the four themes all relate to respecting a participant's rational choice, or their autonomy. Linked to the IC consent process is respect for autonomy. It is important to note that respect for autonomy is not just the capacity to reflect on ones action but also the capacity to critically reflect about the course of action to take, and the capacity to change one's mind "in the light of higher order preferences" as Dworkin (1989[b]; 108) puts it. By being given a choice of actions, and assuring that a potential participant understands the aims of the research, e.g. what is and is not required in participation, the burdens and

the benefits in the context of researcher fidelity and then allowing a decision without prejudice equals validation of one's autonomy (Levine, 1991:207-236).

The participation or not in research studies should be left to the participant's discretion. By implication this means that the participant's choice is voluntary. This is in accordance with respect for their autonomy. The qualifier for voluntariness is that voluntary consent should be void of duress or undue inducement (Darr, 1991:169-170).

The reality is that "voluntariness can be compromised" (Kass et al, 2005;1-5). Some of the factors which may compromise 'voluntariness' are poverty , limited access to medical care , and patterns of decision making related to gender , socio economic conditions, or culture (Benatar, 2002:1131-1141) One of the difficulties in measuring consent and choice is dependent on the type of theoretical underpinnings used to measure them (Jepson, at al, 2005:192-196).

Information, its boundaries and expression, is a difficult problem in the research context. One major hurdle is that the way information is imparted is not value free (Edwards & Elwyn, 2001:9-13). In other words, the values of researchers (e.g. if completion of their study is over-prioritized over actual participant burdens) may influence the type of information provided to the potential participant. Thus the principle of autonomy may be distorted and the type of choices made by potential participants may be skewed unless equipoise is maintained.

While autonomy is the fundamental principle in informed consent, it is closely related to other principles. It is in the participants best interest (the principle of beneficence-to do good; actively pursue the good) of participants to have adequate and pertinent information in order to make their own informed decisions. Respecting participants' capacity to make their own autonomous, informed decisions, has a bearing on respecting human dignity (principle of non-maleficence-to do no harm; to not knowingly inflict harm).

The principle of justice (fairness; equity) requires that one must be treated with in accordance with what is just and fair. It follows that when one participates in research it is consented to on the basis of informed choice and so in the spirit of justice, the participant is being treated justly and fairly.

The difficulties of obtaining informed consent from research participants are well recognized in situations where there are educational, linguistic and cultural differences between the researchers and the participants. A study from Kenya highlighted the challenges confronted by researchers in obtaining truly informed consent as a result of the participants' lack of understanding of the research aims (Molyneux, at al, 2004:2547-2559). This also was of concern in a Malaria study conducted in Uganda (Pace,et al 2005). In this particular research, parents did not fully understand that their children were at risk because of the children would be randomized in the study. Although these represent real hurdles, social and cultural barriers should not be used as a reason to negate the IC process (Newton & Appiah-Poku, 2007:149-156). Rather, such examples

show that there is a greater need to investigate ways in which the IC process can be realized while being culturally and socially aware of inherent difficulties.

Particularly in developing countries, one of the roles of informed consent is to prevent the notion of the therapeutic misconception on the part of participants. "Therapeutic misconception is a major barrier to genuine informed consent" (Lidz & Applebaum, 2002:55-63). Participants who take part in clinical research sometimes mistake clinical research for treatment. It is a fact of research in countries where healthcare resources are scarce that sometimes self interest motivates people to participate in research with the hope of getting some benefit even if the research will not benefit them at all (Gotay, 1991:569-577). Desperate for some type of care, the danger of therapeutic misconception is common and amplified. This naturally impinges on the informed consent process as the patient's perception, or hope of assistance serves as a psychological barrier to a true understanding of IC. This barrier to real comprehension may be taken advantage of by unethical researchers and is a vital issue to consider in research ethics (Schaeffer, Krantz, & Wichman, 1996:261-268).

Justification for this Inquiry

There is a need to constantly review the concept of informed consent and the process of obtaining a valid informed consent in the light of the rapid proliferation of collaborative research in developing regions, especially Africa.

The aim of this paper is to explore whether there is a disconnect between existing guidelines, ethics structures and currently held views and perceptions of obtaining informed consent in developing countries resulting in the fundamental principles underlying it being ignored.

Objectives

- To examine the concept of informed consent and its relation to autonomy.
- To review the streams of thinking that dominate informed consent in literature as it pertains to research.
- To examine the present International and National guidelines on informed consent.
- To propose that informed consent is a vital research process which needs to be continuingly re-evaluated; that there will always be 'unfinished business' e.g. in the light of new information, cultural changes and research developments.
- To suggest ways in which the research process may be fortified to ensure the protection of human participants in research.

Research Methodology

Sources included books, articles and documents pertaining to issues on informed consent in developing countries which were read then reflected upon. The variables for analyses were 1) International and national research ethics

declarations, codes and regulations. 2) Ethical / philosophical theories that speak to informed consent. 3) Other general articles pertaining to informed consent. Print media were the source of information including academic search engines in the gathering of research data. Arguments in support or refuting the claims that the informed consent process is not applicable in developing countries were considered.

CHAPTER 2*:* Ethical and Legal Frameworks for the Analysis of Informed Consent

In this chapter, I will explain the Ethical and Legal Frameworks for analysis of the concept of informed consent and explore the extent the various declarations, codes, guidelines and some regulations pertinent to the obtaining of informed consent in research

Ethical Framework

From a deontological perspective, a researcher has a duty to conduct research for the good of individuals. However, within that duty the line has to be drawn between treating participants as autonomous agents and the stringent requirements of science and research. In a Kantian view, one of the duties we have is to treat all people as ends in themselves, and never as a means to an end. It is morally justified and a moral duty to sanction ethical research for the benefit of peoples' well-being but not at the expense of individual informed consent as the "means does not justify the end".

The Utilitarian theory looks at research in a different perspective. This is because it is a view based on Consequentialism. In this perspective, a right action is one that brings about the best consequences for all concerned. Although doing research is morally justifiable on the assumption of maximising utility (happiness / good / pleasure) or benefits for the majority of a population, the individual participants' value might be considered less than the attainment of good research outcomes which would benefit the aggregate. However, there

are many different ways of interpreting utilitarianism and because it is a *moral* theory, researchers are bound to act within its ethical framework.

The foundational platform for ethical research is strongly influenced by principle-based ethics (principlism) which was developed by Beauchamp and Childress. They based their work on a synthesis of deontology, Utilitarianism and the works of W. D. Ross. From these moral theories, they developed key principles which they consider ground the basis of medical practice. The principles are autonomy, beneficence, non-maleficence and justice. Although each of the principles are *prima facie* and can be overridden by the another depending on the most compelling situation at hand, this way of reasoning became the most common ethical system used by healthcare professionals. In the healthcare setting, respect for persons / autonomy, maximizing benefits and minimizing harm (beneficence and non-maleficence), and fairness (justice) are core concepts of being a professional and in the concept of professionalism.

Application of Principlism in Research

There are four basic principles of biomedical ethics which serve to ground the ethical duties of researchers. These principles are Autonomy / Respect for persons, Beneficence, Non-maleficence and Justice.

Autonomy

As a concept, autonomy or autonomous, can be traced back to the ancient Greek governmental system which assigned 'autonomy' (*auto* – self and *nomous* – governing) to the states within its boundaries. Many philosophers contributed to the idea that humans also should be treated autonomously e.g. capable of and should be given the opportunity to make their own individual choices. One of the most influential was Immanuel Kant who clearly linked the idea of autonomy with that of respect for persons. The obligation to respect the inherent dignity and worth of every human is present in all liberal, moral and political activities which emphasise issues such as individual freedoms and the right to make choices. Any theoretical analysis of informed consent is therefore underpinned by the autonomy momentum (Seedhouse, 2001: 184-185).

The Kantian approach revolutionized the way research participants should be treated by laying the foundation for respect for persons. A person is autonomous when decision making and choice is entirely his/hers. This is the basis of human dignity. Autonomy is likened to two sides of a coin i.e. that of a person making hers/his own decisions without coercion whilst simultaneously making reasoned choices. It follows then that anything less than treating a person as an end in his/herself is tantamount to the denial of his/her autonomy.

Respect for persons as autonomous beings presupposes that they are competent to make choices. Therefore the giving of IC is valid when autonomy is respected (Munson, 2004:780-781). Where the participant is competent and

able to exercise free choice respecting autonomy is pretty straight forward. Problems arise where people are not in a position to do so e.g. inability to understand, low levels of literacy, poverty, mentally impaired or under the legal age of adulthood. In cases where the individual is not competent and thus does not have the capacity to make a valid informed decision, the "best interest[1]" principle must be drawn upon and the individual must be represented by a legal guardian. In such ways, the dignity and worth of each person can be realized.

Beneficence

Ethical research endeavours to ultimately benefit individuals, more importantly to benefit whole populations through knowledge gained or discoveries as a result of the research. The principle of beneficence in the context of research is an act of preventing, removing or improving a particular situation. The principle of beneficence is therefore core to research. This principle obligates researchers to maximise possible benefits (Gillon, 1997:167). It relates to the concept of informed consent in the following manner, firstly, it aims at directing researchers to do everything possible to respect the values and dignity of the research participants. This is done only if researchers put into practice and adhere to the elements of informed consent (Ganzini et al 2005: 100-104). Secondly, through assessing and foreseeing the potential risks and potential benefits of the research and informing the participants about them adherence to beneficence assures fairness. Thirdly, by ensuring that participants are informed about the research process in terms of any conveniences the research will have on their personal lives adherence to the principle of beneficence may prevent

[1] The best interest principle is sometimes relied upon to guide decision-making in circumstances when the patient is incompetent

any misconception on the part of the participant. As mentioned previously, beneficence has been misused by healthcare professionals in the form of strong paternalism. In strong paternalism, the healthcare professional (e.g. doctor, researcher, nurse) does not permit the patient to make his or her own decision based on provision of e.g. available information, understanding and consent. Rather the healthcare professional makes all the decisions for the patient concerning his or her care. In addition, there is usually an imbalance of knowledge, hence power between the patient / participant and doctor/ researcher. A doctor / researcher is generally perceived as more knowledgeable about the treatment / research than is the patient/ participant.

Non-maleficence

The principle of non-maleficence or not inflicting harm stems from the Latin maxim *Primum non nocere* meaning "first do no harm". This principle is particularly apt in the context of research. Medical research history, as demonstrated in this paper, is littered with research that did harm to many people. The transgressions of informed consent processes can virtually do harm to the participants. The application of this principle in informed consent puts an obligation on researchers that potential participants must be told about the risks or harms of the research. These risks or harms can be physical discomfort or pain, psychological, economic or social in nature. Harm also can be at individual level or extended to groups. Harm must be weighed against the benefits of the research. This is a major reason that potential participants must be informed in detail about research processes. For example, it is incumbent upon the researcher to inform the participants about how confidentiality will be observed

by the researcher and to whom the research results will be reported to and whether at any point the anonymity will be broken.

Justice

In research, the principle of justice can be applied at three protective levels. One level is that of obtaining informed consent. Research ethics committees therefore examine whether justice as protective mechanism is applied by researchers through ensuring that provision for obtaining informed consent is included by researchers (WHO, 2001). Can justice be said to have been applied when the participants agree to take part in research when they might not understand the enormity of the risks entailed in the research? In other words, can individual consent to research be sufficient? The principle of justice in research is grounded on protecting vulnerable groups from being forced to take unreasonable risks. By looking at the principle of justice through the lens of risks, research ethics committees on behalf of the participants make a decision of about the reasonableness of the risks. If they are perceived to outweigh the benefits the protocol is rejected. Lastly, the justice principle is applied as a protective mechanism against exploitation (Macklin, 1998:131-145). In developing countries like South Africa this is particularly important where poverty is rife that people are not over researched when there are no benefits. It is particularly so, when perverse incentives[2] are offered.

The principle of justice is linked to the concepts fairness and equity. Justice, particularly its sub-set distributive justice is particularly applicable to research in

[2] A perverse incentive is an offer of a desirable good in excess characterised by inappropriateness. It compromises judgement, may lead to risk taking eroding autonomy and therefore informed consent. This is especially true in vulnerable groups.

developing countries. In the context of research distributive justice requires that participants have equitable access to research or basic healthcare. This means no one must be prejudiced or excluded from being a research participant for non-scientific reasons (especially during clinical trials). Distributive justice also concerns access to information, and the just distribution of goods and services.

Legal Frameworks

"Valid" as opposed to "informed" consent is the terminology usually used in law (Andanda, 2006:41-43). I will use the terms interchangeably in the following section. The legal framework for informed consent was crafted initially for clinical care exclusively rather than research. With regard to consent the law is clear about the duty of a doctor to inform patients and obtain their consent (Veriava, 2004). Injury to the patient as a result of not explaining to the patient the risks of the intervention may result in the doctor being sued for damages and financial compensation may have to be awarded to the patient.

In South Africa, a failure to obtain consent can be treated as amongst other liabilities as negligence. From the legal perspective consent is invalid if any information is withheld that might be considered material to the decision to give consent (Classen & Verschoor, 1992:62-67).

From a legal perspective, the idea of obtaining valid consent was to ensure another course of action was possible in cases of poor outcome e.g. when negligence by a doctor in treatment of his/her patient could be established. In the case of Fortner v Koch (1935), the USA Supreme Court reiterated the fact

that human experimentation must rest on “knowledge and consent” (Katz 1987:3-5). Some legal scholars have argued that adequate disclosure of information is a necessary prerequisite to enable for valid consent (see, for example Rynning 1994). In South Africa, in the case of Castell v De Greef (1994), the reasonable standard of information necessary for consent to be informed was identified. Concerning the issue of obtaining informed consent and voluntarism to participate or withdraw from research, Singh and Ngwena discuss its legal sanction in their 2001 article.

CHAPTER 3: Legal and Ethical Documents Supporting Informed Consent & Good Research Activities with a Focus on the South African Particular

In South Africa, the Bills of Rights as enshrined in Chapter 2 of the Constitution Act 108(1996) as well as the National Health Act 61(2003) are categorical about obtaining informed consent in human research. It must not be forgotten that what trumps law is the moral insight into the informed consent process. Therefore, the deontological – utilitarian - principlism and legal approaches to informed consent may be perceived as guiding tools in the application of the informed consent process.

International Codes and Regulations and Informed Consent

Where research involves the use of human beings, it is crucial to have codes and regulations that have as their objective safeguarding the safety and the dignity of the participants. This need was prompted by the atrocities committed during World War II. Emanating from concerns of these violations it became clear that conditions for experimentation on human beings need to be well defined. According to Pedrini & PImple (2001),

> *All modern codes of ethics concerning research, on human subjects, affirm the moral importance of informed consent*.

International, and National codes and regulations are crucial in guiding researchers concerning their roles in and the importance of obtaining informed consent from research participants. If the guidelines are unclear, they are prone to be misused or applied incorrectly. The two most important international guidelines which are considered applicable in the context of research sponsored by developed countries and conducted in developing countries are the Declaration of Helsinki and CIOMS guidelines.

Nuremberg Code 1947

The historical impetus towards a research ethics was as a result of the atrocities carried out during medical research in German concentration camps during the Third Reich. Prisoners were used as guinea pigs by the Nazi's for so-called scientific medical experiments. Many of these experiments were conducted to allegedly give the Nazi army beneficial information which would aid their troops in air and sea survival. Another aim was to experiment on prisoners to see if it was possible to make other ethnic groups similar to physical characteristics filling in with the ideology of the "Aryan master race" (such as experiments to see if eye colour could be changed). Because they were prisoners, all experimentation was conducted without the permission of any participants. As the extent of the atrocities was revealed, the result was the formation of the formulation of the Nuremberg Code. The first principle as the heading of The Nuremberg Code, (1947) states … [that] "The voluntary consent of human subjects is absolutely essential".

This laid the foundation for the idea of consent and further elaborations moved to obtaining voluntary informed consent from research participants. The code further states that “This means the person involved should have the legal capacity to give consent.” The Code is categorical about the need for the participant to exercise free choice and to have sufficient understanding of the research in terms of type duration and purpose. The legalist approach is dominant in this Code as it was formulated by judges and should have been considered legally binding.

That the Nuremberg Code is not legally binding was abundantly clear in Moreno’s (2001:343-356) description of the USA’s Pentagon’s attempt to circumvent the Nuremberg Code as early as the1950s. This is because Pentagon was motivating for soldiers and prisoners to be used for human experimentations. The Declaration and the guidelines arguably were seen as a hindrance because of their insistence of obtaining informed consent. This lack of obtaining informed consent by doctors is typified by further events that occurred in Jewish Chronic Disease Hospital (1963) and in the Willowbrook Hospital (1956-1970) cases where parents were said to have “consented “to having their children injected with hepatitis under the guise of a vaccination program.” One of the most infamous cases of failure to obtain informed consent (particularly in as the participants were not informed of an available drug which could offer cure, were the Tuskegee Syphilis Studies which ran from 1932 - 1972.

Following close on the heels of the Nuremberg Code, subsequent codes and regulations incorporated an informed consent ethos at various levels. According to Perley, Fluss, Zbigniew& Simon (1992:149-173),

> *… the [Nuremberg] Code influenced the development of codes and guidelines, both in the general field of medical ethics and, more specifically, in the field of human experimentation.*

But despite the flurry of codes and guideline documents Faden,Lederer & Moreno.(2003: 1667-1671) state that between1948-1960 the popular press "was uncritical about experimentation on humans and assumed that those involved had freely volunteered to participate" .The assumption was that these atrocities could have only happened in totalitarian countries and not in democratic countries e.g. the USA. However, this complacently was shattered in a publication by Beecher (1966) which revealed that for many years, there were multiple instances where obtaining informed consent was superficially obtained or in many instances not obtained by researchers in human clinical trials.

The World Medical Association Declaration of Helsinki. (DOH). First document 1964) – DOH October 2008. Ethical Principles for Medical Research Involving Human Subjects

The World Medical Associations' Declaration of Helsinki (WMA, October, 2008) was the first document that was formulated by medical doctors in 1963. It laid the foundation for obtaining informed consent for research purposes. As its purpose it stated, "Recommendations guiding physicians in biomedical research involving human subject". The declaration was amended in 1975, 1983, 1989, 1996, 2000, 2002, 2004, the latter two added notes of clarifications in certain paragraphs culminating in what is termed the "DoH/Oct 2008" document. Principles 24, 25,26,27,28 of the Declaration deal with informed consent at length. Of importance is that both principle 9 of the DOH 1964 and principle 24 of 2008 emphasize the elements of information to impart to the participants. These elements include the aims, methods, anticipated benefits and harms. The principles stress the importance of voluntary participation and a choice to withdraw from the study should be emphasized in the information to be imparted. Furthermore, both Declarations allow for proxy consent in clinical trials for those who are unable to give consent. According to (Schuklenk, 2000:969-977) "proxy consent was introduced by stealth in these guidelines written by doctors for themselves." This document is not legally binding in international law. But it places moral obligations on researchers to obtain informed consent.

The Council for International Organizations of Medical Sciences (CIOMS), International Ethical Guidelines for Biomedical Research Involving Human Subjects in collaboration with the World Health Organization (WHO) 2002

The (CIOMS) Council for International Organizations and Medical Sciences:, 2002), in collaboration with the World Health Organization (WHO) prepared the Ethical Guidelines for Biomedical Research on Human Involving Human Subjects. These guidelines have also had several amendments since 1993. Besides the requirements of informed consent, the guidelines stress the importance of protection of vulnerable groups in research, the guidelines are accompanied by commentary which describes who the vulnerable groups are. (Tangwa, 2004:63-67) is of the view that ethical guidelines drawn from the Western perspective "were basically attempts to universalize and globalize a particular powerful paradigm, Western paradigm". He further urges inclusiveness in crafting international guidelines. By this, he implies that there has not been adequate inclusiveness of expertise from the developing regions where the international guidelines have been compiled thereby questioning whether these documents are truly international and if so by whose standards. Bhutta (2004:771-776) believes current guidelines need revision as they lack clarity in terms of the consent process research in developing countries. However, because both the Declaration of Helsinki and CIOMS guidelines are not legally binding, perhaps this could explain why the US Food and Drug Agency (FDA), at least according to Camporesi (2008), does not regard them as credible.

The World Health Organization's (WHO) Guidelines for Good Clinical Practice (GCP) on Trials of Pharmaceutical Products

Clause 3.3 of the World Health Organization's Technical Report (1995) reiterates the Declaration of Helsinki and CIOMS guidelines on informed consent stressing the issue of *how* information to the participant should be presented about trials, and that "no subject should be obliged to participate in the trial". Of importance concerning the guidelines is that of taking cognizance of safeguarding those participants who are subordinates to their superiors – in other words, the protection of vulnerable groups.

Ethical considerations in HIV Preventive Vaccine Research - UNAIDS Guidance Document 2000

Guidance Point 12 of the document says "Independent and informed consent based on complete accurate and appropriately conveyed information should be obtained from each individual …" (UNAIDS, 2000). What is of interest about the document is that it stresses the fact that informed consent is a two stage process e.g. pre-trial screening for eligibility and second stage once a person fulfils the criteria for inclusion in the trial as a participant.

Operational Guidelines for Ethics Committees that Review Biomedical Research 2000

This is the WHO supportive document for review committees. On the issue of informed consent the World Health Organization (2000) guideline stresses that "a full description of the process for obtaining informed consent, including the identification of those responsible for obtaining consent is necessary". This puts an onus on the research ethics committees to ensure that informed consent is obtained legitimately by the researcher and that solely responsible for it.

The international guidelines appear to be comprehensive in addressing informed consent in research in terms of scope and content. Granted; they are not cast in stone as they can be amended to suit any unforeseen circumstances that arise. The principles however would remain unchanged. It would be the application of the principles that would be altered. Yet despite this, these international guidelines are not fully applicable to the developing world context. However, the importance of international guidelines is nevertheless to ensure that the requirement for informed consent is well entrenched in the minds of research communities worldwide/ Moreover, they serve to signal that at no point in the research process should the practice of obtaining informed consent from research participants be just an option, to accept or reject, and this remains true in both the developed and the developing world contexts.

National Guidelines in South Africa

Many developing countries especially in Africa are signatories to international codes and declarations by way of membership for example, the WHO, the UN, the African Union, SADAC and many other organizations that espouse the values of ethics in research. In addition, many professionals in developing countries are aligned to health care associations and research entities whose scientists are affiliated to international institutions and organizations whose philosophy is to adhere to the ethical values for conducting research.

From the literature, it is obvious in African countries, the incorporation of informed consent in the legislative framework for research purposes is sparse resulting in some instances of unethical research activities partially due to lack of or weak legislative controls (Bazara, 1998:625-626).This is also echoed by Chima (2006:858-852) who observed the circumvention of international regulations and codes by researchers whilst conducting research in developing countries.. Informed consent for example was not obtained by Pfizer during the trials of Trovafloxacin® in Nigeria (Hensey, 2003). This could be attributed to both a lack of a strong legislative framework and the ease in which international rules and codes can be ignored in developing countries. Added to this, there are weaknesses of research proposal oversight at local and national levels by research ethics committees and councils. In addition, these countries are home to large numbers of vulnerable populations who have little or no knowledge of their rights in the research setting and are probably unaware of the courts as a legitimate recourse. It is clear that laws promulgated at national levels on

obtaining informed consent aid in enforcing compliance especially where international or multi site research is envisaged and the probability of harm to research participants a real possibility.

South Africa and the Assurance of Informed Consent

South Africa has one of the most progressive Constitutions in the world. At its core is the protection of the dignity of all persons. The ushering in of democracy in 1994 brought with it a window of opportunity to institute stringent conditions for doing research. The revelation of Dr Bason's experiments during the *Truth and Reconciliation Commission* hearings gave further impetus to address the issues of experiments on human participants. An example of note is the 1967-1999 "Aversion Projects", which were experiments conducted for "sexual alignment" by doctors on White male gay army recruits, of ages ranging from 16-24years (Simo, 2000). Here there was a flagrant disregard for the international guidelines. Of note, South Africa was a member of the World Medical Association at that time.

Chapter 2 of the Bill of Rights (BORS) of the of the Constitution (Act no 108 of 1996)

Chapter 2 of the Bill of Rights (BORS) of the Constitution (Act no 108 of 1996) in Section 10 affirms the need for respect and protection of peoples' dignity. This clause clearly is in keeping with the ethical principle of respect for persons / autonomy. For, example, Section 12(2) states that;

"Everyone has the right to bodily and psychological integrity" which includes the right-

a) 12.2(a) to make decisions concerning reproduction.

b) 12.2 (b) to security in and control over their body, and

c) 12.2(c) not to be subjected to medical and scientific experiments without informed consent."

While Section 36 of the BORS limits all rights on condition the limitation is reasonable and justifiable in an open and democratic society, it is highly unlikely that an argument to limit the right to informed consent in research would be successful

The National Health Act (NHA) 2003 (Act no 61 of 2003)

Section71.1 of Chapter 9 in The National Health Act (No 61 of 2003) deals with human experimentation. Section 71.1 lays down the conditions for experimentation or research on human subjects as follows;

a) Section 71.1 (1b) "with written consent of the person after he or she has been informed on the objects of the research or experimentation and any possible or negative consequences on his or her health."

Section 71.2 explains under which conditions minors may be involved in therapeutic research as follows;

b) 71.2 (a) "if it is in the best interest of the minor"

c) 71.2 (b) "in such manner and on such conditions as may be prescribed

d) 71.2 (c) with consent of the parent or guardian of the child " and

e) 71.2(d) “if the minor is capable of understanding, with the consent of the minor.”

If the research is conducted for non therapeutic on minors the follow should apply;

a) Section 71.3(a) (i) “in such manner and on such conditions as may be prescribed;
b) Section 71.3 (a) (ii) “with the consent of the Minister,”
c) 71.3. (a) (iii) “with the consent of the parent or guardian of the minor;”
d) 71.3. (a) (iv) “if the minor is capable of understanding the information, the consent of the minor”.

Section 71.3.b states the conditions under which the minister may not give consent as follows;

a) Section 71.3.b. (i) “the objects of the research or experimentation can also be achieved if it conducted on an adult.”
b) 71.3.b. (ii) “”the research or the experimentation is not likely to significantly improve scientific understanding of the minor’s condition , disease or disorder to such an extent that it will result in significant benefit to the minor or other minors;
c) 71.3.b (iii) “the reasons for the consent to the research or experimentation by the parent or guardian and, if applicable, the minor are contrary to the public policy;”
d) 71.3.b(iv) “the research or experimentation poses significant risk to the health or well being of the minor or;”

e) 71.3.b(v) “there is some risk to the health or well being of the minor and the potential benefit of the research or experimentation does not significantly outweigh that risk.”

Should Section 71 be promulgated, it will go a long way in ensuring that researchers not only have an ethical responsibility to obtain informed consent from research participants but also a legal responsibility. In the interpretation of the NHA it is clear that the RSA law recognizes obtaining informed consent as pivotal to the research process.

Department of Health (DoH): DoH Guidelines for Good Clinical Practice in the Conduct of Clinical Trials with Human Participants in South Africa (2006 Second Edition)

The South African DoH provides two main guidelines for researchers. These are Good Clinical Practice (GCP) guidelines which were first published in 2000 (revised in 2006) and the Ethics in Health Research: Principles, Structures and Processes, the specific ethics guidelines for health research in the country.

What these guidelines state is that, “informed consent is an essential component of ethical research” (DoH, 2006). Implicitly, this means research done without informed consent is unethical. The main strength of the guidelines lies in the acknowledgment of the context of developing countries like South Africa which is characterised by people coming from disadvantaged and

vulnerable communities. The guidelines are categorical that especially from vulnerable populations informed consent should be obtained.

The GCP guidelines direct researchers to use "culturally acceptable practices including the use of the participant's language of choice" (2006:11). This is aimed to highlight that participants understand the information given to them. The importance of this document is its power to lay down clear conditions of obtaining informed consent from a context where there could be barriers e.g. in language, culture, and socio-economic differences. The document also echoes the health rights and law perceptive embedded in the Constitution of the Republic of South Africa (1996) in section 27 which guarantees the right to have access to health care services. What is of interest is that it stays clear of communitarian directives in that it does not mention how to obtain and the conditions of obtaining what is called "community consent".

Ethics in Health Research: Principles, Structures and Processes (PSP 2004)

The DoH (PSP) document allows the carrying out of research in an emergency situation but initial permission must be sought from a Research Ethics Committee (REC) or the Head of Department (HOD) of the emergency facility. The REC or the HOD must ensure that;

a. "Justification for carrying out the research is sound
b. Cultural and religious sensitivities of the participant have been taken into consideration

c. It has been established that the participant cannot give consent
d. Research has a potential of being therapeutic and does not pose more than the acceptable risk
e. A legal representative would be told if the research has been done and opting out of the research was optional."

If the participant recovers he/she will be told about the research that has been carried and that the right to withdraw will be guaranteed. These conditions ensure that emergency research is not used as a tool to exploit participants. In such situations deferred consent is ethically acceptable

The incompetent participant lacks that psychological maturity to understand and communicate preferences in a coherent manner and this is also an ethical challenge. The challenges are that such a person cannot make rational decisions and therefore from such a person informed consent cannot be obtained. Those who fall under this category are e.g. the very young and the elderly. Informed consent should be obtained from a competent adult on behalf of the participant but after the informed consent process is followed.

Covert research relates to research that could not be done without deceiving or hiding the purpose of research from participants. Deception research while sometimes necessary is in the main unethical The PSP document by DoH however has laid conditions for this action as long as the REC is satisfied that;

a. "The validity of the research would be compromised if there was no concealment.

b. There are strict and well understood limits to the deception.
c. The only way to gather information is by use of deception methodology,
d. Participants are not exposed to higher than the minimum risks participants will be debriefed after the fact.
e. Participants could withdraw the data about themselves after the research has been completed and
f. Finally that the relationship will not be soured between the researchers and the participants after the research".

Many questions are raised by these conditions for deception research stated above including whether it is morally correct to do convert research as it conflicts with ethical norms governing research on human participants.

The pros are that the researcher may discover information which he /or she may not have discovered if the research was done in an open manner, due to unavoidable bias if the participant was aware of all details. The cons are that firstly, it is not ethically sound as it shows no respect for persons. Misleading participants or not divulging all information about the purpose of the research is ethically very difficult to defend and can be seen as using the participants as a "means to an end ". Once people discover that deception was used to carry out the research, they might show antipathy against future researchers. In addition, it does not give participants the chance to ask pertinent questions as the researcher hides information from the participants.

The PSP (2004:4) guideline states that "informed consent must be obtained from participants before the research can begin". Both written and verbal informed consent must be obtained, unless there are good reasons to the contrary, such as a situation of coma, emergency, or mental incapacity (DoH 2004: Sections 5.9 & 5.14) The guidelines entrenches the oversight role of RECs concerning the assurance that informed consent requirements are included in the protocol. It is a generic document for all types of research. The Good Clinical Practice (GCP) document reemphasizes the importance of obtaining informed consent even from the vulnerable communities.

These guidelines have also incorporated the National Health Act (Act 61 of 2003 Section 68) which outlines guidelines on the use of human tissue samples where it states when consent is required and the requirement concerning when consent can waived.

The South African Medical Research Council (MRC): Guidelines on Ethics in Medical Research: General Principles: Book 1 2005

Book 1, Section 5 of the 2005 guidelines produced by South African Medical Research Council (MRC) is titled *The Legal and Moral Justification for Research*. The MRC guidelines basically reiterate the elements of informed consent in their previous documents. Sub section 5.3.1 states, "Consent must be given by someone who is legally and factually capable of consenting." The document further distinguishes competence from the perspectives of adults and minors. What is of interest is that the document tends to take a more legalistic

outlook on issues of capacity. The MRC while given much respect, does not have the legal standing that DoH guidelines have, this is because DoH guidelines are a response to the National Health Act.

Health Professions Council of South Africa (HPCSA)

The HPSCA is the statutory body established under the Health Professions Act No 56 of 1974, which registers doctors, dentists and other allied health care workers. It was formulated to protect the public from unethical behaviour by practitioners amongst other functions. Booklet 9 on Informed Consent of HPCSA (2007:1) states the following,

> *Patients must be given sufficient information in a way that they can understand, to enable them to exercise their right to make informed decisions about their care. This is what is meant by an "informed consent.*

In Section 4 of the same booklet it is stated that "patients should have knowledge and understanding of the harms or risks; appreciate and understand the nature of harm and risks; have consented to the harm or assumed risks and that the consent must have been comprehensive" (ibid:5).

Researchers involved in biotechnology such as gene mapping, DNA sequencing, diagnostics, cloning and genetic modification also have particular

duties. It is for this reason that the HPCSA developed *General Ethical Guidelines for Biotechnology Research 2007 Booklet 7*. Section 2 of the booklet reiterates the importance for the researchers to abide by the four principles of biomedical ethics. In addition, the value of integrity is promoted for all those engaged in research. The principles grounding informed consent are reinforced in the ethical guidelines. The preamble of the section on informed consent states "It is necessary to obtain informed consent from the research participant prior to commencing research" (2007:11). Sections 2.6.4 -2.6.4.4.2 deal with the issue of informed consent in adults, mentally ill or handicapped, elderly, pregnant women, the unconscious patients, the dying, minors and children. For each of these groups' conditions for obtaining informed consent is spelled out.

Patients' Rights Charter (2000)

Although this document addresses itself to health care its scope is wide enough to address issues of research as most health research is conducted in health facilities. Concerning informed consent the Patients'Rights Charter states

> *Everyone has the right to be given full and accurate information about the nature of one's illnesses, diagnostic procedures, the proposed treatment and the costs involved, for one to make a decision that affects anyone of these elements*. (2000:2)

On choices, it states that,

> *Everyone has the right to choose a particular health care provider for services or a particular health facility for treatment provided that such choice shall not be contrary to the ethical standards applicable to such health care providers or facilities, and the choice of facilities in line with prescribed service delivery guide lines(ibid:2).*

This document is rights-centred as it was envisaged to affirm patients'' right to access to healthcare services. Amongst the roles and responsibilities of patients one that is pertinent to this paper is the patient's responsibility, specifically "to respect the rights of other patients and health providers".

Research Ethics Committees and the National Health Act, 2003 (Act No. 61 of 2003)

It is an accepted international practice that research involving human participants should be conducted only after thorough reviews have been carried out by RECs. In many countries, RECs are called Institutional Review Boards (IRB). In the following section, I will use the terms synonymously.

Reviews by RECs are guided by international, national and institutional research guidelines. Their roles, amongst others, include review of the research proposals for risks, benefits, and overall the protection of research participants. In addition to this, REC's have the responsibility of educating and assisting

researchers concerning the ethics of research, monitoring research and to provide accountability to the public. Overall, the key role of the REC according to Dhai (2005:595-59) "is to safeguard the dignity, rights, safety and well being of all participants in human research subjects. Implicit in this is to scrutinise the informed consent documents and processes for its appropriateness, and protection of participants' integrity".

Some of the conditions which developed countries must take cognizant of are under scored by (Cleaton-Jones 2005:267-269) "functioning of IRB……., in a developing country environment requires knowledge of local culture, resources and services". This is not always understood nor accepted by RECs and researchers who operate in resource–rich environments. Ideally, a REC should be constituted of members who have the ability and the expertise to recognize the gaps in the protocol and in the consent form.

Attention to the lack of capacity and infrastructure in developing countries to review protocols is an important point raised by Kass et al (2005). Lack of capacity could result in not examining the consent forms properly during the research ethics committee sittings. This thought relates to the ability of a REC to have a good mixture of people who have sufficient knowledge to review proposals for their scientific validity and ethical acceptability (WHO 2007). One of the major criticisms of RECs at their current stage of development is that the membership may be socially and culturally removed from communities for which the protocols are being reviewed. A way to overcome this is for RECs to invite community members and community advisory board representations to

meetings which involve participants from those particular communities are being discussed.

It is commendable that although the main aim of the National Health Act (NHA) (Act No. 61 of 2003) is to ensure that everyone in South Africa has access to heath care, part of the Act reiterates the necessity to establish research ethics committees in "institutions, health agencies, and health establishments where research is conducted" (see No 61, Chapter 9 Sections 73, 1 and 2). This is because of the importance of research for the improvement of the population's health. Of equal importance in the Act is the protection of research participants' rights and dignity. Therefore, to ensure that the research is conducted ethically, ethical clearance for protocols must be issued by the research ethics committees after comprehensive and competent ethics review.

Research conducted a few years ago by Moodley & Myer (2007) showed that membership in the RECs was not adequately diversified. There was variability in terms of capacity, operational systems and infrastructure. In addition to that their study also revealed that "previously advantaged universities seem to be faring better compared to the formerly historically disadvantaged institutions." (It will be interesting to see what the situation is now especially since the National Health Research Council (NHREC]) has started registering RECs and will soon be auditing their processes.)

Despite these concerns, there is a National Directive as to REC composition and functioning. Currently, twenty RECs have been registered with the NHREC; two of them are private RECs (Dhai, Personal communication 2009). Just how

these function, is not known, making it much harder to assess their capacity especially on the issue of informed consent. According to van Bogaert (2007:240) the lack of political will to support and promote the value of provincial RECs is the major hurdle to their development. Until comprehensive audit and assessments are done, the effectiveness of these committees in ensuring informed consent may not be known.

Overall, South Africa has strived to produce world class guidelines for conducting research in an ethical manner. These guidelines are unequivocal on issues of informed consent. Of importance is the legal framework in buttressing the guidelines by articulating the conditions of obtaining informed consent. But what remains doubtful is the capacity of the many research ethics committees to play their roles effectively as an enforcing arm. It is hoped that as more opportunities open up locally to train health professionals in bioethics and research ethics, capacity will gradually be built to include them into RECs functioning. However, it must be emphasized that guidelines rules and codes are only one part of the matter-the monitoring of research and education of research participants concerning their role is vitally important.

This chapter explained how informed consent has been incorporated in international guidelines and the conditions under informed consent should be applied in research. It has further demonstrated that a developing country like South Africa views the obtaining of informed consent as a precondition prior and during the research process. These are principles enunciated not only in the codes and guidelines but also in the law.

CHAPTER 4: Informed Consent in Research: An Ethical, Legal & Cultural Commentary

The value of informed consent has already been detailed from the ethical perspective in the last chapter as that of respect for persons and of enabling autonomy and allowing autonomous decision making in competent participants in research.

There are other additional ethical arguments supporting informed consent. For example, it can be argued that obtaining informed consent could have secondary positive ramifications. One of them is that of establishing a platform for a researcher-participant relationship based on mutual respect. Such a relationship is characterised by transparency trust, accountability and communication. By communicating in a transparent manner about the aims of the research and risks and probably potential and mutual benefits, mutual respect and trust is built paving the way for an ethical informed consent process. According to Wear (1993: 100-112) this can also result in a reduction of psychological distance whereby the participant and researcher see each other as moral beings. Accordingly, each other would be seen as equals and any benefits gained would also be seen as mutual. These mutual benefits should be seen in the light of a give and take relationship in that research participants voluntarily sacrifice their time to participate in the research while the researcher gains experience and knowledge. The research participants, by giving, ought therefore to benefit, either directly or indirectly as a result of involvement in the research.

Open and truthful communication also encourages participation in discussions thus reducing misconception about each other as well. Common in developing countries, therapeutic misconception, especially in clinical trials, may also be avoided through a properly executed informed consent as many of participant preconceptions would be clarified. Therapeutic misconception occurs when a trial participant misconstrues the purpose the research as therapy. It is therefore important for the researcher to explain to the participant that he or she is in a state of equipoise in order to prevent therapeutic misconception. Equipoise, according to Freedman (1987: 141-145) is

> *... a state of genuine uncertainty on the part of the clinical investigator regarding the comparative therapeutic merits of each arm in a trial.*

Informed consent also ensures that privacy is protected from unwanted and unsolicited physical or psychological intrusion. According to White & Zimbelman (1998:477-499) informed consent "can serve as foil to culturally or professionally embedded values and practices that undercut patients' values and goals". By that I understand they mean informed consent is a protective mechanism against health workers' prejudices which include a belief that by virtue of being professionals their culture is superior to that of patients. Although they were writing about clinical care, this is also apt for contemporary research endeavours.

Researchers in many instances meet social values and cultural beliefs that are different from theirs for the first time during the research process in developing countries. Much has to be done by these researchers prior to conducting the research. Researchers need to develop collaborative partnerships with communities and potential participants from the onset. . This would serve as the entry point of the informed consent process, as discussing and raising awareness of the communities' burdens and benefits is pivotal for ethically conducted research. Raising awareness, understanding and respecting community culture, traditions, and sensitivities, will result in facilitating the recruitment and enrolment process. Moreover, it will assist with compliance, and retention of participants in the research. If practiced, application of this process will serve to circumvent the high attrition rates in the context of poor understanding.

When informed consent is treated truly as a process, commencing from the time of community consultation prior to the actual research and continuing into the research where the principle of respect for persons is consistently upheld, exploitation and manipulation of research participants may be circumvented. These are some of the ethical perspectives which are part of the research process.

Concerning law, informed consent, according to Montange (1974: 1632-1664) came about as a result of medical malpractice where a doctor gave treatment to a patient without consent. Because this case involved touching a patient's body without valid consent it was regarded in the court of law as "battery". The case

of Pratt v Davies (1905) tells of the case of a Dr Pratt who performed a hysterectomy on Mrs Davis to cure her of epilepsy. Of importance of the case (as it would be considered medically suspicious by modern standards) is that Dr Pratt intentionally deceived Mrs Davis concerning the nature of the treatment he would perform. This was because the medical doctor simply wanted the patient's cooperation to perform the operation. The case confirmed that consent includes the legal (and ethical) concept of fidelity.

The importance of disclosing risks associated with an intervention was also clearly shown in the landmark case of Canterbury v Spence (1972). In this case, Dr Spence operated on Mr. Canterbury to repair his spinal defect. But the doctor failed to explain in full the risks associated with the surgery. This case confirmed the need to impart information including risks that a reasonable prudent patient would consider relevant in giving consent to a procedure. Informed consent from the legal perspective serves as a protective mechanism against illegal bodily invasion.

Amongst its other functions, consent, according to Schuck (1994:899-959) defines the law of contract. At its core is respecting ones dignity to make informed consent and choices. This implies therefore that fiduciary duties are owed to the research participant. This is particularly important in the globalisation of research where most funding is from international consortiums with the likelihood that although research is being carried out in developing countries the benefits may accrue which mainly advantage developed countries.

Regarding South Africa, the legal arguments in Chapter 2 of this research report emphasise the legal responsibilities concerning informed consent in detail. Based on the arguments stated above one would imagine that there is an agreement amongst researchers that informed consent should be obtained at all costs and in every situation from competent persons before any type research can be carried out.

However, there is a growing amount of literature to suggest that there are circumstances and contexts that dictate flexibility and should be considered. It is argued that in many cases it is not only unreasonable but also not germane. Defending such arguments, points are made about the questionable 'universality' of application of informed consent in the current manner as suggested in the international guidelines. This is because the context in which the research takes place reflects different worldviews, ways of life, perspectives and outlook. This is not to say that the process of informed consent is totally negated, it is to say that some arguments are given for greater flexibility in the informed consent process for various reasons.

There are views that reflect paternalistic and pseudo anthropological perspectives on the issue of research participants in developing countries. This is based on the assumption that the researchers know the needs of the-would-be-participant. This knowledge is based on superior knowledge about the research process coupled with an understanding the prospective participants' worldviews. Some further argue that insistence on strict criteria of seeking informed consent retards scientific progress as research participants just cannot

grasp the technical information given. There has been also an acknowledgement by Macklin (2004), a strong proponent for autonomy, of the need to adjust the process of obtaining informed consent in response to local level needs. However, Gostin (1995:844-845) cautions against deviations from prescribed standards set for obtaining informed consent.

Some skeptics harp on the fact that the allure of better health care (a coercion factor) is the driving force behind the participation in research amongst poverty stricken communities. It would follow that as autonomous decision making is compromised, so is informed consent. Additionally, it is argued that participants may not understand the research jargon like “placebo” as there may not be an equivalent term in their particular vernacular.

Critical to obtaining IC therefore is the ability of the researcher to understand the educational, linguistic, social and cultural backgrounds of the participants in order to communicate clearly. Researchers need to learn from communities in order to build in culturally appropriate research designs which take care of ethically appropriate principles.

What is proposed is of paramount importance - to have the safety of participants safeguarded - without the stringency of the informed consent process. Some have gone as far as rejecting the bureaucratic procedures involved in informed consent stating that that processes of informed consent are social constructs which are not in keeping with social changes. A point is also raised that one should consider that consent practices developed in early

twentieth century are not perceived as having the same meaning in the early twenty first century. From these perspectives; another view which is important comes from that of culture.

Culture and Informed Consent

A topical debate is that of the confluence of culture and the obtaining of informed consent in developing countries in non-intrusive ways that are ethically acceptable. In this perspective, because autonomy is relative and viewed as a social construct, the consent practises developed for individualistic Western societies may be cultural inappropriate and therefore is not applicable especially in some communitarian cultures. This is because autonomy and its limits are determined by the will of the community.

The criticism emerged because of wholesale application of informed consent based on a Western construct upon developing countries. Because, it is argued, autonomy is a Western concept which stresses individualism it is an anathema to communitarian self-identity in traditional developing countries like Africa. The debate intrinsically implies that the configuration of the informed consent process in the current form is not a universally applicable concept.

African philosophers have argued that it is fallacy to equate communitarian consent as divorced from individual consent just because informed consent has a multi step process is a mistake. Some have criticised the focusing on autonomy alone, which is a norm in Western cultures. The suggestion is that

there should be a considered effort by “Westerners” to understand and embrace the cross cultural context where each person sees him or herself in relation to others. Mansoh (2008: 104-114) contends that “ … Acting within the contexts of cultural norms and institutions does not by itself imply lost, diminished or compromised rights of autonomy and self determination”. He defends this statement by giving an example of how even in the West that a researcher wishing to conduct research in an institution would need permission from the authority of that institution. From a principlist point of view he sees this more no different than seeking community consent.

My argument however is that generally, African cultures are gradually loosing homogeneity and societal changes within communities have gradually shifted the ethos of decision making to be more participatory. This change includes autonomous decision making. Hence, the obtaining of individual informed consent versus communitarian consent is gradually taking root. As an example, the HIV / AIDS pandemic has clearly demonstrated that individuals will make autonomous decisions about participating in research regardless of so-called communitarian bonds. I argue that although community consent is required, one cannot ignore the importance of respect for individual consent. Perhaps, when it comes to the community aspect of the process, “permission” as opposed to “consent” terminology, should be used.

The debate is strengthened further, it is argued, by the fact that in some cultures decision making is often deferred to family members, the elders, chiefs

or religious leaders. Therefore, it is sometimes assumed that individual self-determination is null and void.

A cursory examination of the reasons that dictate exceptions in obtaining of informed consent is admittedly tempting and indeed may have value. However, closer scrutiny yields pitfalls because they do not admit that cultures always change and negate (for right or wrong) the effects of globalization. For those engaged in REC processes, a major concern is that if current guidelines and codes are modified, greater avenues are opened for unscrupulous research to take place which will cause great harm to vulnerable populations. .

The scientific quest for knowledge should not trump respect for persons. It is possible to explain information in simple ways that allow ordinary people to understand medical and scientific jargon. Doing so has the potential to empower research participants to make truly informed decisions. Although it may appear that the bureaucracy is overwhelming, they are necessary to ensure that informed consent is obtained for the protection of research participants. Bureaucracy in this instance refers to e.g. oversight of research ethics committees regarding the standard of the information sheet for obtaining informed consent (Farham & Bradbury 2000). The danger of ignoring the bureaucracy has been shown to have done harm to research participants.

As examples, one may point to the recent South African case where Professor Werner Bezwoda subjected patients in his clinical trials to inappropriate research protocols without their informed consent and without the knowledge of

the University of the Witwatersrand. At a 1999 international conference, Bezwoda claimed he had successfully treated breast cancer patients with very high doses of chemotherapy. He claimed that these high doses, combined with bone marrow transplant on women with high risk breast cancer, resulted in lower remissions and lessened morbidity. International experts on breast cancer showed great interest in the studies and came to South Africa to verify his data. It then transpired that he had falsified his data. Of interest is that many patients were Black and had not given their consent to be in the trial.

Pfizer is another example case of an international company that conducted unethical clinical trials in 1996 by administering Trovan© which was not approved by the (US) Federal Drug Administration (FDA) in an oral form for paediatric use. The drug was administered to Nigerian children with meningococcal meningitis without their parents' consent. Some of these children died. While permission to conduct the drug trial was allegedly given, after years of court disputes Pfizer eventually compensated the families of the victims (Howden, 2009). The ethical issues include that of REC approval or not, informed consent or not, and importantly the clinical testing of a non-FDA approved oral form of a drug in an emergency situation on a vulnerable population.

In both cases, it appears that bureaucracy was circumvented by the researchers. It also appears that it was no accident that these occurred in developing countries. It is also critical in this fast-changing world where exchanging of data is fast and highly sophisticated, that human tissues can be

sold to the highest bidder without the informed consent of the participants. It is also doubtful that the processes for obtaining informed consent developed in early twentieth century really have a radically different meaning in the early twenty-first century. A way forward is to have the processes enriched. Respect for persons as a concept is core to informed consent and respect for persons must remain a research ethics imperative to uphold.

That being said, there are instances when it is ethically acceptable to circumvent the informed consent process. Some examples include emergency situations, or when the identified participant is incompetent to directly give consent because of age or mental incapacity (deferred consent). In the latter, however there are regulations concerning proxy consent which are applicable,

These last two chapters have demonstrated that informed consent is extensively addressed in the international guidelines, coupled with national codes and guidelines. Guidelines are dynamic and may well change over time in response to changing circumstances. In addition there is general agreement that they are applicable even where the social environments are different. The main aim is to ensure that no one participates in any research without informed consent being obtained in order to fulfil the principle of respect for persons.

CHAPTER 5: Highlighting "Unfinished Business" in Informed Consent and Recommendations for Its Further Development

"Unfinished Business"

Is there an unfinished business in the obtaining of informed consent? What do I mean by the term "unfinished business?" In this paper I meant areas or gaps which, if not urgently remedied may ethically compromise the genuine obtaining of informed consent.

At the beginning of this paper, I demonstrated that codes and guidelines concerning research involving human participants do incorporate the importance of obtaining informed consent. Moreover, many are quite detailed providing guidance on how to obtain informed consent whilst protecting communities regardless of their cultural differences. They are universal, making their application acceptable as respect for autonomy, in spite of material and social differences, is their prime goal.

However guidelines are only a roadmap. This means that there must be properly constituted structures and effective mechanisms in place to ensure compliance. A major function of developing world RECs is to ensure that clinical / medical research conducted in their countries adheres to the ethos of good research practices.

I now propose five broad categories under “unfinished business” which have the potential to threaten the obtaining of informed consent in developing countries.

1) The Capacity and Training of Research Ethics Committees

The capacity and training of research ethics committees in institutions and health establishments in many instances is not uniform in developing countries. Most research ethics committees conduct their business on a voluntary basis without payment. Members are recruited for their expertise in a particular field that does not necessarily reflect ethics training. As expected many of them are burdened by their own service delivery and may not necessarily have the skills to unpack or even see the nuances in the protocols to discern that the informed consent and other ethical issues are in danger of being infringed. The “publish or perish” culture in tertiary institutions has resulted in an increase in the number of protocols to be reviewed adding extra work to ethics committee. According to (Cleaton-Jones & Vorster, 2008:38-43) “general research application increased from 439 to 553 in 2007” at the university of the Witwatersrand. In addition, there is a high likelihood that committee members, if they are not properly trained, may be partial to colleagues held in highest esteem in the research arena. This could possibly result in the committee allowing infringements of ethics including informed consent processes. Training of Research Ethics Committees is important but it is not sufficient as institutions need to support their functioning which may include the employing of full time reviewers. It is imperative that the functioning of the committees need to be monitored by the National Research Ethics Councils through yearly reports.

2) *Monitoring of Research Processes in the Field*

It is generally agreed that informed consent is a process which means it has to be instituted before the research process and reinforced during the research. This has a bearing on how informed consent should be monitored. The fact that there is a paucity of literature on the monitoring of informed consent, whether the process is actually continued throughout the research is a complex thought. The lack of information concerning monitoring may be due to the difficulty of observing the process on an ongoing basis during the conduct of the research. In addition, difficulties are also experienced because of the need to uphold confidentiality and anonymity of participant's data. Participants have been promised these values as part of the informed consent process.

What is critical to quality assurance is the role of RECs in monitoring whether informed consent is being obtained as reflected in the protocol. It is argued that it is one thing to reflect the desired requirements on paper but what happens in the field may be totally different. While the REC's monitoring of the informed consent process ought to be the gold standard, it is highly aspirational. Even in the developed world where the IRB's do not function under the terrible resource constraints of RECs of the developing world, monitoring the conduct of research is not always the norm.

South Africa, like many developing countries is a hotbed for research activities. At the same time there is an exponential growth of independent ethics committees. It is important that the functioning of these research ethics

committees need to be monitored. At present in South Africa it is informally reported that there are about twenty such committees, most are not attached to universities or research government entities or institutes (interview: A Dhai) . The researchers, quiet a number of whom are medical doctors in private practice do research for private companies. Although in general, a current Good Clinical Practice certificate is a requirement to conduct research it is not clear how many of these researchers adhere to the principle of GCP training. In addition, conflicts of interest can be generated by e.g. large sums of money paid to the researcher for every patient in one's practice enrolled in the study could easily compromise ethical principles in the informed consent process. There is a paucity of studies on the obtaining of informed consent from one's own patients in the private sector. This raises ethical concern especially in light of the fact that the funders are profit making entities.

At a practical level how does one ensure that the process of obtaining informed consent is continuous and following the strict criteria laid out in the protocol? This is especially critical in the context of a background with proliferation of collaborative research between developed and developing countries, where funding agreements are tightly controlled and based on tight schedules within limited time. Currently despite a history of research misconduct, researcher integrity is relied upon. REC functioning is based on good faith agreements with the researchers: The question that begs an answer is "Is this enough?

3) Political Interference in Research Activities

Research activities also reflect a political agenda therefore raising ethical problems about informed consent processes in developing countries. The promise of anticipated health care services to be given to research participants can raise poise ethico-political problems through the interference of politicians. Politicians may insist on reviewing and approving protocols, despite no training in health or ethics, thereby threatening the independence of a research ethics committee. A case in point was in Mpumalanga in South Africa where the REC rejected a study on scientific and ethical grounds because it was perceived that it would harm some of the research participants (van Bogaert 2007) and mostly likely the informed consent could have been jeopardised. It transpired later that a newly appointed Member of Executive Committee (MEC) for Health approved the study without informing the REC.

Heads of ministries could even demand expedited reviews and approval of ethically flawed projects. They may even facilitate research where trials have not undergone the review process. This has been aptly demonstrated in the case of Mathius Rath who conducted clinical trials with his products of vitamins which he publicly claimed cured AIDS. DoH did not stop this vagrant act of misinformation until the Treatment Action Campaign (TAC) took Dr Rath to Court for making false claims. In the case (TAC and SAMA v Matthias Rath , 2008), Rath was interdicted and the Department of Health was ordered to investigate him. He was also told to stop breaching the (Medicines and Related

Substance Act, 101 of 1995). The Act among other objectives gives power to the Department of Health to control use of unregistered medicines

4) *Slowness of Governments to Facilitate the Formation of National Health Research Ethics Councils*

National Ethics Councils play a pivotal in setting norms and standards for conducting research on human participants, auditing processes and outputs of research ethics committees. The advisory role to government and Non Government Organisations on issues of research ethics including informed consent is also important. There is also a need for the public to air grievances and seek redress in matters concerning informed consent in research. However with the exception of a few countries, very few functioning councils have been established. One of the reasons could be that, where the burden of disease is such a high priority and research is urgently needed for solutions by governments, research ethics committees are perceived as stumbling blocks to initiating research. In South Africa the National Health Research Council (NHREC) was established in 2006. The functions of NHREC according to NHA, includes among others registering and auditing of research ethics committee and also give guidance on how research ethics committees should function. Thus far the functioning of the committee has remained an enigma. It was only recently that the NHREC registered RECs. As the Council serves a three year term which comes to an end in 2009, it is clear that not much has been achieved by the first council. However, of importance the administrative structures are in place.

5) Open Debate and Civic Engagement

Despite the proliferation of research in developing countries there is hardly any public debate concerning on the ethical issue of informed consent in biomedical research. Granted, community involvement should take place prior to research where informed consent is discussed, but this is usually within the circumscribed areas where research is to take place. I argue that there is a need to open the debate to a bigger audience. This failure may be explained by the fact that firstly biomedical researchers on human participants are programmed to announce positive results to the public especially if the research results are of high political national interest, the processes leading to the actual research results take low importance. Secondly, as informed consent in developing countries is a contentious issue, not many researchers might be amenable to public debate when the key challenges and concerns might be that of recruiting sufficient participants and sourcing adequate funding. This does not in any way infer that there is unethical intent on the researchers' part, or that there are ulterior motives to keep down the debate. Thirdly, as the concept of obtaining informed consent for research purposes is so complex and contentious, researchers may be wary of discussing such an issue because of the media's tendency to distort facts. Research agencies have are also to be mentioned because when they put calls in the local media for recruits to participate in research issues of informed consent are not clarified up front in the criteria for participation.

The public in general including health workers are not conversant about ethics of research especially on the issues of the ethics of obtaining informed consent. This might be explained by the fact that bioethics is still a new field in developing countries. This is true also of South Africa. This is borne out by the fact that bioethics teaching at university level in South Africa as an example has only recently been made compulsory in the curriculum of health science students. Increasing awareness and dialogue would ensure that that people know that they have the right not to participate in research and, if they do so under what the conditions should be to ensure ethical research. There role of civic society should not be undermined in the facilitation of this process. Civic groups are in touch with communities at grass root levels as they have tremendous capacity to network. They also have the ability to galvanise community participation, especially the poor, thus acting as a vehicle for them to voice their concerns.

Recommendations

In this report I have identified unfinished business areas in the issue of informed consent. I have detailed the issue of IC in International and National documents and from ethical and legal views; I have shown that such documents do not present a deterrent to obtaining informed consent. I have further suggested that it is naive on the part of some persons who claim that the guidelines should be relaxed because of cultural differences. This is because they fail to include the fact that all cultures change, the more-so with globalization. In the previous chapter I have pin-pointed the areas to target. The areas can be summarized as

follows; capacity strengthening and training of research ethics committees to asses protocols, strict monitoring of research processes in the field, curtailing of political interference in research activities to ensure that research ethics committees do their work independently and by actively encouraging of vigorous debate on issues of informed consent in research by civil society .

This is not to undermine the complexes of obtaining informed consent .Although there was an outcry about the individual autonomy in developing countries, the acceptance of the multi step approach in obtaining consent in communitarian societies has eased this tension as it has not overridden individual consent which is core to ethics. This is great step forward in matters concerning informed consent for developing countries.

I have highlighted the importance of informed consent in research and its elements have been dissected fully, recommendations about its universalism in its application in diverse communities is well explained , but much more work needs to be done in the areas I have mentioned.

Is there some unfinished business in informed consent in developing countries? Yes there is.

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