STORAGE AND FUTURE USE OF HUMAN BIOLOGICAL SPECIMENS IN RESEARCH: KNOWLEDGE AND ATTITUDE OF NIGERIANS

BY

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ABSTRACT

BACKGROUND:-The globalization of health research and international health collaboration has led to increased interest in the use of human biological samples (HBS) by researchers. In spite of this, there has been limited research into the perspective of individuals and communities in developing countries like Nigeria on the ethical challenges surrounding the use of stored HBS in research. One principal ethical conundrum is whether researchers should be required to obtain individual informed consent before conducting future research on stored samples and if required, how such consent should be obtained. Nigeria, with her large and heterogeneous population, readily serves as a valuable source of information on this issue.

METHODOLOGY:- A cross-sectional survey of 401 adult Nigerians living in Enugu, South-eastern Nigeria was conducted between 2008 and 2009 to determine their knowledge and attitude to the use of stored HBS in research. Participants completed interviewer-administered questionnaires. Focus group discussions involving 52 participants were also conducted. The study was approved by the University Nigeria Teaching Hospital (UNTH) Health Research Ethics Committee.

RESULTS:- There were 50.1% males and 49.9% females in the survey, with mean (SD) age for the men being 35.7(13.3) years and for women 30.4(9.9) years. Most, 220(54.9%) were of the view that fresh consent was not necessary for every new research conducted on stored HBS and63% were willing to donate for future unspecified use research (FUUR) but only 38.9% were willing to grant one-time consent. Multivariate analysis showed that the willingness to donate HBS for FUUR was significantly associated with gender (p-value=0.003, O.R=1.86, 95%CI=1.23 – 2.82) and marital status (p-value =0.02, O.R=1.39,95%CI=1.05 -1.84).

Findings from the FGDs indicated that there was low public awareness of the potential use of stored HBS for FUUR and the attitude to the concept of FUUR was guarded possibly due to lack of trust in researchers.

CONCLUSION AND RECOMMENDATIONS: There is an urgent need to educate the public on the potential use of stored HBS in research while ensuring adequate levels of accountability and transparency among researchers. An adequate option for consent for FUUR in Nigeria may be to encourage the concept of general one-time consent subject to ethical review/oversight as well as a practical “opt-out” option for interested participants

Keywords: Stored samples, future, unspecified use, research, Nigeria, consent

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CERTIFICATION OF ORIGINALITY

The work presented in this dissertation is to the best of my knowledge and belief, original except as acknowledged in the text. I also declare that i have not submitted this material either in whole or in part ,for another degree at this or any other institution.

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CERTIFICATION BY SUPERVISOR

I certify that this work was carried out by Onochie I. Okoye in the Department of Surgery, University of Ibadan, Nigeria.

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DEDICATION

This work is dedicated to all the potential research participants and health researchers in Nigeria. It is also dedicated to all the persons in the bioethics movement globally.

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LIST OF ABBREVIATIONS

FUUR	-	Future Unspecified Use Research
HBS	-	Human Biological Specimen/Samples
HREC	-	Health Research Ethics Committee
IRB	-	Institutional Review Board
UNTH	-	University of Nigeria Teaching Hospital, Ituku Ozalla

CHAPTER ONE
INTRODUCTION

1.1- Background

Medical Research involving human participants has increased tremendously globally, including the developing world. With this globalization of research has come increased interest in the use of human biological specimens (HBS) by researchers. Increasingly, genetic and biomedical researchers are developing protocols to examine and re-examine human biological specimens (tissues/fluids) which were obtained and stored during previous medical/surgical care or previous research studies.

With the recent advances in biomedical technologies, there has been a dramatic increase in the scientific and commercial value of human tissue and fluid samples stored all over the world; thereby raising profound and multi-dimensional ethical, legal, socio-cultural and economic questions about the use of these stored tissues. The collection of human biological specimens from research participants and their retention in a tissue bank (bio-bank) for future use, typically unspecified at the time of sample collection, is another area where concerns about consent, storage and ethical practices have converged.

There is controversy about whether researchers should be required to re-consent the individuals from whom the samples were taken before conducting research on them; if required, how should such consent be obtained; what are the rules about ownership, access and control of stored HBS; how is confidentiality of data, privacy of sources, ownership, access and control of stored HBS managed; what about commercialization, benefit-sharing, disclosure of research findings/results, risk of commodification, risk of group harm in the light of conflicting community and individual interests, and the risk of exploitation.

1.2- Statement of problem:-

Despite the increase in international collaborative research (Benatar and Singer,2010;Marshall et al,2006), there is very little discussion in developing countries such as Nigeria about the ethical problems posed by the use of stored human tissues for research or exploration of the perspectives of potential research participants on the ethical challenges associated with the use of stored HBS (Van Schalkwyk et al ,2012; Wendler D. et al ,2005;Langat ,2005; Upshur et al ,2007;Zhang et al,2010; Emerson et al,2011).One principal ethical conundrum is the informed consent process required for the future use of stored tissues in unspecified research. Although, guidelines for human tissue research are being developed

by stakeholders in the research enterprise, most of these rarely take the preferences and perceptions of the potential tissue donors into consideration.

1.3- Research questions

- **Consent Issues (Disclosure):** In the light of the potential ethical problems associated with use of stored HBS, how much information should be provided to individuals before they are asked to consent to use of their stored HBS for research in future? If individuals are well and properly informed, are they likely to consent or refuse? Are they predisposed to granting one-time consent for future unspecified use research on stored HBS? What would be the preferred consent model for these potential donors? Would individuals consent to the storage of HBS from their dead relatives for future unspecified use research?
- **Consent Issues (Comprehension):** The extent to which participants understand the rationale, benefits and drawbacks of future unspecified use research on stored HBS is unclear. Which types of HBS would potential research participants donate for storage and re-use? How do potential research participants perceive their relationship with their body tissues and fluids submitted for research or treatment purposes? It is not even clear whether patients' attitudes to donating residual tissues for research would be affected by knowledge of how these tissues (sometimes considered ''surplus'' or ''waste'') are handled and disposed of post-treatment and that it is these tissues that may be used in research. How should results of uncertain significance or new useful information be communicated to the HBS donors?
- **Issues of Ownership, Property, Access:** It is also unclear if and how the issues of ownership and property rights are resolved with individuals whose tissues are used in these researches. Some of the other research questions that arise include–Who owns the residual specimen between the researcher, the institution and the research participant? Should donors be accorded control or access to the specimens or data derived from the samples? What are the obligations of the researcher, research institutions or research sponsor towards such research participants and the community?

Nigeria, with her large and heterogeneous population, for whom body tissues and fluids may be socio-culturally significant, could serve as a valuable source of information on this issue.

1.4-Aim and objectives

The aim of this research is to determine the knowledge and attitude of potential research participants in Nigeria to the use of stored human biological specimens (HBS) in future unspecified use research (FUUR). The objectives of my research are:

- To determine the understanding and concerns of potential research participant in Nigeria on FUUR with stored HBS.
- To determine the willingness of potential research participants in Nigeria to grant consent, and the type of consent they are willing to grant for FUUR on stored HBS.
- To determine the types of HBS that potential research participants in Nigeria are willing to donate for FUUR on stored HBS.
- To determine the views of potential research participants in Nigeria on ownership, access and control of HBS; privacy and confidentiality of data; benefit sharing; commercialization and disclosure of research findings with respect to future use of stored HBS.
- To determine the views of potential research participants in Nigeria on promoting and encouraging donation of HBS for future unspecified use research.

1.5- Significance:-

The information obtained from this relatively novel research will inform researchers about the potential for conducting research on stored HBS in a typical low resource and low literacy environment like Nigeria. It will also contribute to understanding the acceptable types of consent and the types of HBS that prospective research participant and communities in environments like Nigeria are willing to donate to researchers who require stored human biological specimens.

The information obtained from this research would be important in improving community engagement and how ethics committees resolve requests for use of stored HBS, thereby enriching informed consent/community engagement processes and enhancing trust in research. It will help develop genuine, legitimate, pragmatic, respectful and inclusive research partnership between the research participants in Nigeria and local /international researchers. The information garnered would be helpful in the development and implementation of local and international guidelines for future unspecified use research on stored HBS. In the long term, this study could contribute to development of bio-banking facilities and their use in Nigeria.

CHAPTER TWO

LITERATURE REVIEW

2.1- Human biological specimens and research

Research involving the use of human tissues and fluids (biospecimens), or the use of information derivable from such, remains a fundamental cornerstone of medical research and scientific knowledge. Human tissues and fluids donated for research purposes, removed at surgery or at coroner or consensual autopsies, left over from diagnostic and therapeutic requirements, or held in archives are important sources of research material. The overarching objective of such researches is to develop generalizable knowledge to improve health and/or increase understanding of human biology; with persons who participate being the means of securing such knowledge (Emanuel et al,2000).

The ethical use of human tissue banking and analysis is rapidly becoming an important issue with the growth of clinical and basic research worldwide, particularly in the developing world (Upshur et al , 2007). Increased participation of individuals from low-income countries in research in recent decades (largely stimulated by the HIV pandemic and the need to carry out clinical trials expeditiously on large numbers of patients), has intensified the debate on over these issues, particularly as they relate to international collaborative research that may require use of stored HBS (Benatar and Singer, 2010).

With recent advances in genetics, molecular biology methods, and the rapid growth of biomedical studies in low and middle income countries (LMIC), there are growing concerns about the risk of research to the citizens of these countries. In response to such concerns, researchers are increasingly confronted with various ethical guidelines relating to the exportation, storage and use of stored specimen as well as data protection policies that are increasing the cost of research. This development is leading many researchers and research organizations to conduct research in developing nations where costs may be lower (Reymond et al ,2002;De Vries and Pepper,2012;Dickenson,2005)

Stories of ''parachute, tourist and mosquito'' researchers who come in from developed to developing countries just to collect specimens and leave a bound (Muula and Mfutso-Bengo ,2007); Mudur,2002;Dickenson,2005).This approach to research impedes the development of scientific capacity in the developing world and negatively impacts the willingness of potential research participants to trust researchers and participate in future research (Hall, 1989; Leach et al ,1999).

In addition to the ethical issues surrounding the use of HBS in future unspecified use research, the social meaning of HBS in different societies and contexts is not known. Some societies may see such materials as a something that connects a person to a community or place thereby creating an identity that may play an important role in the prevention and healing of illness. Others may see it as waste materials that needs not be accorded any special treatment.

Some people may assert that while human tissue cannot be said to have human dignity, human dignity is nevertheless implicated by human tissue, making what is done with HBS and how it is done worthy of moral consideration. These considerations lead to an emphasis on showing respect for human material (Jones et al, 2003). Irrespective of the tissue type, storage and use of HBS in research makes it imperative that the research be done ethically. (Kirchhoffer and Dierickx, 2011; Parker, 2011). When such proper understanding of meanings attached to HBS is ensured, it can facilitate the crafting of ethically acceptable approaches to the collection, storage and use of HBS (Jenkins and Sugarman, 2005).Moreover, there are complicated issues underlying public trust in medicine as well as scientific and genetic research that must be addressed. Any innovative strategy for public education and community engagement should also take into account cultural settings and historical experiences, which may have contributed to distrust or lack of interest in the past. All these point to a critical need for further empirical research on innovative approaches to the process of informed consent for research use of stored HBS that take into account scientific, social and cultural factors (Rotimi and Marshall, 2010).

2.2- Some controversial cases involving use of stored human biological specimens in research

1 Genetic information derived from blood samples taken from members of the Arizona Havasupai Tribe and used for research which was not covered by the original informed consent process (Mello and Wolf, 2010). Though Arizona State University agreed to pay US$700,000 to 41 members of the tribe to settle legal claims that the university's researchers improperly used these stored blood samples in research, the case threw up crucial questions on what constitutes adequate informed consent for HBS collected and stored for future unspecified use research. The Havasupai India tribe case highlights the need for researchers to adequately understand and consider the perspectives of their study population. It also shows the need for community consultation or community engagement which can help to identify areas of concern regarding possible future uses of HBS.

2 In the 1960s and early 1970s, blood samples were collected from the Amazon's Yanomamo Indians by a group of researchers and stored in laboratories in USA for decades. After about

10years of seeking the return of their blood samples, the indigenous group finally succeeded in retrieving their samples. The case was triggered of by a controversial book by an investigative journalist in which researchers were charged as having acted unethically in their dealings with the Yanomamo, especially with respect to the informed consent process (Couzin – Frankel ,2010).

3 In the Adler Hey Scandal, there was unauthorized retention and disposal of human tissue including children organs removed during autopsies conducted in several British hospitals including the Adler Hey Children's Hospital, Liverpool from 1988 to 1995. During this period, organs were retained in more than 2000 pots containing body parts from around 850 infants. Until the public inquiry in 1999, the general public was largely unaware that hospitals within the National Health Service (NHS) were retaining organs of their patients without family consent. Following the revelation of the Adler Hey scandal, many public figures openly expressed concern for the potential harm that could be done to scientific research and organ donation. The scandal led to the Human Tissue Act of 2004, which overhauled legislation regarding the handling of Human Tissues in the UK and created the Human Tissue Authority (Wikipedia, 2012).

4 In the AutoGen case, DNA samples were obtained from the Tongas by AutoGenand stored to study genes involved in diabetes, obesity and other diseases (Rotimi and Marshall ,2010). Serious ethical questions were raised about privacy, ownership and the commercialization of genetic material in a resource-poor setting such as Tonga. Eventually in 2002, AutoGen indicated that they would not pursue the development of a genetic database in Tonga.

5 In 2008, a University of Tokyo team retracted a research paper because researchers had failed to obtain informed consent from tissue donors or approval from an Institutional Review Board (Normile, 2008).The tissue samples used for the retracted paper were collected and stored for future unspecified use research long before Japan's Ministry of Health issued guidelines for IRBs and informed consent in 2003. This case brought to light the fact that few researchers in Japan at that time were aware of the ethical issues surrounding use of stored samples because the ministry's guidelines did not have anything about such legacy samples.

6 A newspaper report of the export of millions of HBS from Uganda for storage in other countries (Upshur et al 2007). According to records from the Uganda National Council for Science and Technology (UNCST) a regulatory body response for research in the country, of all the biomedical studies done, 80% of the human biological samples collected had reportedly been exported. Uganda consequently had lost millions of dollars. Records had shown an average of 200 studies being carried out in Uganda per year, 50% of which were biomedical

studies involving biological samples and 51% of the total studies being on HIV/AIDS. The foreign researchers who came into Uganda then used excuses like lack of storage facilities in Uganda, and a short supply of staff and equipment to work on sophisticated experiments to justify the exportation of the samples. Some claimed they had limited budgets so they could not stay in Uganda for a long time. Others stated that there were more experienced personnel and specialized laboratories overseas to ensure quality assurance, especially as regards multi-center trials. The practice had to be nipped in the bud to prevent more loss of foreign exchange accruing to the health sector as a result of the biomedical researches.

7 In the case of the Karitiana Indians in 1996, a team of researchers visited, promising them medicines in return for their blood samples which was collected for storage and FUUR but they got nothing in return (Rohter,2007).

8 A study by molecular biologists at the University of Cambridge analyzed DNA from stored saliva specimens of 958 individuals from Kerala, India. These samples were exported from India without following the Indian national guidelines (Mudur, 2002).

2.3-Ethical issues in stored tissues and research

In developed countries, the number and scope of large-scale biobanks/biorepositories has rapidly increased. By allowing researchers an unprecedented ability to identify fine-grained relationships between genetic, environmental and lifestyle factors, these biobanks promise enormous benefit for society (Cambon-Thomsen et al,2007;Cambon-Thomsen,2004). For the last 50 years, the main sources of guidance on the ethical conduct of clinical research have been the Nuremberg code, Declaration of Helsinki, Belmont Report and the International Ethical Guidelines for Biomedical Research involving Human Subjects. In spite of this, complex ethical issues are now being raised and widely debated with respect to the use of stored human tissues in FUUR that are not adequately addressed by these guidance documents. These issues arise because of rapid advances in research technology and genomics. These issues border mainly on informed consent, ownership of samples, privacy/confidentiality, benefit-sharing, commercialisation, and disclosure of research findings among a host of others.

One prominent concern identified in relation to the long-term storage (either as isolated collections or in bio-banks), future use of HBS and derivable data relates to the most appropriate informed consent process to be adopted under these circumstances. Whereas most guidelines and codes also require that informed consent be properly documented, informed consent is much more than signing a consent paper. It is a continuous process of communication between the investigator and the research subject. As the body of knowledge impacting a study often changes, research subjects should receive information from

investigators after they have enrolled in a study, such as significant new findings that may affect their decision to participate in research or clinically useful tests results (Wendler and Rackoff ,2002; Renegar et al ,2006;Resnik,2009). This is relevant with respect to cases where re-consenting may be required.

In addition to consent, other ethical challenges relating to use of HBS include concepts of ownership, access and control of HBS; privacy of sources and confidentiality of data, disclosure of research findings, benefit sharing and commercialization. There is an extensive array of literature on the perspectives of research subjects regarding the use of their tissues in the developed world but little is known about the perspective of those in the developing world (VanSchalkwyk et al,2012).

Informed consent:. Various approaches to consenting potential research participants had been adopted in settings with established bio-banking practices. Although the collection, storage and research use of bio-specimens and data are typically thought to involve minimal risk, information must be conveyed during the consent process that can be complex or controversial. (Beskow et al, 2012) In the initial consent methods, a no-consent method will not approach persons regarding participation as regulations for exemption from human subjects research are being met. (Simon et al, 2011). In the prospective opt-out method, potential research participants are provided with information about the bio-bank and given the opportunity to signal any desire to be excluded from the research. In the prospective opt-in method, potential research participants are provided with information about the bio-bank and given the opportunity to actively signal their willingness to be included in the research. Although opt in consent is widely considered better at promoting individual autonomy and active decision making than opt out consent as they provide more information ,many problems have been associated with opt-in consent process including the potential for participant burden, misunderstanding of contents, sample biases, and adverse study accrual rates(Simon et al,2011; Jegede, 2008).Though opt-in consent processes are resource-intensive often, they are better suited to some research protocols than opt-out consent, including protocols seeking to recontact, reconsent or subsequently collect additional data from participants.

With respect to the scope of permission to use donated, stored biological samples and health information in future research, the approaches used so far include a one-time “general” or “blanket” consent approach, study-specific/reconsent approach and categorical/tiered approach. In the general consent approach, participants prospectively agree to their samples and health information being used in any future research deemed appropriate by a biobank, relevant health research ethics committee, researchers, research organisation and/or other

entities. In the study specific consent, participants are re-contacted and asked to consider participating in specific research studies for which they are eligible. This is preferred by some experts because it bears the traditional hallmarks of informed consent, namely the capacity to thoroughly inform individuals of the various elements of the research in question, including information on potential benefits and risks (Beauchamp and Childress, 2008). Moreover, so much public confusion, misunderstanding, and mistrust have been associated with the use of general consent for future research use.

In the tiered approach, individuals prospectively choose from a list or "menu" of disease categories or research methodologies, or designate those areas of research their specimens or health information should not be used. Though this method is considered by many to be a "best practice" that enhances autonomy by allowing for greater choice and control over research participation, it is known to be unwieldy, burdensome and largely uninformative (Simon et al, 2011; Beskow et al, 2010).

After so many decades of health research ethics, fundamental ethical milestones are being questioned in the light of challenges being thrown up by demands for stored human biological samples. The UK Human Tissue Act of 2004 focuses on the identifiability of human tissue as being the main detail of importance with regards to the need for consent. That is, assuming normal approval for the research project has been obtained, the Act allows for the waiving of explicit, individual consent only when non-identifiable tissue is used (Parker, 2011; Furness, 2006).

While some authors have abandoned informed consent in favour of general consent (which in itself does not meet the common rule benchmarks for adequately informing participants of the specific nature, risks, benefits and other elements of the future research), others have opted to enlarge the definition of what constitutes non-identifiable samples and data (Elger and Caplan, 2006). It then follows that any research using non-identifiable samples does not create an obligation to obtain informed consent and approval of the protocol from an IRB or a research ethics committee. The advantage of enlarging the definition of non-identifiable is thus obvious:- researchers can maintain high standard of informed consent but are provided with a simple means to escape strict regulation by entering agreements that prohibit them from access to one code for a biological sample, without having to destroy the link. Until 2004, Europe and USA considered coded and linked anonymized samples as identifiable and requiring subjects' consents to future use. Only if this link is irreversibly destroyed are samples and data considered unidentifiable, and thus, research using such samples was not considered human subject research in accordance with the Declaration of Helsinki.

However, with the enlarged definition as given by the US office for Human Research Protection {OHRP}, a number of issues come into prominence .Firstly, research involving biological samples still implies risks for identifiable groups and communities because the anonymity of the individuals does not translate to the anonymity of the group. (Elger and Caplan, 2006). Secondly, if researchers use coded samples without having access to the code, this means that a link exists, which may still be used to contact donors at any time. Thirdly, there is the possibility that the code could be broken for less justifiable reasons than alerting donors of a possible future harm. Moreover, one might question the sense of a solution whose main goal is to escape existing regulations so that most biobank-based researchers can take place without further monitoring.

As part of the debate, it had since been established that as long as samples contain any trace of DNA, they are not fully anonymous. (Lin et al, 2004). Rather, the term "anonymous" had been deemed to be more appropriate when referring to biological materials stored alongside associated information, but with all information that would allow identification of the participants being stripped, either irreversibly (unlinked anonymized) or reversibly (linked anonymized). In the case of linked anonymized sample, identification is possible by code, to which the researchers and other users of the material do not have access. Coded samples, on the other hand, have the same characteristics as linked (reversible) anonymized samples but researchers and users have access to the code. Finally, samples are considered to be identified if the information that allows identification is associated directly with the samples (Elger and Caplan, 2006).

The debate over when investigators should obtain consent for research on anonymizable biological samples suggests a new paradigm for understanding individual's involvement in research and competing models of research participation; namely the subject model, experiential model and contribution model (Wendler, 2002). Involvement in most researches includes 3 distinct elements; participants are exposed to risk, they have to perform certain behaviours or tasks prescribed by the research project, and their contributions help answer the research question.

The discussion of the 3 models of informed consent was based on these 3 elements. The subject model identifies the need to obtain informed consent in the participant's exposure to risk from the research. Consent to use existing tissue specimen is needed only when the samples are linked to personal identifiers. In the subject model, it is believed that there is no reason to solicit sources' informed consent because research using anonymized samples poses no direct risks to sources.

The second model finds the need for informed consent in research procedures that have some personal effect on the participant- where they interact with the investigators or are asked to do certain things. Under this model, research that uses tissue samples obtained for other reasons and that contain no personal identifiers would not necessarily require consent, since the source of the tissue specimen is unaffected by whether the research is performed or not. Similarly, in experiential model, there is no reason to solicit sources' informed consent because anonymized research may not affect sources personally, particularly for samples that were obtained in the past.

The third model focuses not on risk or interaction, but on whether the individual makes a contribution to a particular research project. An individual contributes to a particular research project anytime information about that person is included as data in the project. Wendler concludes that although the contribution model would argue for obtaining consent for a specific project if such consent would impose a serious burden on researchers, the potential value of research may outweigh the individuals interest in controlling precisely which research project they contribute to (Wendler,2002). In other words, individuals can ethically provide a general consent to future research on their biological samples without knowing of and approving of every use of their samples. In the same light, some believe that even when a person is not asked to do anything additional for a research project, that person may wish to make decisions about whether to contribute to a certain research project (Mears, 2002). It was stressed that if any member of the research team can identify the source of the samples, an IRB must review the research use. If the source or the sample is not identified, an exemption from IRB review may be required. In her reaction to Wendler's work on the 3 models, Mears also highlighted that previous recommendations for collection of new tissue samples that might be used for research in the future have included informing patients about the possibility of notification in the event of a clinically important discovery, and warning patients about possibility of incidental findings (Mears ,2002).

Some bioethicists have suggested that a gift model may be better than one-time general consent for research with human biological samples (Caplan and Moreno, 2011). Giving a gift involves voluntarily transferring control of something of value to another person without any anticipation of reward or compensation. Typically, the giver is not informed of how the recipient will use the gift, and recipient is free to use the gift as one chooses or decides (Murray , 1987). On the other hand, one-time general consent involves asking individuals to prospectively consent to allow investigators to store samples indefinitely and use them for a

broad range of researches. Because this type of consent is obtained years in advance, it is not possible to describe the specific studies for which the samples will be used.

In analyzing the 5 central challenges which arise in the context of obtaining and storing human biological samples for future research, it was suggested that one-time general consent is better than a gift model (Wendler,2012).With respect to providing information to potential donors, one-time general consent seems better suited even if it cannot describe details of future uses. Wendler however failed to mention that one-time general consent may not explain most possible risks and benefits of future researches (Wendler, 2012). With respect to which future studies are allowed, one-time general consent sets explicit limits on the use of donated samples, while recipients are typically free to decide how to use the gifts they receive.

Proponents of the gift model however posit that a gift model could incorporate similar safeguards. One-time general consent supporters believe that it gives investigators the flexibility to decide which approach to use on the basis of the needs of the study in question, when it concerns the possibility of donors changing their minds. Under one-time general consent, potential donors can then be informed that they will or will not be allowed to change their mind. Because donors relinquish control of the gifts they give, a gift model may seem consistent with a situation where investigators plan to strip samples of identifiers, thereby making it impractical or impossible to remove previously donated samples. With respect to research involving children and adults incapable of consenting, a gift model might inadvertently block investigators from obtaining samples in these contexts because of lack of competence (Committee on Bioethics, 2001).

Given the points of difference, it is noteworthy that an Advance Notice of Proposed Rulemaking issued on 26 July 2011 by the United States Of America (U.S) Department of Health and Human Services considered the endorsement of one-time general consent for research with human biological specimens and its possible incorporation into U.S. federal regulations (Wendler, 2012). Some commentators continue to argue that, as with other types of research with humans, donors should only consent to the specific studies for which their samples will be used when the studies are proposed. However, this approach will require researchers to keep track of donors for long periods and to obtain consent repeatedly for studies which may merely vary in inconsequential details (Clayton et al, 1995; Hansson et al, 2006).

A number of surveys in the developed nations especially have been conducted to determine the attitude among donors to the use of human biological materials for research. Conceivably,, the heterogenous picture this has created reflects the fact that surveys explore different types of donors, different applications of researchers in relation to different types of biobanks, using

different methodological approaches and asking different questions (Hoeyer,2008). In as far as surveys seek to measure public attitude to help shape legitimate policies, the resulting measurements contain contradictory conclusions with few messages.

With the plethora of research done on this topic, few general insights are noticeable. Firstly, the types of tissue asked for and the position of the donors in relation to the research project seem to influence the view of research on tissue. Cancer patients are generally very supportive of research on their tissue (Pentz et al, 2006); potential participants on cohort studies are less willing but still relatively supportive (Kettis –Lindblad et al, 2005), while the close relatives of potential cadaveric donors are least likely to accept donation (Womack and Jack, 2003). Secondly, only a minority would never participate in a bio bank research (Chen et al 2005; Goodson and Vernon, 2004) but the social groups most likely to abstain differ between national contexts (Pentz et al, 2006; Wendler and Emanuel, 2002; Hoeyer et al, 2004; Kettis-Lindlad et al, 2007). Thirdly, a majority or at least a substantial minority, think the donor should be involved in a consent process that enables one to have a say concerning retention of tissue, but whether people prefer broad consent or specific consent differs between surveys (Chen et al, 2005; Wendler and Emanuel, 2002; Stegmayr and Asplund, 2002; Igbe and Adebamowo, 2012).

A review of 30 studies that reported the views of individuals on consent for research with human biological samples showed that most respondents want to decide whether their samples can be used for research purposes (Wendler,2006). Of the 20 studies which assessed willingness to donate, 17 found that at least 80% of respondents would donate a sample if asked (Wendler, 2006).Consistent with these findings, four of the five studies that specifically asked about left-over samples found that most respondents (93-99%) were willing to donate them for research. In six of the studies which examined different consent options, 79-95% of people were willing to provide one-time general consent and rely on ethics committees to determine the studies for which their samples would be used. One limitation of these studies was their focus on blood samples. The data analyzed in this review of thirty studies were consistent across many different groups, including religious leaders, participants in past and present research, and the general public. This consistent and widespread support indicates that one-time general consent offers people the choice reasonable people want to make when deciding whether to donate samples for future unspecified use research.

In another related study, data was gathered using a telephone survey of 504 individuals living in the United States, comprising 2 cohorts. Of the respondents, 65.8% would require their consent for research on clinically-derived samples with personal identifiers, 27.3% would

require it for research on clinically derived samples that are “anonymized” (Wendler and Emanuel, 2002). The investigators concluded that it appears that most sources want to control whether their samples are used for research purposes, are not concerned with the particular disease that will be studied, and want to receive results of uncertain clinical significance. Because there were very few minority respondents, these results may not accurately reflect the views of minority populations like African-Americans in the United States.

In a general reaction to this contribution of Wendler and Emanuel, it was argued that the first question to be answered is not what is the size of the majority needed to override the requirement for informed consent of research subjects; rather it is whether there are any circumstances under which persons, tissue samples, or information about them, may be used for research without their consent. The argument goes further to state that the pluralism of American culture does not permit, in principle, universal policies based on a majority vote to decide who and what can be used for investigational purposes (Sade, 2002).The unconsented use of anonymized human samples or information derived from them generally had been justified by the claim that if individuals who provide samples cannot be identified, they therefore cannot be harmed or at least can be harmed minimally. This had been held to be true whether harm is viewed in terms of physical harm or psychological harm. Sade argued that the claim is not persuasive as it assumes that there is some universal measure to establish a ranking of severity of harms; when no such measure exists (Sade,2002). Only the subjects can weigh the severity of potential harms to themselves or to their communities, in terms of their own values, preferences or concerns. He argued that though research subjects’ reasons for not wanting their anonymized biological materials or information to be used in a study may be plausible or implausible, reasonable or unreasonable, it was critically important to assert the principles of personal self determination.

The issue of accurate use of words in describing human research, in order not to obscure the actual status of research subjects, was also raised. Sade also made reference to the work of Wendler and Emanuel in which they used the term “Source” when referring to research subjects ,and argued that referring to research subjects as source diminishes their status, suggesting that they are things rather than willing persons (Wendler and Emanuel,2002;Sade,2002). Subjects are individuals whose bodies, body parts or responses are studied for the purpose of gaining new knowledge and these individuals have thought processes and certain rights as moral agents. Using the word “source”, carries no connotation of values preferences or using reasons to agree or decline to be part of a particular research project (Sade, 2002).The conclusion reached in this work is that what is at stake in developing

policy for the use of stored samples is the fundamental right to decide whether and how one's body and its parts will be used in research.

In another study of 1,670 consent forms signed by research participants that offered options for future research with participants' samples, 87.1% of research participants chose to authorize future research on any medical condition (Chen et al, 2005). Only 6.7% of those given the option to refuse all future research did so. Although African-Americans were less likely to permit future research with their samples,75% of them still authorized unlimited future research with their samples. One major drawback of this study was the fact that their findings may be limited to major research institutions, and may not be generalizable to research institutions or private practices with smaller research portfolios. Also, because the study was conducted at a research institution, the findings may not apply to samples obtained in the course of routine clinical care.

In a study involving 48 FGD participants and 751 survey participants in the USA, majority of participants reported little or no prior knowledge of biobanking, a recognition of the potential value of biobank-based research, and a preference for making a one-time active and informed choice regarding biobank participation through means of a prospective opt-in consent process(Simon et al,2011). Although their perspectives on general consent model were very favourable, participants did express some concerns over the model. They recognised that biobank participants would have little choice or control over the kind of research their samples would be used in and that they would need to trust the bio-bank to appropriately manage researcher access to their samples and health information .When discussing study-specific consent, participants again emphasised the value of having prior knowledge of the research in question, choice and control over how samples and health information would be used. However, it was considered impractical and likely to stretch biobank resources given the "time" and "money" that many FGD participants felt would need to be invested in this approach. Survey participants who preferred opt-out consent more often preferred broad consent, but the difference was not significant. Age and income were shown to be significantly associated with consent preferences. One limitation of this study is the fact that the research was conducted with members of the public and not with the actual biobank participants. In some cases, attitudes and concern between these two groups markedly differ. Also, the findings are largely specific to Whites and English speakers, and the study addressed only the issue of consent for a competent adult, not the surrogate consent which would be given for paediatric populations, or for impaired adults.

In a related study, almost all clinical patients, regardless of site of care, ethnicity or socio-economic status, were willing to provide a biological sample for research purposes and allow investigators to determine the research to be done without contacting the patients again (Pentz et al, 2006). This study compared two cohorts, one of which was largely African-American and the other largely white. The finding from this study supports the recommendation to offer individuals a simplified consent with a one-time binary choice whether to provide biological samples for research. This contrasts with the findings in another study that preferences for consents model may vary based on ethnicity (Murphy et al, 2009).

In another study to understand the general population's attitudes towards consenting and banking of genetic methods, an anonymous survey was conducted among North Shore Long Island Health System (NSLIJHS) patients and their families in 2009 and 2011 (Kerath et al, 2013). Majority of the respondents (82.24%) here were supportive of the genetic research, as well as their own participation in such research. The results show that 44.4% of the respondents were satisfied with the "opt out" approach for obtaining consent, and 20.7% definitely opposed the idea. In addition, over 80% of those who responded were uncomfortable with a study being done without a specific explanation and without their knowledge. Demographic factors were not found to be descriptive of personal willingness to participate in genetic research, or of approval for the opt-out approach to consent. This study demonstrates a continued concern for the ways in which genetic materials are safeguarded once they are collected, as well a general lack of understanding about the various consent processes that go along with genetic research. One limitation of this study was the fact that the convenience sample used may not be necessarily representative of the population living in the study area.

In another study involving 1,583 subjects participating in the 1990 risk factor survey of the WHO's MONICA project, 1,311 gave their consent for their blood samples to be used for academic genetic research, provided that the ethics committee had approved the study (Stegmayr and Asplund ,2002). The investigator believed this was the first report from a "real life" situation – that is, people's willingness to give consent to genetic research on their own blood donated more than a decade previously when genetic research was not yet an issue. They concluded that it is feasible to obtain individual consent for genetic research many years after blood was donated.

Some investigators were also able to show that many members of the US public support the prospect of making an active and informed initial decision about bio-bank participation but that they have concerns about the need for and potential adverse impact of future – use consent mechanism such as categorical and study specific consent (Simon et al ,2011). In

contributing to the discourse, another commentator suggests that in order to respect donor interests, it is necessary to pay more attention to diversity with regard to bio-bank types and different contexts for donation (Hoeyer, 2010).

A study, examining native Hawaiian preferences for informed consent and disclosure of results, was conducted and modelled after a national study of consumer preferences, allowing a comparison between the national sample and the Hawaii-based sample. The interview schedule included two scenarios on research requiring the re-use of clinically derived and research-derived biological specimens. In this study, 78% of a sample of native Hawaiians would want to be asked for their consent for the re-use of identified specimens and about 35% would want to be consented for the re-use of anonymized specimens, regardless of how they were obtained. In both cases, Native Hawaiians in the Hawaii sample were more likely than whites in the previously conducted national sample to want an informed consent process (Fong et al, 2004). These findings call into question the "Common Rule" and the guidelines of the American Society of Human Genetics, which do not require researchers to obtain informed consent for research use of anonymized specimens .Data from another 1998 American survey showed that of 2,621 respondents, 42% were in favour of blood donation and long term storage for genetic research (Wang et al,2001).

When potential tissue donors in the Swedish general public had to strike a balance between the values at stake, i.e. the autonomy of the donor versus the research value, most (72%) preferred general consent, i.e. where consent is asked for at the outset only. They want the research ethics committee (REC) alone to decide on the use of stored samples, and they would allow storage as long as the sample is useful for research. The minority of respondents who were in favour of specific consent were more likely to be young, well educated, have negative experiences of healthcare and low trust in healthcare authorities (Kettis – Lindblad et al, 2007). The same researchers demonstrated that a majority of 2,928 respondents in a cross sectional survey in 2002 had a positive attitude towards general research. Most (86%) would donate a linked blood sample for research purposes; a total of 78% would agree to both donation and storage, with the most common motive being the benefit of future patients (Kettis – Lindblad et al, 2005).

In Sweden, a randomised sample of 1200 donors who had donated blood and signed informed consent forms for a bio-bank and a biotech company was conducted (Hoeyer et al, 2005). Despite effective informed consent procedures being given as a reason for deeming these facilities ethical, the donors were found to be not well informed. However, only a small number reported their information levels to be of particular importance when bio bank-based

research is assessed in relation to other issues pertaining to research politics, ethics and few of them were unsatisfied with the information they have been given. This study called for a reconsideration of the importance attributed to informed consent in debates about ethics of bio banks and genomics companies and for in-depth exploration about what is at stake for donors in various contexts. In a related study in Sweden, patients refused consent to either storage or use of their samples in about 1 in 690 cases. Rather than having their samples destroyed, about 1 in 6,200 patients wanted to restrict their use. Of those who had previously consented, about 1 in 19,000 withdrew their consent. This gives the impression that refusal to consent to bio-bank research in Sweden is rare. However, a system of presumed consent with straight forward opt-out would correspond with people's attitudes, as expressed in their actions, towards bio-bank research (Johnson et al,2008).

Generally, studies in Sweden have shown that a majority would consent to donation and storage of material in bio-banks, with the most common motive being benefit of future patients (Melas et al, 2010). They recommend a need for guidelines on benefit sharing, as well as trustworthy and stable measures to maintain privacy, as a means for increasing personal relevance and trust among potential participants in genetic research. In the same light, strong emphasis has to be laid on the importance of transparency and accountability in the conduct of research in order to maximize donor participation and confidence and public trust in general (Otlowski ,2007; Lemke et al ,2010).

Among the Finns, a survey conducted in 2007 demonstrated that 34% would not attach any condition on their consent, while 42% said that it was important to obtain consent when the new study contains diverging steps. One-third (30%) were unequivocal about the need for fresh consent for every new research project, and 44% would like to decide what type of research their samples would be used for, if they were included in a normal bio bank. Though majority of the respondents in this study considered their knowledge of bio banking to be limited, they wanted the ability to control how their samples are used (Tupasela et al, 2009)

Findings from THE STRATUM PROJECT (Strategic Tissue Repository Alliance Through Unified methods) suggest that the general public in the United kingdom are keen to donate human biological samples for medical research, with participants preferring less restrictive informed consent models. They were of the opinion that an opt-in approach to tissue donation would provide the most control for the public. General consent and tiered consent for donating left over tissues were equally popular and preferred over specific consent. Most participants in this study would still agree to donate their samples, even if their preferred model of consent was not an option. (Lewis et al, 2012).One other study obtained prospective research subjects'

perspectives on an array of issues affecting participation in bio-banking research within the context of detailed information provided in a consent document (Beskow and Dean, 2008). Considerably, more than half of the 40 interviewees were comfortable with unlimited duration of bio-specimen storage and periodic contact to inform them of additional research opportunities.

In a Jordanian study, it was concluded that the Jordanian population appears to be willing to take part in bio banking- based research, although more effort would be required to increase awareness and promote wider participation (Ahram,2012). Almost two-thirds of respondents in this survey agreed to donate both bio-specimens and relevant information for bio banking. The responses obtained here demonstrated a significant correlation between intention to participate with both younger age ($r= 0.12$, $p<0.001$) and increasing education ($r= 0.08$, $p<0.001$) independently, but not gender. The study also highlighted the need for deeper interaction of the public with researchers as an avenue for easing doubts and concerns about bio banking-based research.

In a multi-country study involving researchers, IRB members, policy makers and collectors of HBS, from China ,India, Japan ,Egypt and Korea, it was demonstrated that in non-western countries they agree that prospective donors of tissue samples for research should be able to provide specific conditions under which their tissues are used for future research. A substantial portion of them believed that one should allow tissue donors the option to be re-contacted for consent for any future research use of their HBS (Matsui et al, 2009).In the study, the majority (44.9-59%) of the respondents favoured the multiple-type of content option to be given to the donors, rather than the binary type of option. The study findings did not support the notion that the requirement of specific informed consent to future research is culture-specific .Some investigators had held the opinion that it is necessary to pay more attention to diversity with regards to bio-bank types and different contexts for donation, in order to respect donor interests (Hoeyer, 2009). This is predicted on the view that tissue type, procurement situation including who is asked to provide consent, and the biobanks geographical, social and historical context influence how various potential donors view the issues of consent, reconsent and feedback of research results. Findings from various surveys show that there are differences in attitude depending on the type of tissue collected in a given bio-bank. Apart from the common biological samples such as blood, urine and saliva, other tissue types which may be donated include gametes, embryos, umbilical cord blood, cadaver and left over (residual) material, post surgical biological samples, and samples obtained from minors and pregnant women.

Concerns have also arisen following increased bio banking-based research initiatives in obstetric and paediatric populations around the world. Several bio banks have focused on collecting samples during pregnancy, often with cord blood taken post-delivery. Others have specifically enumerated pregnancy and paediatric complications as a focus of the bio-banking researches. In a study related to the Chicago Lying-in Pregnancy Program (CLIPP), it was shown that enrolment into research correlates directly with trust and minority women are willing to donate blood samples for research, despite the frequent finding of low research participation in minority populations (Joseph et al, 2008; Murphy et al, 2004). Two major limitations of this study were the use of a convenience sample and a non-standardized survey instrument.

In a similar study in Halifax, Canada involving 443 pregnant women, most of the women (86%) would elect to store cord blood in a public bank; many citing altruism as the reason for this choice. Apart from using it for bone marrow transplantation, 67% mentioned research as an additional acceptable use of cord blood, (Fernandez, 2003).

Public concern over the research use of oocytes , spermatozoa, embryos and foetal tissue have been noted, in many countries, though isolation of human embryonic stem cell lines has opened a promising and pioneering area of research. In a prospective study of 300 couples who underwent IVF/ICSI treatment, 54% consented to donate their surplus embryos for research. Couples of ethnic minority origin were less likely and willing to consent for research compared to caucasian couples (Choudhary et al, 2004).Similar studies suggesting a variable level of willingness to donate supernumerary embryos for research had been conducted; with the level ranging from 92% in Sweden (Bjuresten and Hovatta, 2003), 50% in the UK (Brett et al, 2009), 57% in Denmark (Bangsboll et al, 2004), 30% in Australia (Burton and Sanders, 2004) and 30% in Spain (Luna et al, 2009). Research purpose, treatment stage, embryo quality, religious beliefs and altruism appear to be important factors for donation. Being at the beginning of IVF/ICSI treatment, not knowing the aim of medical research, having strong values about life, or having good quality embryo appear to motivate those not willing to donate embryos (Hug, 2008). One study indicates that people are much more willing to donate their own tissue than that of their children (Goodson and Vernon, 2004). In childhood cancer research, however, parents are generally willing to consent on behalf of their children and again it might reflect what could be termed an assessment of relative danger and whether researchers are construed as outsiders or helpers in the specific situation. In one study, for example, couples in fertility treatment were inclined to donate so-called spare embryo because they judged fertility doctors as health professionals who had been helping them, (Hoeyer,

2009). In this case, donation was viewed as compatible rather than in potential conflict with caring for a future child.

Another area of concern is the use of left-over biological materials in research. In a study conducted on patients' experiences on donation of their residual biological materials, four conclusions were reached. For left-over tissues to be used, patients must clearly understand the following:- the type of consent they are providing (opt in or opt out);the parameters for the future research use of their tissues; the safeguards put into place to protect the individual and the donated tissue from unethical use; and the commercial implications of their consent (Chan et al, 2012). Studies show that tissue excised during operation (e.g. tumours, breast tissue) is described as alien and 'not mine' by patients and readily donated (Hoeyer, 2009). When tissue is collected as part of clinical care or national screening programme, assent rates are generally high. Donation rates and donor support for tumour banks are generally very high compared to other types of tissue banks. When people feel threatened by cancer or some other disease, research can be construed or misconstrued as part of a fight against the disease, whereas participation in cohort studies with healthy participants introduces potential risks where there might have been none.

In the same light, blood and urine tests are generally seen as routine measures of limited significance, and blood for instance is accordingly seen as easier to donate than the DNA it contains. One study in the United Kingdom (UK) suggests that the majority of respondents would be willing to consider giving open-ended consent for the use of blood left over from routine clinical tests in general practice to be stored and used later for medical research. Despite general supports for these collection methods, respondents expressed concern about future uses (Treweek et al, 2009). Three limitations of this study include the low response rate, under powering of the study and the difficulty respondents had with the questionnaire.

Some other writers have also addressed the issue of postoperative informed consent. It was concluded that there was no reasonable objection to the process of postoperative research consent for the use of surgical tissues and associated medical data, provided it is properly regulated (Hewitt et al,2009). In a study involving 264 cancer patients in the Netherlands, three different consent procedures were offered, and 99% of the patients consented to research with their residual tissues. (Vermeulen et al, 2009). Patients preferred "opt-out plus" (43%) above one time consent (34%) or opt-out according to the standard hospital procedure (16%). The majority of respondents preferred information to be given before or during hospitalisation.

Studies in other settings have reported similarly high consent rates for the use of residual tissue in medical research (Stegmayr and Asplund, 2002; Womack and Jack, 2003; Furness

and Nicholson, 2004; Chen et al, 2005; Bryant et al 2008) Patients are known sometimes to consider their tissues to be special, as it allows them contribute to medical progress. Earlier studies found that surgically resected tissue had no special emotional value for most respondents (Start et al ,1996). Among the Chinese, 64.7% of the respondents were willing to donate residual samples; of which 16.7% desired the option to withdraw their donation anytime afterwards. The overall assent rate for future unspecified use research was as low as 12.1%; this not being un-associated to the low level of public trust in medical institutions (Ma et al, 2012). Respondents who trusted medical institutions were more willing to donate bio-samples, which might be due to their lack of concern about the eventual use or outcome of the donation. The strengths of this study were the high response rate, the diverse population examined and the integrity of the data gathered from face-to-face interview. The investigators recommended specific consent approach as a better method to encourage Chinese to donate bio-specimens. This issue of some degree of distrust of medical institutes and medical research was also emphasised by some other authors (Jianping et al, 2010).

Numerous surveys have actually demonstrated that most individuals who have had tissue removed for other purposes have no objection to the unlimited use of excess tissue in future research studies. The findings – as well as the position that the law appears not to recognize donors' personal ownership rights pertaining to surplus tissue specimens taken from those individuals for diagnostic or therapeutic purposes - underpin the contention by some that a patient's valid consent for future research uses of previously collected tissue specimens should be made on the basis of a binary choice (either authorizing all future research uses or none all) rather than requiring investigators in every new research protocol to track down and obtain specific consent from every tissue donor, even if the specimen is identified only by a code (Hakimian and Korn ,2004; Chen et al,2005).

Regarding obtaining consent for left-over body materials, it had been suggested that the reasons why consent was not being obtained in the past for the research use of left-over materials included the presumed limited availability of materials for scientific purposes, bureaucracy, the right of self-determination which may be considered relative with regards to left-over biological materials, the principle of solidarity, the fact that lack of consent had not caused problems in the past, the possibility of safeguarding patients' privacy and interests without a consent system and the fact that the alternative use for leftover body material is to discard it which helps no one (Van Diest,2002). Van Diest pointed out that the general feeling among his colleagues is that the vast majority of patients are not very afraid that their privacy is breached and their interest is harmed by re-use of their leftover body materials, and will

trust doctors/scientists to use them properly for educational/scientific purposes instead of discarding them. He, however, suggested that permission to use these materials be obtained especially in the case of non-anonymous use (Van Diest et al ,2002). Results from another survey conducted in the UK also confirm that the vast majority of patients are indeed happy for "surplus" biopsy material to be used for research; the situation though not being parallel to the use of autopsy tissue (Furness and Nicholson ,2003).

Regulatory proponents, however, additionally cite evidence that at least a significant minority of patients polled want to be informed in advance and be afforded the opportunity to consent to or refuse the use of their tissue for research purposes (Goodson and Vernon, 2004). This desire bolsters the argument that the storage and use of tissue specimens in research protocols is a matter about which people really care and therefore, strongly want their autonomy respected. The subjects for this study (Goodson and Vernon, 2004) were recruited from a National Health Service dental practice rather than primary or secondary care to remove bias attached to studies of surgical patients or patients attending primary care physicians for conditions relating to tissue removal. A critical review of the questionnaire applied in this study gives the impression that it is a vaguely worded and ambiguous one which may give misleading results.

Another investigator argues that the best way to retain tissue for research is through educating and encouraging people to donate their redundant tissue, not by taking them without their knowledge (Savulescu ,2002*).* Among the reasons cited for obtaining consent are – research on tissue can harm patients by disclosing health or other information resulting in discrimination in employment or insurance; patients may have values regarding research, especially commercial research or genetic research; seeking consent promotes public confidence in medicine and research, prevents exploitation and regulates the behaviour of researchers; it may benefit participants by allowing the identity of participants to be known and results with implication for the health of participants to be reported to them (and their families); it may benefit researchers by allowing further information and samples to be gathered from participants and to link databases; it allows sensitivity to be shown cultural values and it empowers research participants and may enable them to share in the proceeds of the research.

Another investigator argued that a current research project ,unlike a future research, can be described to allow for meaningful informed consent, irrespective of being linked to present treatment of a patient or totally separate ;the argument being that it is difficult, if not impossible, for a participant in a research protocol to give meaningful prospective consent to

the use of tissue in a possible future research protocol that is devoid of all relevant information (Kapp, 2006). Along this line, others argue that sometimes it may be necessary for subjects to reaffirm their decision to participate, to re-consent, or to sign or re-sign a document. They went on to suggest that IRBs should determine when it is necessary to re-consent subjects, ask subjects to reaffirm their commitment to research, or re-sign a consent form; with the IRBs providing investigators with guidance for these procedures (Resnik, 2009).

Further with respect to research on medical records and archived information derivable from left-over tissues, some investigators outside the US and Europe have argued that retrospective research on medical records or leftover tissue may be ethically conducted without the explicit consent of individual interests under certain conditions; where individual interests of confidentiality is outweighed by the expected utility of the research (Al-Quadire et al, 2010). This has remained widely controversial. In prospective studies, investigators can readily seek consent and in retrospective studies, participants might not be practically contactable and contacting them might cause distress. Among the Saudi Arabians, 37% of participants required a consent (general or study-specific) for the use of leftover biological materials in research; 49% did not require a consent, while 14% believed that these tissue should be used only for personal medical care. The study also found out that although only about 37% of participants required consent, most participants (>77%) do not, in principle, oppose retrospective research. The respondents were more concerned about medical records research than residual tissue research. This is rather expected as the information in medical records are more profound, more readily identifying, and more related to patients-comprehended information than the information that can be obtained from leftover tissue. However, this may indicate less awareness of the potential wealth of information in leftover tissue as a source of DNA, which can identify the tissue source even with fully anonymized sample; is a diary of the future; and relates not only to tissue but also to one's family. Researchers in Saudi Arabia were able to show that consenting to use of medical records and leftover tissue samples are perceived differently in their population and there was considerable diversity among Saudis' views about consenting for research which may be related to health status (Al-Qadire et al, 2010). The limitation of this study includes being based on a single hospital and on perception and preference rather than on actual consenting/participation.

A similar picture was also shown from preliminary findings based on focus group interviews in Japan which indicated that the lay public and medical professionals may have different attitudes toward the use of archived information and samples without specific informed consent (Asai et al ,2002). Protecting a subjects privacy, maintaining confidentiality

and communicating the outcomes of studies to research subjects were regarded as essential preconditions, if researchers were to have access to archived information and samples used for research without the specific informed consent of the subjects who provided the material. Although participating physicians in the FGDs thought that some kind of prior permission from subject was desirable, they pointed out the difficulties involved in obtaining individual informed consent in each case. Some of the limitations of this study include the need to validate their findings through quantitative research with a nationally representative sample, and the fact that the interview did not focus on epidemiological studies that used genetic analysis thereby making it difficult to apply the results to genetic research. In comparison, a survey of the Irish public suggests that prior consent agreements allowing the supply by general practitioners of anonymous personal health information to researchers may be widely supported, and that populations willing to opt in to such arrangements may be sufficiently representative to facilitate further research (Buckley et al,2011).

Others have also raised the issue of presenting a rationale for mandatory research biopsies and they have offered suggestions for standardization to ensure that high-quality, patient-centered, clinical trials continue to be designed with scientific and ethical rigor. Ethical concerns had been raised when a participant's enrolment on a clinical trial depends on their consent to undergo a mandatory research biopsy. Most research biopsies ordinarily will not result in direct personal benefits to the patients, and the outcome of these tests generally will not have an impact on the clinical care of the trial participants. It is the observation that patients are willing to put themselves at a risk in order to gain access to novel therapies that raises the concern of whether these patients could be subject to a form of coercion when consenting to mandatory biopsies as part of a novel therapeutic trial (Olson et al, 2011). Supporters of mandatory biopsies argue that it is unethical to avoid analysis of biomarkers that could benefit future cancer patients (Cannistra, 2007); participants are not harmed by making access to the experimental treatment conditional on a research biopsy, as a mandatory research biopsy does not interfere with access to standard medical care; required biopsies are acceptable when investigators appropriately weigh the risks against the necessity of the correlative question ;required biopsies should be considered if the correlative assay has been validated, addresses a yet unknown scientific question, and has the potential to impact the clinical care of the patients ;and optional biopsies that are statistically underpowered to answer a scientific question can be un-interpretable (Olson et al, 2011). Opponents of mandatory research biopsies hold that they should be optional if the scientific value of the correlative question is

not yet well established, and also mandate that a separate opt-out section be included in any consent form where a research biopsy is required.

The debate over the storing of organs and tissues at post-mortem examination, without fresh consent from the next-of-kin, has led to a re-assessment of the justification for, and circumstances surrounding the retention of any biological material after post-mortem examinations and surgical procedures, (Jones et al, 2003). After completing the usual autopsy, there is usually a rather large volume of leftover material comprising sections, paraffin blocks and wet material. These materials may be kept for quality control, future diagnostic procedures as requested by the deceased's family members, and sometimes for research and educational purposes. In many instances, overtime, these specimens are not identifiable and be disposed of, used for teaching, used for research or remain in storage. Some posit that with stringent safeguards, such materials may be used even in the absence of consent in research and teaching .The general assumption is that it is the consent of the living people that is crucial in cadaveric tissue donations, because they are the ones principally affected by whatever research is conducted. This consideration has led to an emphasis upon showing respect for human material as well as ''doing no more than what can be justified in advance on reasonable and decent criteria for the benefits of science, justice and society " (Jones et al, 2003; kirchhoffer and Dierickx, 2011).

The lowest donation rates seem to be in conjunction with procuring tissue from recently deceased, especially when commercial partners are given access to the tissue (Hoeyer, 2010). Most people feel that no allowance should be made for commercial use of tissue of tissue unless consent was obtained when collected. If appropriate consent for future uses has not been included in the consent obtained for recently acquired tissue, the tissue cannot be used in further ways. To do so, is to override the dimensions of the consent provided, and show lack of respect for those providing this consent. The low rates of consent to cadaver donation might also be related to reluctant attitude towards donating the tissue of others. It can be important whose tissue that is procured because it relates to whether the person asked to consent will view consent as compatible with care. Protection of the body integrity of a recently deceased person might appear more appealing than acceptance of tissue requests for research. In a caring relationship, the relatives may feel more comfortable protecting the defenceless cadaver against outsiders, including researchers (Hoeyer, 2010).

There are few empirical studies on the research participants' perspectives on stored HBS in Africa. In a Kenyan study that reviewed research protocols submitted to two Ethics Review Committees, 25% out of 388 protocols sought permission for re-use of HBS and only half of

these actually informed subjects of the contemplated re-use. Less than 20% requested storage and again about half of them sought consent from subjects. The findings are strong pointers to the fact that these investigators did not see the need to seek consent for storage, exportation and reuse of samples (Langat,2005).This is problematic particularly, in the light of the growing amount of research taking place in Africa, and with the rise of bio-banking in Africa. The boom in bio-banking has spawned a 'boomlet' of regulations and guidelines, which has created controversies, especially about the importance and definition of informed consent. There does not seem to be an easily identifiable bio-bank policy in most African countries.

An early study involving parents or guardians of children participating in a malaria clinical trial in rural Uganda showed that most participants (95%) were willing to permit blood samples to be stored and exported for future use research and were willing to waive additional consent. These results may not be generalizable to other Ugandans or other Africans. Moreover, since parents or guardians were interviewed regarding future use research of their children's biological samples, and these results may not reflect individuals' views concerning the future research use of their HBS (Wendler et al ,2005). Majority (97%) want to know the kinds of possible future research, suggesting that their expressions of willingness to donate samples for storage and exportation was not exhaustive of their interests in the fate of their tissues. The study did not ask respondents about the deeper issues of community identity, and whether this was of concern to them, and if so, how such concerns might be addressed in the context of the research collaboration (Upshur et al ,2007).

A South African study showed that the majority of participants were supportive of granting one-time general/blanket consent to the future use research of stored HBS. Additionally, a significant minority requested that they be re-contacted if a future use was not stipulated on the original consent. The investigators also reported the expression of great deal of trust in the researches by the participants. This study was conducted with research participants in a TB study in the Western Cape, South Africa (Van Schalkwyk et al, 2012).

Conflicting results were found in a study of adult Egyptian patients(Abou-Zeid,2010).Less than a majority of the Egyptian patients (44.3%) thought that informed consent forms should provide research participants with an option to donate a linked blood sample for future unspecified research. The reluctance to donate a blood sample for future unspecified research was probably due to issues surrounding storage or the undefined nature of the future research involving blood sample. Only a slight majority of the study population (66%) were willing to have their linked blood samples used in genetic research, even with assurance of confidentiality. Many of these individuals did not favour the donation of a blood sample for

future research. Of those who approve of such future research, many favour a consent model that includes an option restricting the future research to the illness they had when HBS was removed. Also, many Egyptians were hesitant to have their blood samples donated for genetic research or exported out of the Arab region to the USA and Europe (Abou–Zeid,2010). Factors to account for the unwillingness of the study population to share their blood sample with other countries, especially those from western world, might revolve around issues of confidentiality, commodification of the samples, religious values or a concern that once blood samples leave the country it might be more difficult to provide oversight on the types of research performed on them. One major limitation of this study was the fact that a large proportion of the study population was illiterate, and as such may have found in difficult comprehending concepts and terms such as genetics informed consents'. The strength of the study, however, was the large sample size and the diverse representation of individuals from different socioeconomic strata.

In a related study in Nigeria, it was demonstrated that the participants accepted bio banking once they were educated about it, though there were different attitudes to elements of biobanking such as types of consent. Half of the discussants supported broad consents, a quarter supported restricted consent while the remaining were in favour of tiered consent. The majority of the discussants did not mind if their specimens are stored for future unspecified research, with only a few wishing to be re-consented before their samples are used for future studies. The main reason for choosing tiered consent was a desire to maintain control over the type of research conducted with donated samples. The major limitation of this study was that it used only qualitative method of data collection. The study further highlighted the need for a careful documentation of the population attitude to elements of modern scientific research and the consenting process (Igbe and Adebamowo,2012). The conclusion realized in this study was that Nigerians are willing to participate in bio- banking but have specific ethical concerns which need to be taken into cognizance.

The consent of participants is usually required before bio-bank samples can be used in research, but the nature of this consent, and how it is obtained, vary widely. Many European guidelines take the view that general consent is acceptable to use samples for future unspecified research projects; US and Canadian policy follows a more rigorous standard (Elger and Caplan ,2006;Hall et al ,2010; Sebire and Dixon-woods, 2007);Beskow et al,2010);Cambon-Thomsen,2004).In Africa, there does not seem to be a consensus in policy. This lack of regional or international consensus, if left unchecked, will likely interfere with the efficiency of biomedical research which makes use of stored human biological samples in several countries.

Ownership, access and control: Over the years, research on stored human biological samples had been conducted with no clear ownership interest being established. The presumed right of researchers and their institutions to collect, store and use these specimens have remained largely undefined. With renewed interest in stored HBS, new questions are being raised about ownership and control of these biological materials (Hakimian and Korn, 2004).

More attention seem to have been focused on ownership of tissue collected specifically for research purposes, than on tissue originally collected for diagnostic purposes and now residing as formalin-fixed, paraffin-embedded tissue blocks within the pathology departments in the world. (Dry, 2009). Though, most of these pathology laboratories are recognised as the legal caretakers of these diagnostic blocks, the distinction between this guardianship and ownership is laced with some confusion. This is so because the notion of "ownership" includes the right to control property, products derived from the property or control profits derived from the property.

People are also asking if tissue banks should assume exclusive control over donated samples, or should donors retain property rights over their tissue and the ability to determine who gets to use them and how? Reduced to a fundamental level, patients' control over donated samples amount to a little more than their right to "withdraw" from a study by having their donated tissues removed or destroyed.

In a number of cases, law courts have considered the question of whether an individual retains an ownership interest in his/her excised tissue that would authorise that person to share in the profit of any commercialization of research results, dictate who controls the sample, or determine how and if the sample will be used in future research. Some court rulings suggest individuals may retain some property rights (and thus "ownership") of certain tissues, especially concerning embryos, ova, sperm and donor organ for transplantation. In most cases involving tissue excised for clinical purposes and tissue donated for research, courts have decided that individuals do not retain of ownership or control of biological material contributed for research, regardless of whether commercial benefit accrues.

In the seminal case of Moore Vs Regents of University of California, decided in 1990, George Moore signed a consent form for a splenectomy as part of the treatment for hairy cell leukaemia. Unknown to Moore, his physician had conducted a research on his spleen cells and created a cell line which was later patented and used by the University of California for commercial gain. Moore then went to the courts and made claims of conversion (when a party takes away or wrongfully assumes the right to goods which belong to another or deprivation of a property interest), lack of informed consent, and breach of fiduciary duty for the use of

his excised tissues and for the failure to disclose personal interests. The court held that the patient did not have property right in excised tissues used to develop new products, holding that even if the excised cells initially belonged an individual, those cells were legally and factually distinct from the resulting research product. The court also decided that the patient could pursue a breach of fiduciary duty claim. It held that when a research relationship exists along with a therapeutic relationship, it is necessary to notify the patient of additional research or economic interests (Hakimian and Korn, 2004; Allen et al, 2010). The court noted that a contrary ruling would couple medical research because it would bestow a continuing right for donors to possess the results of any research conducted on their tissues.

A decade later, precisely in 2003, a group of plaintiffs sued an investigator and a hospital when the investigator developed and later patented a predictive prenatal genetic test from research on donated biological samples from afflicted children, their parents and relatives. The court ruled that the patients had no property right in tissue voluntarily donated for medical research. In the case of Greenberg Vs Miami children's Hospital Research Institute, the judge found no duty to disclose willing participants the potential for future economic benefits from the research, and thus, no misuse or fraud by the investigators (Hakimian and Korn, 2004). In another case of Washington University Vs Catalona, the University refused to relinquish custody of tissues obtained for research purposes when one of the investigator (a professor of Urology, formerly in their service) and 6000 of the patient-donors requested that the samples be transferred to another institution (the professor's new place of employment). The court held that donors made a gift of their samples and did not retain a right to direct that they be transferred elsewhere (Charo, 2006; Allen et al, 2010).

Contrary rulings have also been reached in other cases in which the evidence showed that there was a clear understanding that the patient would retain ownership of the excised tissue(Allen et al,2010), or evidence of fraud on the part of the researchers. In the case of York Vs Jones in 1989, a couple signed agreement regarding procedures for freezing their fertilized eggs, and permitting use for research if they no longer desired to initiate a pregnancy. Later, the couple sought to have the prezygote transferred to another medical school for implantation. The court ruled that the relationship was that of bailee/bailor and the couple did have property right and could re-possess the prezygote (Andrews, L, 2006).

In the Mansaw Vs Midwest organ bank case of 1998, a father sued for right to control the removal of tissue and organs from his deceased son's body, and the court in acknowledging the father's property interest held that it was minimal (Hakimian and Korn, 2004). In the Havasupai tribe vs Arizona State University case of 2004, a native American tribe filed lawsuit

claiming samples donated to local Universities for diabetes research were used for studies on inbreeding, schizophrenia, metabolic diseases, alchoholism, and population migration. The case was settled out of court, with the university paying some money to the tribe, providing other forms of assistance and returning the blood samples (Mello and Wolf, 2010).

In the case of Adams Vs King country of 2008, a donor's organs were sent to medical research institute for research. The family sued, contending that the donor's consent was limited to transplantation. The court held that the family had a claim based on their interest in proper treatment of the body; and not a property interest. In the more recent 2009 case of Beleno Vs Texas Department of State health services, the parents sued the State for the use of over 5 million leftover blood samples that were collected for new born blood screening and were used in research for which parents had not given consent. The case was eventually settled out of court, with the state destroying all existing leftover specimens.

All these court rulings tend to suggest that there is no basis to establish individual ownership of or right to control the use of excised tissue collected or used to develop research product, even while affirming the applicable principles of informed consent. At the same time, it can be inferred that tissue donors do retain certain rights in the tissues, depending on how the informed consent forms are structured. The outcomes of some of these cases also demonstrate that the ownership question does not depend on whether a patient consented to the use of his or her excised tissue for research. Though it is increasingly clear that donors of research specimen do have continuing rights regarding the use and secondary use of their samples, they do not own those samples or control their disposition.

At present, research regulations are built on a theory of autonomy that is independent of any property right in ones tissue. Currently, no laws or regulations exist regarding ownership of leftover materials. The law regarding donor control over excised tissue sample is still evolving. In as much as most of these cases have tended to reject claims that tissue donors retain property interest in excised tissue, there are ongoing efforts to address questions about the donors' right to control the future use of such stored tissues. In as much as this is especially applicable to specimens that would normally be discarded (particularly if it is diseased or no longer necessary for human functioning) if they were not put to an alternative use, a different analysis comes into play when the donor has a continuing use for the excised tissue, like in the York vs. Jones case. One major fear on the part of researchers is that the research enterprise would be greatly crippled by administrative and other bottlenecks, if donors ownership of tissue is allowed across the board.

It has been argued that if ones' body is property, then uninvited removal of specimen could constitute theft or trespassing (Charo, 2006), and this would be considered as an injury and a "deprivation of liberty" .Others hold that treating specimens as property raises fresh question such as :- is a person entitled to sell their specimens? Do their specimens become the property of their heirs and could they profit from their sale? Or should bodies and tissues be viewed as part of a common heritage of humanity, to be used for the collective good? Assuming patient or donor privacy is protected and their liberties are not deprived, this would suggest that the public has a right to excised specimens. Alone this line, society may justify the expansive use of human biological samples based on the principle of justice because the benefits of medical knowledge derived from tissue research will potentially accrue to all individual and future generation, (Hakimian and Korn, 2004; Allen et al, 2010). Most current literature appears to be focused especially on the issue of property rights that the tissue donors may have in tissue samples. The issues of intellectual property right in clinical research generally ,and collaborative research especially become more complex when these samples are obtained from developing countries and exported to developed countries for analysis and research (Andanda, 2008). Informed consent and strict confidentiality rules are recommended as mechanisms which can accomplish the same result as a property right, without the liabilities of an exclusive entitlement (Spinello,2004).

Benefit sharing and commercialisation There are strong grounds to believe that the potential for commercial exploitation of donated human biological samples is a very relevant consideration for potential research participants to take into account in deciding if to consent to participation in research, particularly given that most subjects participate on the basis of altruism. There is a widely held view that while "the human body and its parts shall not, as such give rise to financial gain" intellectual property based on human tissue research is generally acceptable.

The commercial exploitation or comodification of human tissue is associated with widespread anxiety and raises a lot of ethical concerns about 'self' , 'personhood', 'body', 'identity', 'genealogies', ' group continuity among other issues. It is believed that the buying and selling of human biological samples debases the value of human life, and antithetical to the gift paradigm of tissue transfer. In order to avoid feelings of exploitation and possibly even deception, it is crucial that potential donors be given the opportunity to consent to participation, in the knowledge that there is a possibility of commercial gain being made from their donated biological materials. Though, court decisions related to this matter have created the impression that research participants have no right based in any property interest in their

samples entitling them to share in the profits from the commercialisation of the research using their genetic materials (Otlowski, 2007). It may be more ethically appropriate to inform participants of the commercialisation potential of a research than offering them the opportunity of sharing in the financial gain of future commercialisation. The latter option may be misinterpreted in some quarters as inappropriate inducement.

There is presently no clearly enforceable legal requirement stipulating that the consent of the source must be obtained before the biological material be used commercially in the creation of a patent. If prospective donors are adequately informed about the potential commercial use of their material and they waive any right to financial compensation, it will greatly minimize potential misunderstanding and possible litigation arising between donors and users of these materials. This will ultimately encourage openness and transparency in the research industry, and may not necessary be a deterrent to research participation, (Otlowski, 2007, Wilkinson, 2005).

Exploitation can be avoided if the benefits and burdens of research are distributed in a way that does not take unfair advantages of people's vulnerability. Despite the absence of general principles for working out which distribution of benefits and burdens are fair, however, people have strong intuition about fairness in certain cases (Millum, 2011). For instance, with respect to the equitable distribution of profits derived from human tissue, patients or tissue donors must be allowed to decline commercial use of products developed from their cellular material, as an exercise of control over the terms and conditions of their participation in clinical research. Alternatively, patients may choose to share in the profit from commercial ventures that utilize their tissue or its products by entering into contractual agreement with the researchers. However, it should not be expected always that patients in general will benefit financially from research involving their cells or cell products, because most research on human tissue does not result in substantial commercial profits.

Whilst research participants may have no legal rights to share in the profit of commercial exploitation of their samples, there is now strong support for some form of benefits sharing. The benefits may come in the form of health care development program or broad humanitarian assistance, and it may involve the individual donor, the group/class to which the individual belong or even the wider community. Disagreement still exists as to whether or to what extent the benefit that come with bio banking research should be shared with sample donors only or the groups/communities from which these donors are drawn (Millum, 2011, Thiessen el al, 2007).

Whilst the push for general benefit sharing is gathering momentum, the case for benefit sharing at the level of the individual or group is buttressed by the Article 19 of the UNESCO International declaration in human genetics data (2003) which goes to acknowledge that in giving effect to this principle of general benefit sharing, benefits may inter alia, take the form of special assistance to the persons and groups that have taken part in the research, (World Health Organisation, 2004). Where benefits and burdens of a research are shared fairly, it provides a major pathway for preventing exploitative international collaborative research. It is a potent means of demonstrating genuine reciprocity between tissue donor and researchers, and to acknowledge the important contribution that participants make to the research endeavour. In this way, it can also play a vital role in fostering public trust in research, especially in research with commercialisation potential. In circumstances where such benefit sharing is not going to be feasible or appropriate, this should be made clear to prospective tissue donors (Otlowski, 2007).

Disclosure of research findings: A lot of debate has continued over the obligation of researchers to communicate the results of research to the research participants. Though, there seems to be a consensus that in addition to public dissemination of results, investigators also have a responsibility to communicate certain types of findings directly to study participants. This surge in interest after disclosure of findings may not be unconnected to the dramatic increase in genetic research globally, in which individual's genotypes often become known to researchers and results increasingly have the potential to be relevant to participants' clinical care and personal lives (Shalowitz and Miller, 2008).

Differences exist among the various policies and guidelines on communicating research results. Nobody is certain whether investigators have an obligation to proactively contact participants or simply respond to requests. Nobody is certain whether the investigators should communicate aggregate or individual results, or both. Nobody is certain if research results should be clinically relevant before disclosure is considered, and to what extent research results need to be verified prior to disclosure. Associated challenges include distinguishing between aggregate and individual results, and determining the potential clinical relevance of results. Recommendation from a 2 year project finding by the National institute of Health, USA are in favour of the bio banks research system being enabled to discharge four core responsibilities, when re identification of individual tissues, donors is possible (Wolf et al, 2012) . These responsibilities are to clarify the criteria for evaluating findings and the roster of returnable findings; to analyse a particular finding in relation to this; to re identify the individual contributors and to recontact the donor to offer the findings. Along the line, findings

that are analytically valid, reveal an established and substantial risk of a serious condition, and are clinically actionable should generally be offered to consenting donors.

In contrast, the public generally expresses great interest in learning their personal genetic information, regardless of clinical relevance or utility (Wendler and Emanuel, 2002; Halverson and Ross, 2012). Even at that, some would ask if there is a duty to share genetic information, especially among family members. Some would argue that most genetic information shared among family members is done in a weak way that does not necessarily lead to the actual manifestation of particular disease. On that basis, they suggest that the idea of the familial nature of genetics does not provide enough justification for moving towards a system in which by default genetic information is shared among family members (Liao, 2009). Another argument also exists in support of non-disclosure of paediatric results. The advocates, while admitting that healthy children may only be enrolled in bio-bank based research on the consent of their parents, also note that these minors do mature and need to be re-consented on attaining adulthood. As such, such children have the right not to know one's genetic predisposition; these children have the right to privacy, even from their own parents; these children have a right to wish to avoid labelling and stigmatization, and the need to reduce the risks of parents seeking non-validation therapies and preventions to counteract any identified genetic risks in their children is another reason in support of non-disclosure of paediatric results (Halverson and Ross, 2012).

Despite the fact that many studies show an overwhelming interest on the part of tissue donors in feedbacks of research results, there is still a minority insisting on a right not to know about research results. There also appears to be some regional differences. American and Irish respondents seem to want research results irrespective of the availability of treatment options, while Swedes prefer getting individual results only when they are of validated clinical use (Hoeyer, 2009). In fact, some research participants see feedback on research results as a basic right and an indisputable entitlement. Studies indicate that such people tend to expect an element of reciprocity when contributing to bio bank research. They rarely want money in return; they expect respect and care (Igbe and Adebamowo,2012).

The bottom-line remains that people care about the research they contribute to in ways which incur enduring obligations on bio- bank researchers. As such, researchers, should within the context of the socio-cultural research environment, first and foremost bear in mind whether feedback on research findings in fact represent care (Hoeyer, 2009).A review including 28 empirical studies concerning communication of research results (7 genetic researches) found that a median of 90% of participants wished to receive any study results (Shalowitz and Miller

(2008). A study involving 45 African-American adults showed that participants did not distinguish between the results they wanted to receive regarding themselves and her children. They also believed that their children should be allowed access to their health information but they wanted to be involved in deciding when and how the information was shared (Halverson and Ross,2012).The main reason to return individual results is to incentivize participation and show respect for the wishes of the subjects (Shalowitz and Miller ,2008). Several authors conclude that researchers in general have an ethical or moral duty to communicate research results to participants. However, it has been argued that decisions about the communication of individual research results should be based upon a case-by-case approach (Meulenkamp et al, 2010).

Privacy and Confidentiality: In order for researchers to recruit potential participants, the public must believe that the privacy and confidentiality of their information will be adequately protected, and that the benefits of participating in research outweigh the risks associated with potential issues of medical and genetic privacy, or not be concerned about privacy issues. Concerns about privacy are multi-faceted and may relate to the types of information being collected and shared, the form in which samples and related information are kept, the degree of control that participants will have over access to their information, the types of researchers and other parties that may have access, as well as what could be with the personal information for harm or exploitation of study participants.

The magnitude of harm caused by a breach of privacy may depend on the types and clinical relevance of the disclosed data and findings, the likelihood that the participant could be identified from the data and the additional harm that could result. Even, when a person cannot be identified or his study data cannot be used for harm, the perception of a loss of medical and genetic privacy may be harmful in itself (Kaufman et al, 2009). Failure to maintain the privacy of research subjects may prevent them from maintaining and controlling social relationship that are affected by the information shared or disclosed. Losing this control can erode personal anatomy and the dignity of individuals. In bio bank-based researchers, the privacy of participants' information is usually protected by removal of personal identifiers before data and samples are made available to researchers.

In many cases, the value of the sample lies in the potential for linkage, and therefore complete anonymisation is not desirable (Otlowski, 2007). Capacity to link data however, carries with it privacy implications. Details of how the data will be kept secure through encryption, coding or other security measures should be given to prospective research participants. This will help a gender trust and confidence in the research. However, emerging

forensic methods have shown that a third-party with access to a sample of an individuals' DNA could use DNA sequence data of the type collected and shared by genetic biobanks to determine that the sample belongs to a biobank participants (Kaufman et al, 2009). As attention turns to models for optimal protection of privacy in connection with genetic research especially, there had been growing interest in the concept of a gene trustee- as earlier suggested in Australia- an independent third party to hold codes linking genetic sample or information with identifiers. The gene trustee becomes the gatekeeper and plays a key role in maintaining the integrity of the system. The gene trustee acts as an intermediary between the person maintaining the database and the individual who provide genetic samples and information. This model has potential as a means of promoting public trust (Otlowski, 2007).

Against the backdrop of all the ethical issues associated with research on stored human biological specimens, it is obvious that they are closely interrelated and underlying almost all of them is a tension between the rights and autonomy of individual donors and the collective benefits that biobank-researches deliver to individuals, groups and humanity. All the emerging concerns ,especially in the light of increasing international collaborative studies, make it all the more imperative for the perspectives of potential tissue donors for these researches be enunciated and documented as a means of encouraging and promoting ethical conduct of research.

CHAPTER THREE
METHODOLOGY

3.1- Research design and scope

The scope of this cross-sectional community based study, using mixed qualitative and quantitative methods, was limited to determining the knowledge and attitudes of respondents with respect to issues associated with the storage and future use of human biological specimens in research.

3.2- Study area and population

The study was located in Enugu metropolis of Enugu State in South Eastern Nigeria. Enugu metropolis comprises 3 local government areas, namely Enugu East, Enugu North and Enugu South. Enugu East consists of TransEkulu and Abakpa Nike areas; Enugu North of Asata, Independence Layout, New Haven and the Government Reservation Area; and Enugu South of Uwani, Achara Layout, Idaw River, Gariki and Awkunanaw areas.

According to the 2005/2006 population census, the population of Enugu State was put at 3,257,298, with 1,624,202 being males and 1,633,096 being females. The population figure for the three Local Government areas in Enugu metropolis was put at 722,664. The Igbo ethnic group predominate the study area. Majority of the population are civil Servants, traders, artisans, and students.

3.3- Sample size and sampling procedure

Using the following formula $n = \frac{Z^2Pq}{d^2}$

Where n = desired sample size

z = The standard normal deviation usually set at 1.96 which corresponds to 95% confidence level.

p = The proportion in the target population estimated to have a particular characteristic i.e. In this case, population that would want information retrospectively on the research done on their specimens = 54% from the Uganda study done by Wendler et al,2005.

q = 1.0 – p

d = degree of accuracy desired usually set at 0.05.

$n = \frac{(1.96)^2 (0.54) (0.46)}{0.0025} = \frac{0.9543}{0.0025} = 381.7$

$\underline{\Omega} = 382$

.. Minimum sample size = 382

Desired sample size = 400

A multi- stage random sampling technique was adopted. Out of the 3 LGAS in Enugu metropolis, one LGA was selected using ballot method. In the selected LGA, using the National Population Commission 2005/2006 enumeration areas (EA) scheme, (which has a population threshold of 450-500), 10 EAs was randomly selected (using table of random numbers) in which 40 respondents was interviewed in each EA. To get these respondents, a route/road/street was randomly selected from a junction. The randomly selected direction was followed and the households along the route was visited and selected by systematic random sampling. For a household to be eligible, there must be at least one adult aged 18yrs and above. To achieve gender balance, if a male is interviewed in a household, a female was purposively interviewed in the next household and vice-versa. Selection of the respondents in the households was by simple random sampling (balloting) of eligible members of the appropriate gender.

3.4 - Instruments and methods for data collection

Qualitative data was collected through the use of focus group discussions (FGDs), initially as part of the pilot study which came before the administration of the final project questionnaires, and eventually after the survey. The focus groups were designed to further explore issues such as informed consent, privacy and confidentiality, ownership, future use of biological specimens and derived data, and disclosure of research results. Focus groups were chosen as a less structured method of eliciting data to allow for open discussion, varying viewpoint, discovery of unanticipated findings and clarification of information. Standard FGD procedures were followed, with a trained female moderator and the investigator conducting and audio-taping the focus groups. Informed consent was obtained from all the FGD participants prior to the discussions

A detailed discussion guide was developed to systematically explore participants' knowledge and attitudes in the domains of interest. A total of 8 FGDs was conducted with 6-8 persons in each group. The FGDs were stratified on the basis of age and gender, into young (18-35years) and old adult females (above 35 years); and young and old adult males. Discussions were held with homogeneous groups and the moderator was of the same sex as each group. Before the commencement of data collection in the study areas, the permission of the relevant authorities and local leadership was sought. Participants in the FGDs were not interviewed in the cross-sectional quantitative study.

For the quantitative study, we used a 38-item questionnaire. The initial development of the questionnaire was informed by the available literature. Content validity and feasibility were ensured by repeatedly reviewing the questionnaire with experienced researchers and members of the public, who suggested revisions. To further evaluate the final questionnaire, a pilot study was done on a random sample of 50 members of the public, in a community separate from the study area. The questionnaire was divided into three survey domains; namely socio-demographic factors, knowledge about use of stored HBS in research and attitudes to the use of stored HBS in research .Some of the questions were to be administered to only those respondents who indicated willingness in donating HBS while the other questions in the questionnaire were applicable to all the study respondents. This was interviewer-administered. The average duration of each interview was between 30 – 45 minutes. For this purpose, one female field assistant was recruited and trained on the methods and objectives of the study. The language of administration was Ibo or English, depending on the respondent's preference.

3.5- Data management and analysis

Data editing and validation was done on a daily basis, starting from the field. All data were double entered into the computers. All the tapes from the FGDs were transcribed by the investigator, and an independent check by a sociologist confirmed accurate and verbatim transcriptions. A descriptive content analysis method was adopted. Analysis of the FGD data placed emphasis on the interpretation, description and recording/writing of what is actually said. In going through the transcriptions, phrases with contextual or special connotations were noted and pulled out as illustrative quotes in completing the statistical data. The data were then re-arranged according to the thematic contents to facilitate comparison. After re-immersion and member checking, outcomes were determined, concepts defined and explanation provided in some cases.

For the data collected by the quantitative method, the research participants' characteristics and choices were summarized as frequency counts and percentages. The principal outcome variable in this study was whether a potential research participant is willing to donate HBS for future unspecified use research and ultimately give a one-time consent for storage and unspecified future use of his or her biological specimens. The independent variables were cross tabulated with this outcome and some other outcomes. These independent variables are the socio-demographic variables such as gender, age, occupational status, religious association, educational level, marital status and status as a previous tissue donor for research. The association of each type of independent variable with the principal outcome and other outcomes was tested in a bivariate fashion with the odds ratio (where applicable) and chi-

square tests. Additionally, multivariate logistic regression analysis was done to determine which socio-demographic factors are related to the choice of whether to give a one-time consent for future unspecified use of stored HBS in research and willingness to donate HBS for storage and future use in research ,as well as some other outcome variables. Quantitative data analysis was done with SPSS version 17.0 and initially, with Stata 10®. A p-value of less than 0.05 was considered statistically significant for all analyses .With the exception of age, only those significant variables were considered for presentation in the logistic regression analysis models ,with the required covariate adjustments being made at every point of running the models .Only those predictors which remained statistically significant in the most parsimonious model were accepted as having a relationship with the outcome variable being studied.

The study variables include:

(1) Independent Variables

- Socio-demographic Characteristics

  i.e Age, Sex, Occupation, Level of education, Religious affiliation, Marital Status, status as a previous donor of body tissues / fluids for research

(2) Dependent Variables (outcomes)

- Proportion willing to consent to storage and future use of their biological specimens in research.
- Proportion willing to give at the point of collection of specimen, a one-time consent for the storage and future use of their specimens irrespective of the type of research.
- Proportion willing to be re-contacted for consent before future use of their specimens in research.
- Proportion who feel that even after specimen collection, that donors own these specimens used in research
- Proportion who desire disclosure of findings from future unspecified research on their specimens.
- Proportion who wish to share in the benefits of research on their specimens.
- Proportion who have concerns over privacy / confidentiality of data from future research on stored tissues
- Proportion who would consent to long-term storage of their specimens for research.
- Proportion who would want payment before giving consent for storage and future use of their specimens in research.
- Proportion who have previously donated specimens for research.

- Proportion willing to donate for FUUR body tissues/fluids from their dead relatives
- Types of body tissues and fluids which can be donated for storage and future use in research.

3.6- Ethical considerations

Approval was obtained from the appropriate research ethics committee (the University of Nigeria Teaching Hospital Committee) before commencing the study. A research consent form was administered to each participant, which they were required to sign as a mark of their willingness to participate and proper comprehension of the information given. All interactions with the participants were guided by the 4 main ethical principles of respect for autonomy, beneficence, nonmaleficence and justice.

3.7- Dissemination of findings

- Feedback to relevant study areas through the leaders and possible dissemination workshop.
- Dissertation to be presented to the University of Ibadan
- Publication in relevant peer-reviewed journals

CHAPTER FOUR

RESULTS

A total of 453 participants were involved in the study, with the qualitative arm having 52 participants**.**

Qualitative methods – summary of results (FGD)

The sex distribution of the participants in the focus group discussion was 24 males and 28 females. Their ages ranged from 18years to 69years. More than half of them (59.6%) were married and the remaining (40.4%) were single. All were Christians. Civil servants were in the majority (55.8%) followed by persons in the private sector (23.1%), house wives (11.5%) and students (9.6%). All of the participants had completed at least primary level of education, and had lived in the area for more than six months.

Topics explored in the FGDs

1) Human biological samples and donation for research

2) Storage and future use of HBS

3) Informed consent process i.e. withdrawal of consent

4) Ownership of tissues, property rights, control over tissues, commercialization, benefit sharing

5) Identifiers, privacy and confidentiality

6) Disclosure of research findings to individuals/communities

Themes identified and selected representative quotes

1) Participants displayed a wide spectrum of understanding of the place of HBS in research. The impression many have is that research is for the university community and academicians, and that it is not a financially lucrative field. They expressed reservations over the use of some body tissues and fluids for research. They expressed some distrust of some researchers and would not be in a hurry to give them their specimen.

One man in the FGD asked, “Why should someone wish to store and use my hair, nail, skin or even my semen for research? Which kind of research is that?”

Some of the male participants agreed with the comments made by one of them in the FGDs , “There is really nothing wrong with storing human tissues for research but we have to be sure that they will be put into good use”. Some of the older female participants also agreed with the view of one of them who said, “You do not have to worry about when giving your specimens to the laboratory man because it is for your health. But when it comes to giving it to a total stranger for the sake of research you need to be careful. You do not know who is who”. The attitude of majority of respondents to research is best described as guarded.

2) There is low public awareness of the concept and practice of storing HBS and using stored HBS for research. Majority of the participants seemed unconcerned about storage of their HBS, either within the country or outside. They were also not too bothered about duration of storage. According to some of the older participants:

"Even if they decide to store them forever, or for one minute, I cannot put them back in my body"

"The thing you are talking about, it is like keeping money in a bank. You mean people will collect my semen and store. Why?"

"I had always thought they will take the specimens, use them and discard them. This thing about storing these things for years…it is strange and sounds odd to the ears"

"Are you saying that my nails and other tissue can be kept for years in a fridge without spoiling? What about faeces?"

3) In weighing pros and cons of granting one-time consent for future unspecified use of stored specimens, there is a willingness to granting one- time consent for FUUR, if trust is assured.

One of the participants remarked:

"Once I give my consent, I don't think I wish to be bothered again about the specimens. But what if they are doing funny things with my specimen in future?"

Another FGD participant also stated:

"If I am sure that nothing will go wrong in the future, I will do so. But how can you know? Are you God?"

An older female participant remarked, "I will permit them to use it for that time only. After, they should throw it away. But how do you know they have thrown it away?"

Majority of the participants agreed that, "All things being equal, it would be ideal to give permission once and for all. But the people need to assure us that they would keep to their words.

4) There was mixed public reaction to issues of ownership, control, sharing of benefits

Most participants remarked, "If you give it out for research, it is no longer your own. It now belongs to the researcher. I can only give them my specimens for research if they assure me that I can control what they will do with them."

"Even if they make money from using my specimens, how will I know? The best thing to do when you give out your specimen is to forget about it completely."

One young female participant strongly admitted that "I will not find it funny with anybody who sells my specimen which I gave them freely."

5) No serious concern over identifiers

Majority expressed their feelings by asking "If they remove information linking the samples to you, how will they know it is yours if they need to get back to you?"

"If you have problems about being associated with your specimens, then you should not donate them."

"Whether they put or remove anything connecting me to the sample, it is their business."

6) Strong desire for feedback of research findings

Majority, especially the older participants, stated that they would wish to have results of researches which affect them. One man asked, "Why shouldn't they tell me if they find something bad about my health? It is for my good so that I can start treatment early."One lone voice among the young male participants inquired, "What if they find out you have AIDS.

QUANTITATIVE METHODS-RESULTS

Some 401 participants were involved in the survey. The mean (SD) age for men was 35.7 (13.3) years and for women, it was 30.4 (9.9) years. More than half of the respondents were single, and students were the commonest occupational group. More than half of the respondents belonged to the Roman Catholic Christian denomination. All the respondents had completed at least primary school education. The distribution of 401 respondents with respect to their religion showed the following: Roman Catholic 206 (51.4%), Protestant 103 (25.7%), Pentecostal 83 (20.7%), Muslim 1 (0.2%), Others 8 (2.0%). With respect to their educational level completed, the distribution showed the following: Primary school 51 (12.7%), Secondary school 161 (40.1%), Tertiary school 182 (45.4%), Commercial school 6 (1.5%), Others 1 (0.2%). The distribution of the other socio-demographic characteristics of these respondents is shown in table 4.1

Table 4.2 shows distribution of the 401 Respondents with respect to either having participated in any previous research requiring HBS or having submitted HBS for laboratory investigations. Almost 90% had no experience of research involving HBS, while a significant majority had a positive history of past laboratory investigations (recalled having willingly submitted HBS in the past for the purpose of routine/special laboratory investigations).None had ever been told that their specimens could be stored for future research.

Responses were sought on the following issues:

a) Knowledge that body tissues and fluids are sometimes stored for long periods in research.

b) Knowledge that body tissues and fluids are sometimes reused.

c) Awareness of any risks and benefits associated with storage and future use of HBS in research.

d) Awareness of any law, code or regulation in Nigeria guiding storage and future use of HBS in research. Table 4.3 shows the distribution of the respondents with respect to their views on these four issues.

Table 4.1: Distribution of 401 respondents according to their socio demographic characteristics

CHARACTERISTICS	FREQUENCY	PERCENTAGE

	Male	201	50.1
Gender	Female	200	49.9
Age	18-35	265	66.1
	35-59	113	28.2
	>=60	23	5.7
Marital	Single	232	57.9
Status	Married monogamous	153	38.2
	Married Polygamous	5	1.2
	Divorced	4	1.0
	Widowed	7	1.7
Occupation	Civil servant	48	12.0
	Professional	63	15.7
	Housewife	12	3.0
	Artisan	21	5.2
	Farmer	4	1.0
	Businessman	90	22.4
	Student	143	35.7
	Unemployed	18	4.5
	Others	2	0.5
Religion	Roman Catholic	206	51.4
	Protestant	103	25.7
	Pentecostal	83	20.3
	Muslim	1	0.2
	Others	8	2.0
Education	Primary school	51	12.7
	Secondary school	161	40.1
	Tertiary school	182	45.4
	Commercial school	6	1.5
	Others	1	0.2

Table 4.2: Distribution of 401 Respondents with respect to having participated in previous research requiring HBS or previous Laboratory tests requiring HBS.

PREVIOUS EXPERIENCE		FREQUENCY	PERCENTAGE
HBS research	Yes	39	9.7
	No	360	89.8
	Uncertain	2	0.5
HBS Laboratory test	Yes	336	83.8
	No	65	16.2

Table 4.3: Distribution of 401 Respondents with respect to their knowledge of storage, future use, risks and benefits of HBS use in research, and awareness of laws/regulations or codes guiding use of stored HBS in research.

CHARACTERISTICS		FREQUENCY	PERCENTAGE
Knowledge that HBS can be stored for long periods	Yes	157	39.2
	No	232	59.7
	Not sure	12	3.0
Knowledge that HBS can be reused in research	Yes	116	28.9
	No	261	65.1
	Not sure	24	6.0
Risks associated with HBS storage and future use	Yes	89	22.2
	No	291	72.6
	Not sure	21	5.2
benefits associated with HBS storage and use	Yes	114	28.4
	No	271	67.6
	Not sure	16	4.0
Awareness of Nigerian laws, regulations or codes regarding storage and future use	Yes	29	7.2
	No	357	89.0
	Not sure	15	3.7

Respondents' willingness to donate HBS for storage and future use research

Majority of the respondents were willing to donate body tissues or fluids belonging to them and/or their children for research purpose. Figure 4.1 shows the distribution of 401 respondents in relation to their willingness to donate HBS for storage and future use research. Only 2.5% of the 401 respondents would require payment alone before donating HBS while 66.6% would require all relevant information on the research alone, and 19.5% would require both relevant information and payment. In bi-variate analysis, gender (p-value = 0.003, O.R. =1.88) marital status (p-value = 0.02,) education (p-value = 0.02) previous HBS research experience (p-value < 0.001) knowledge of storage of HBS for research (p-value = 0.003,) knowledge of reuse of stored HBS in research (p-value = 0.02) awareness of risks in reuse of stored HBS in research (p value = 0.008) awareness of benefits of reuse of stored HBS in research (p-value = 0.01) were associated with willingness to donate body tissues or fluids belonging to them and/or their children for research purposes (see appendix 1).

Among the 252 participants willing to donate HBS for storage and future use in research 70.1% were men and55.8% were women(p-value = 0.003). Multivariate analysis of these predictors demonstrates that gender (p-value =0.003, O.R= 1.86, 95% C.I.=1.23 - 2.82) and marital status (p-value = 0.021,O.R = 1.39, 95% C.I. = 1.05 – 1.84) were associated with the willingness to donate body tissues and fluids belonging to them or their children for research purposes.

Willingness of the 252 respondents to grant one-time consent for future unspecified use research on their stored HBS

Out of the 401 respondents, the 252 who were willing to donate HBS for FUUR were investigated for their willingness to grant one-time consent for such research. In bivariate analysis, occupation (p-value = 0.02) and awareness of benefits of the use of stored HBS in research (p-value = 0.03) were associated with willingness to grant one-time general consent for future unspecified use of HBS in research (see appendix 1. Multivariate analysis showed that occupation (p-value = 0.01, O.R = 2.08, 95%C.I. =1.18 – 3.67) is associated with willingness to grant one-time general consent in FUUR. Figure 4.2 is a pictorial representation of the distribution of 252 respondents with respect to granting one-time general consent for future unspecified use of stored HBS in research.

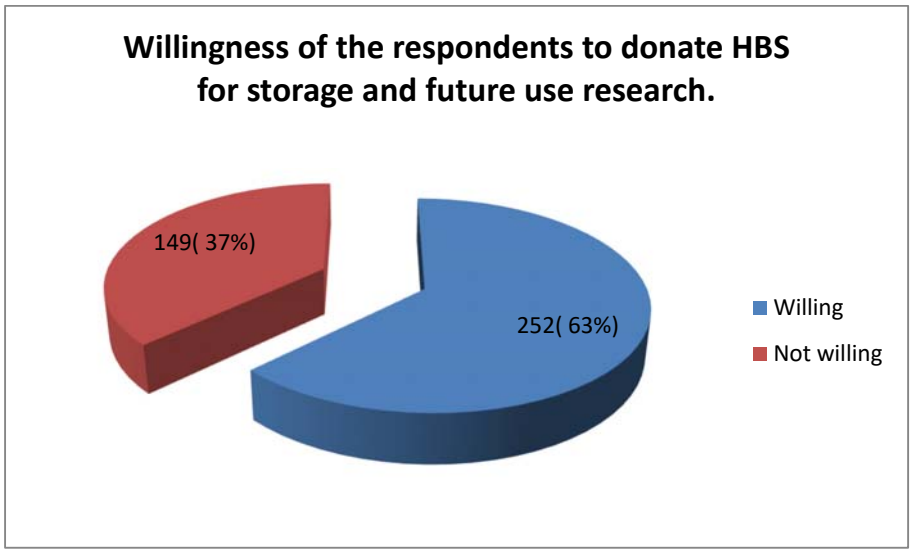

Figure 4.1 below shows the pictorial distribution of 401 respondents with respect to willingness to donate HBS for storage and future use in research.

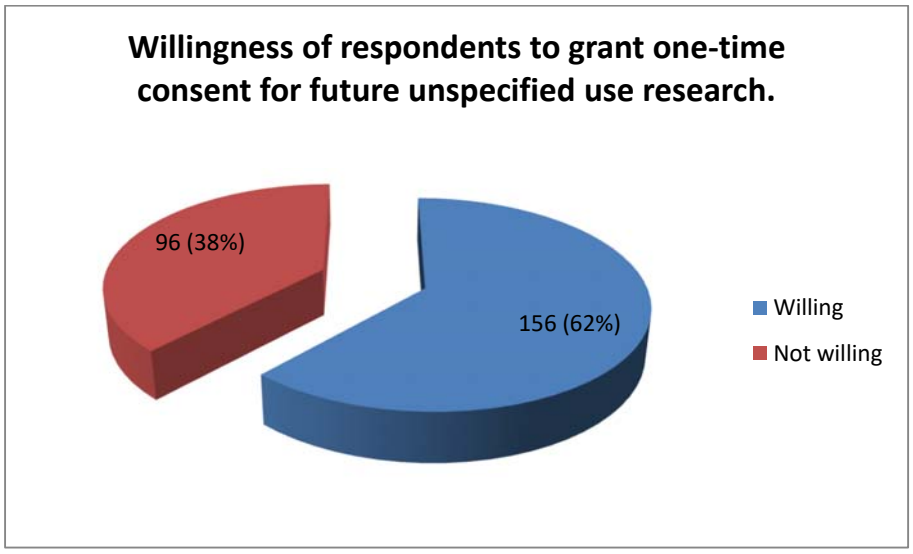

Figure 4.2: Pie chart showing the distribution of 252 Respondents with respect to granting one-time consent for future unspecified use research.

Types of HBS that the respondents were willing to donate.

Respondents were willing to donate various types of body tissues and fluids. These include urine, stool, sputum/ saliva, blood, swabs from ears/nose/throat, eye swabs, nail clippings, hair strand, skin snips and semen and vaginal swab. The distribution of the 252 respondents who were willing to donate HBS for storage and future use research is shown in figure 4.3

Preferred consent model for future unspecified use research(apart from blanket one-time consent)

Out of the 252 respondents who were willing to donate HBS for FUUR, 96 were not willing to grant one-time consent but preferred other consent models for FUUR. The other consent models considered by these respondents were the following: one-time consent limited only to the same research for which the HBS was originally donated, one-time limited to some researches, re-contact for fresh consent on every new research conducted on donated HBS, and only HREC approval being sufficient for any fresh research on donated HBS. Table 4.4 shows the distribution of the 96 potential donors of HBS who are unwilling to grant one -time consent for future unspecified use research.

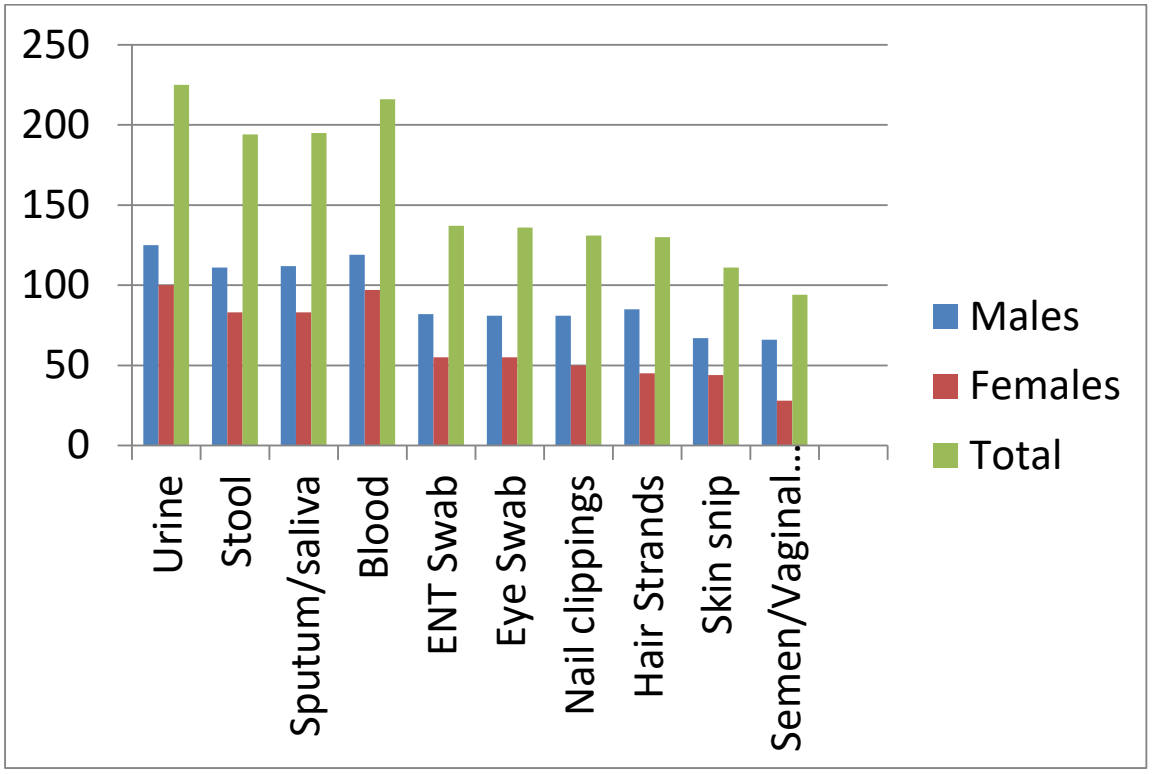

Figure 4.3: Distribution of the 252 respondents with respect to the types of HBS they were willing to donate for FUUR (all consent models inclusive)

Table 4.4 Preferred consent model for future unspecified use research (n=96)

Consent model	**Number**		**Total(%)**
	M(%),	**F(%)**	
One-time consent limited to some researches	1(1.96)	5(22.2)	6(6.3)
One-time consent limited to same researches	14(27.45)	8(35.56)	22(22.9)
Re-contact for every new research	32(62.75)	31(37.78)	63(65.6)

HREC approval for re-use is sufficient	4(7.84)	1(4.44)	5(5.2)
Total	51(53.1)	45(46.9)	96(100)

The views of 401 respondents over the necessity for fresh consent on every new research on stored HBS

Figure 4.4 shows the distribution of these respondents according to their views.

One major reason given by respondents to justify the need for fresh consent for every new research on stored HBS is that the donor may no longer be interested in further research on his/her samples. The predominant reason for those who said 'no' to the need for fresh consent on every new research is that it would be a waste of resources and time. They also stated that it would be a cumbersome task tracking down every research participant in a country like Nigeria. In bivariate analysis, knowledge of HBS storage in research (p-value =0.02), knowledge of HBS re-use in research (p-value =0.001), marital status (p-value =0.01) and occupation (p-value =0.006) were associated with the view that it was necessary to obtain fresh consent for every new research (see appendix 1). None of these were significant in multivariate analysis.

Consent for use of stored HBS removed during surgery

Figure 4.5 shows the distribution of these respondents over this issue.

The predominant reason given by the respondents for allowing HBS removed from their bodies during surgery to be stored for future use in research is that these HBS are usually diseased parts of the body and may no longer be useful to the patient. Also, the surgeon may use such materials in making a better diagnosis or offering better treatment. For those not willing to give consent, they felt those materials should be discarded if they would not be useful in providing further treatment to them. In bivariate analysis, occupation (p value=0.03) and knowledge of HBS re-use in research (p-value=0.03) were associated with willingness to grant consent for the use of stored HBS removed during surgery (see appendix 1). Multivariate analysis showed that only occupation (p-value=0.01, O.R =1.12, 95% C.I. = 1.03 – 1.22) was significantly associated with this outcome.

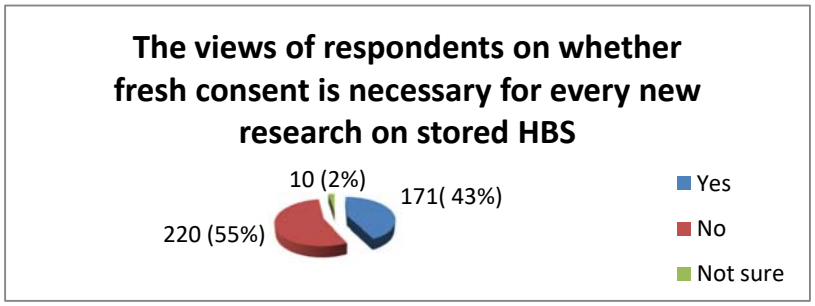

Figure 4.4: Distribution of the 401 respondents with respect to their views on whether fresh consent is necessary for every new research on stored HBS.

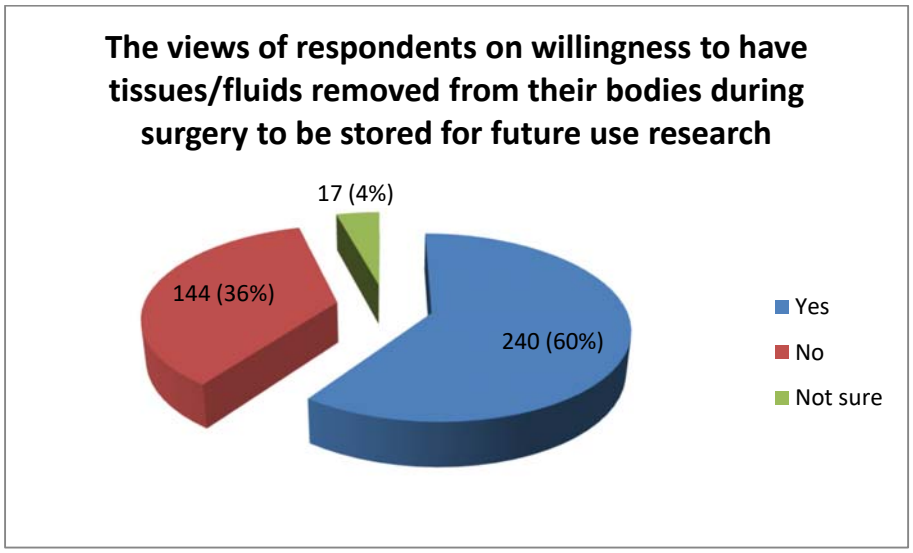

Figure 4.5: Distribution of the 401 respondents with respect to their views on willingness to have tissues/fluids removed from their bodies during surgery to be stored for future research.

Consent for use of HBS removed from bodies of dead relatives

Figure 4.6 shows the distribution of the 401 respondents with respect to this issue.

The major reasons cited by the respondents in support of using HBS from dead relatives for FUUR were that those materials are no longer useful to the dead and some useful information may be derived from the research, which may help the dead person's family. Those respondents who were not in support of using specimens from dead relatives stated that corpses should not be desecrated and that only the dead person has the right to give such permission. In bivariate analysis, religion (p-value =0.001), gender (p-value =0.006), previous HBS research experience (p-value =0.01) were associated with willingness to grant consent for the use of HBS removed from the body of dead relatives (see appendix 1). Multivariate

analysis showed that only gender (p-value=0.002) was significantly associated with to this outcome.

Parents/guardians acting as proxies for children/incompetent persons

Figure 4.7 shows the distribution of the 401 respondents over this issue.

Majority of the respondents were in support of parents/guardians being allowed to give consent on behalf of children and other incompetent persons. The major reason cited is that these persons cannot think properly for themselves.

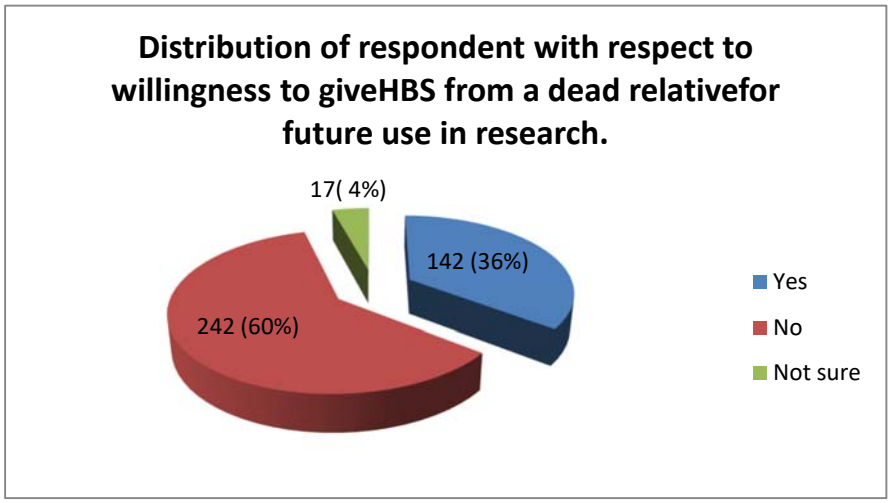

Figure 4.6: Distribution of the 401 respondents with respect to willingness to give HBS from a dead relative for future use in research

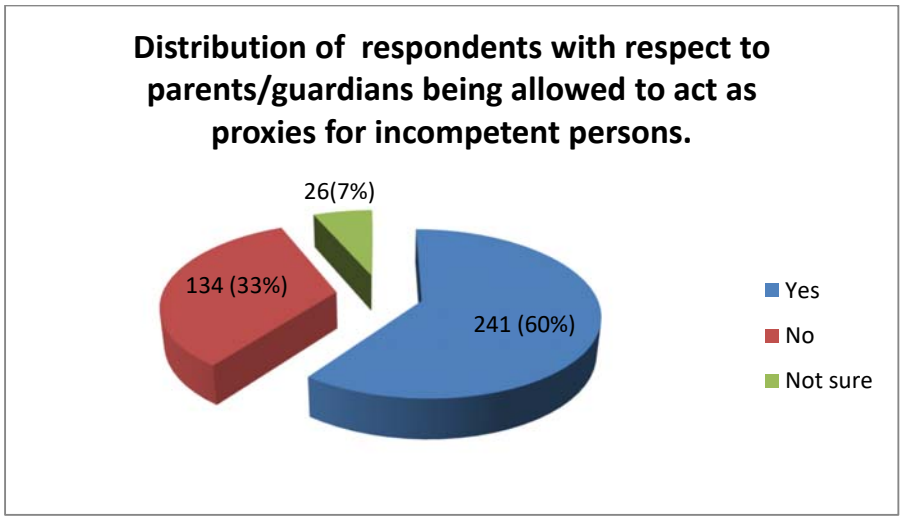

Figure 4.7: Distribution of 401 respondents with respect to their views on parents/guardians being allowed to act as proxies for incompetent persons.

Withdrawal of consent/stored HBS at any time of the research

Figure 4.8 shows the distribution of the views of these respondents.

The major reason cited for supporting tissue donors being allowed to withdraw their consent/samples at any time of the research is that it is their fundamental right to do so as situations unforeseen in the course of the research may arise. Those who did not support this stated that doing so would jeopardize research. In bivariate analysis, age (p-value =0.02), marital status (p value <0.001) occupation, (p-value =0.004) history of previous lab tests, (p-value =0.009), knowledge of storage of HBS in research (p-value <0.001), knowledge of re-use of HBS in research (p-value =0.02), knowledge of risks in re-use (p-value =0.03), knowledge of benefits of re-use (p-value =0.02) were associated with the view that research participants be allowed to withdraw their consent/stored HBS at any time of the research (see appendix 1). Multivariate analysis showed that only education (p-value=0.002) was significantly associated with this outcome.

Ownership of stored HBS

Table 4.5 shows the distribution of 251 respondents(missing data noted in one respondent) over their views on ownership of HBS. Majority of the respondents were of the opinion that the stored HBS belong to the researcher.

Majority (75.8%) of the 252 respondents would consent to storage of HBS for any period of time.

Commercialization, benefit sharing, and disclosure of research findings

Table 4.6 shows the distribution of the 401 respondents views over these issues. Bivariate analysis showed that marital status (p-value = 0.002), previous lab test, (p-value = 0.03), knowledge of risks in HBS re-use in research (p-value = 0.04) were associated with willingness for disclosure of findings from future use research on stored HBS (see appendix 1). Multivariate analysis showed that only marital status (p-value=0.04) and previous lab test (p-value=0.02) were significantly associated with this outcome.

Respondents views over Identifiers on samples, confidentiality/privacy, HBS as property, access/control of stored HBS, storage of HBS outside Nigeria

Table 4.7 shows also the distribution of the 401 respondents over their views. Majority did not have concerns over identifiers linked to their stored HBS and storage of HBS outside Nigeria.

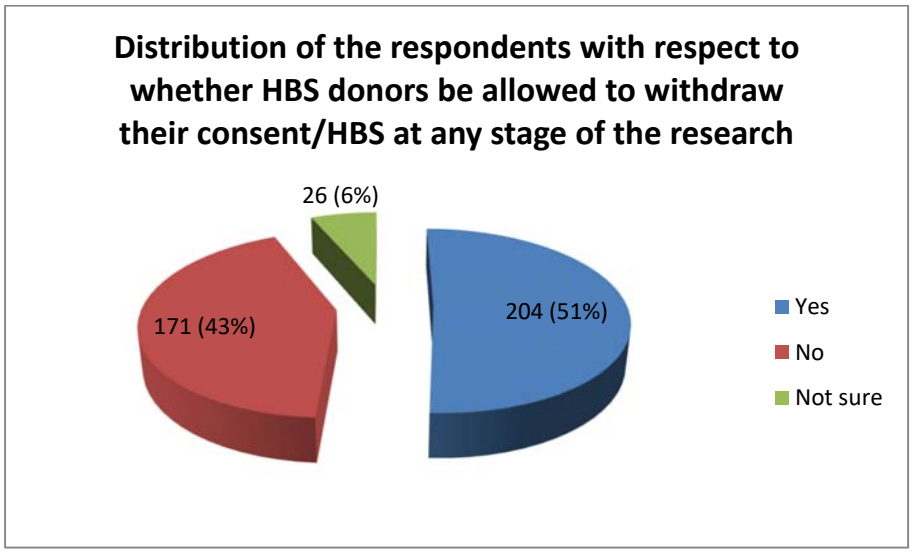

Figure 4.8: Distribution of the 401 respondents with respect to whether HBS donors be allowed to withdraw their consent/HBS at any stage of the research.

Table 4.5: Distribution of 251 respondents over views on ownership of HBS

	Male (%)	Female (%)	Total (%)
Tissue Donor	50(35.46)	35(31.82)	85(33.9)
Researchers	57(40.43)	49(44.55)	106(42.2)
Sponsor	9(6.38)	2(1.821)	11(4.38)
HREC	13(9.22)	11(10.00)	24(9.56)
Not Sure	12(8.51)	13(11.82)	25(9.96)
Total	141(56.2)	110(43.8)	251(100)

Table 4.6: Distribution of respondents on their views over commercialization, sharing of financial benefits and disclosure results from future use research on stored HBS

Item	Yes(%)	No(%)	Uncertain(%)	Total(%)
Willingness to donate HBS for future research to commercial companies	53(21)	165(65.5)	34(13.5)	252(100)
Desire for researcher to share financial benefits from future use of stored HBS	134(53.2	103(40.9)	15(6)	252(100)
Desire for disclosure of results from future use research on stored HBS	205(81.3)	37(14.7)	10(4)	252(100)

Table 4.7. Distribution of 252 respondents over their views on other associated issues.

Item	yes (%)	No (%)	uncertain (%)	otal (%)
Concern for Identifiers linked to Stored HBS	87(34.7)	153(61)	11(4.4)	252(100)
Concern for privacy/confidentiality	195(77.4)	50(19.8)	7(2.8)	252(100)
HBS as property	131(52.2)	97(38.6)	23(9.3)	252(100)
Access/control of stored HBS	104(41.4)	132(52.6)	15(6)	252(100)
Concern over storage of HBS outside country of collection	72(28.6)	169(67.1)	11(4.4)	252(100)

CHAPTER FIVE

DISCUSSION

5.1- Stored tissue research in Africa

This is one of the few empirical studies on the knowledge and attitudes of Nigerian potential research participants on the storage and future use of human biological specimens in research. Prior to these studies, discussions over ethical issues concerning the storage and re-use of HBS in research in Nigeria had probably taken place with paucity of data on the perspective of the actual or potential tissue donor.

Our findings in this study suggest that there may be subtle differences between the attitudes of Africans from the various regions of the continent to the donation of HBS for FUUR. A study from Uganda (East Africa) showed that the vast majority of the Ugandan respondents were willing to contribute a coded sample of their children's blood for future unspecified use research, even outside their country (Wendler et al,2005). A previous study in Egypt (North Africa) showed that many of the respondents did not favour the donation of their blood samples for future unspecified use research and their subsequent transportation to USA and Europe countries (Abou-Zeid et al, 2010). Findings from South Africa also suggest that participants are willing to have samples stored anywhere for future unspecified use research (Van Schalkwyk et al, 2012); the same thing as the Nigerian participants recruited for this study.

However there are differences between this study and those ones that may account for the differences seen. The Ugandan study surveyed parents or guardians of children participating in a randomized trial comparing chloroquine and sulfadoxine-pyrimethamine (CQ/SP) to amodiaquine plus sulfadoxine-pyrimethamine (AS/SQ) for uncomplicated malaria while the Egyptian study involved rural and urban adult patients (largely illiterate) receiving medical care at different public and private hospitals/clinics at the time of the survey. The South African study was a qualitative study of participants in a tuberculosis research project in a high-density, low-income urban area in the Western Cape, South Africa.

In contrast, this study involved healthy individuals living in an urban area of Enugu state, Nigeria. Being healthy, they may not be as vulnerable as those enrolled in the other studies from Africa This study population probably provides a more balanced representation of the perspective of urban dwelling Nigerians.

The study sample was better educated compared to the average educational characteristics of the Nigerian population. While few had participated in previous epidemiological research,

none had ever taken part in a clinical trial and none remembered ever being told that their specimens would be stored for possible re-use in the future.

The level of participation in previous research reported by participants in this study is almost similar to that in the Egyptian study in which 94% of the participants stated that they had never been asked to participate in research study; a probable pointer to the level and magnitude of health research activity obtainable in Africa. While most, 83.8%, of our respondents had given a biological specimen in the past for laboratory investigation, they were never told that there may be left over materials that could be used for educational, research or clinical purposes. Reasons for this situation may include a low level of research actually occurring in these environments and/or lack of capacity for storing HBS for research. Nevertheless, this failure is a reflection of how much information is provided to research participants or patients prior to, during, or even after collection of their biological specimens.

5.2- Awareness / knowledge about storage and future use of HBS in research

Our study shows that most respondents were ignorant of bio-banking; a finding corroborated in some other studies(Igbe and Adebamowo, 2012; Kettis-Lindblad et al, 2005; Ahram et al 2012). This is worrisome given that the respondents were literate and they live in a city with 6 tertiary universities and teaching hospitals.

There appeared to be a variable spectrum of understanding of the benefits of research involving human biological specimens among our respondents. This is consistent with the findings in a related Nigerian study that there is limited knowledge of bio-banking and its implications among lay Nigerians; though with majority acknowledging that such bio-banking researches could be of direct benefits to their communities and humanity(Igbe and Adebamowo, 2012), and even another study in the USA in which 86% of the participants reported never having participated in a medical or clinical research study before, and 74% reported not having ever head of a bio-bank before the survey (Simon et al, 2011).In our study, there were no clearly dominant expressions of religious or cultural- based views on storage and future use of HBS in research. Judging from observations made during the FGDS, majority were seemingly unfamiliar with the notion of storing and using specimens such as hair, semen, nail clippings, skin snips or foetal tissue for research. All these may be a pointer to their low level of awareness of health research activities in their communities, or even a low level of research activity.

While majority felt that such researches could be of obvious direct benefits to humanity, and possibly their communities, others felt otherwise and regarded the research enterprise as

merely an academic activity reserved for university workers and their students, which could be only beneficial to them.

Those in support of research felt it could be used to improve health conditions, cure diseases and solve a myriad of other problems The predominant reason or explanation given by the respondents for the storage of HBS by researchers is the need to prevent decay or spoilage against possible future use; for re-use of HBS in research; the need to get more results, repeat the research or to complete a previously incomplete research. The only recurring benefit accruing to researchers by storing HBS for research which was cited by most respondents was that the researcher would no longer need to search for the donor to collect more specimens and, with respect to risk, the predominant risk was that the stored specimens or the research findings may get into the hands of fraudulent or corrupt persons.

The few who claimed they were aware of a regulation or a research-regulatory agency in Nigeria cited the Nigerian constitution and the Federal Ministry of Health. This level of awareness may not be a cause for concern as long as the general public appreciates the fact that there are functional agencies or operational regulations guiding the conduct of human and animal research in the country. There may be a need to create awareness on this issue as this may help ensure societal trust in the research enterprise.

5.3- Attitude towards storage and future use of HBS in research

The willingness of the public to contribute their body tissues and fluids for research is reasonably high in the developed world as attested by empirical studies done in America and Europe(Wendler and Emanuel, 2002;Kettis-Lindblad et al, 2005;Ahram et al 2012;Stegmayr and Asplund, 2002; Chen et al, 2005; Wendler, 2006; Goodson and Vernon, 2004; Pentz et al,2006). Such attitudes might not be generalizable to other cultures and countries, as the perception and familiarity of health research might be different in developing countries. *Abou-Zeid et al (2010).*Our findings suggest that the attitude of the public is at best guarded and characterized by lack of trustin research/researchers requiring storage of HBS. Nevertheless, there was a positive attitude towards future participation in such researches, if trust can be assured. Recent well-publicized incidents of research misconduct in Nigeria may have contributed to erosion of trust in health research. *Jegede(2009).*

As was mentioned in the focus group discussions especially, distrust in researchers' and health workers' moral characters may be a problem when participants consider taking part in research, and especially for researches in which the researchers/ health workers happen to be the very ones they distrust. Participants' decisions to donate tissues for research may be based

more on a general trust that those responsible for the collection and use of the samples do it for a good cause and have made all necessary considerations for protection of their welfare and interests. Trust has an impact on the acceptance of new ideas, methods and techniques. Consequently, maintaining or improving the trust of the public is as important as having informed citizens. It is widely known also that adverse publicity is usually given to bad news, particularly if unethical research is exposed (*Lemke et al, 2010)*.

Although providing appropriate and adequate information to participants is vital, there will probably be people who do not wish to or cannot inform themselves by using the information provided. There is also the possibility of them misunderstanding the purpose, risks and benefits of the research. Despite the guarded public attitude to the use of stored HBS in research and lack of trust in researchers, many respondents were willing to donate HBS for storage and future use in research. Gender and marital status were shown to be statistically associated with initial willingness to donate HBS for storage and FUUR. A much greater proportion of males than females were more willing to donate their HBS for storage and future use in research. This may be due to the strong patrilineal culture of the population from which the sample studied was drawn. Though there may be a clear element of gender collaboration and mutual dependence in the traditional Igbo indigenous socio-political arrangement, the man as the head of most households takes certain decisions especially those concerning the overall interests of the household. Considering the manner the traditional or modern Igbo society is constituted, the females (whether married or single) are more likely than their male counterparts (husband, father, brother or fiancé) to seek advice from the opposite gender before engaging in such health related decision-making processes.

With respect to the statistically significant distribution of the marital status of our study respondents concerning their willingness to donate HBS for storage and future use in research, majority of the respondents were single. A much greater proportion of them were more willing to donate than those not willing, when compared to the other respondents who were not single. This may suggest that a single person is more likely or more predisposed to participate in researches requiring stored HBS than his/her married or previously married counterpart. Because of the dynamics involved in the decision-making process within the matrimonial institution in Nigeria, it may be less cumbersome for a single person to take a decision on research participation and tissue donation than for a married person, who may have to consult with the spouse.

A contrary observation was made in Egypt where it was shown that women were more likely than men to donate blood samples for general research (Abou Zeid et al, 2010).In

another study, though general attitudes towards societal importance of genetic research were significantly associated with age and marital status, the individual willingness to participate in genetic research was not influenced by gender, education, race or age (Kerath et al, 2013).We did not include age in our multivariate analysis. In another study, those more likely to donate blood samples for bio-banks were the middle-aged, those who had children, had personal experience of genetic disease, were blood donors and had a positive attitude toward genetic research, and had trust in experts/institutions. Gender did not influence the willingness to donate (Kettis-Lindbland et al, 2005); this being consistent with other studies (Wang et al,2001; Wong et al, 2004).

Though education showed no association with willingness to donate HBS for FUUR in our study, it may also sometimes be an important factor in respondents' willingness to donate HBS, as it was noted that those who had secondary/tertiary education were much more willing to donate HBS than others. The level of literacy in the study area is relatively high, especially with the strong concentration of tertiary institutions (government, private, mission) in the capital city of Enugu. It can be safely postulated that the better educated and academically exposed one is, the better informed the individual is, and invariably better placed /equipped to make certain decisions, without necessarily having to consult others.

Participation in previous researches requiring HBSmay also sometimes play a role, with respect to willingness to donate HBS for storage and future use in research. Among those who had previously participated in such researches, there was a considerably greater proportion that were willing to donate HBS; when compared to those who had never participated in such researches. Having a previous research experience presumably makes it easier for such individuals to being more willing to participate in future similar researches, especially when such experiences were not associated with untoward or unpleasant outcomes.

Though it can be argued that the flip-side of this situation is that involvement in research where the subject feels that he /she has been exploited may make such persons more reluctant about participation in future research, and in that sense, it may even be easier for one without any research experience to donate HBS for research. The Pfizer Kano Trovan study is a clear case of controversial research work probably adversely influencing recruitment /accrual of participants for future related research in that part of the globe.

In the same vein, those respondents who were aware that HBS could be stored and re-used for research, and that there were risks /benefits associated with such practices, were much more willing to donate their HBS than those who lacked knowledge about these issues. This may be important considering the fact that most of the study respondents actually were noted

not to be aware that HBS could be stored for future use in research, and as such, were not even aware of any associated benefit or risk. Considering that the study population is a largely educated group, it brings to fore the need for information, education and communication (IEC) programs in health research targeted at the public. People need to be told more about what health research entails, especially the ones requiring HBS. Obviously, there is an information gap in this aspect existing in the community.

The willingness to donate was mainly based on altruistic motives for most people. The desire to do some good and get associated with a good cause or to contribute to knowledge may have served as sufficient motivation for some of them. Majority of the respondents would donate HBS, without hoping for some compensation or reward. Some bioethicists however state that though there is nothing wrong with altruism per se, it fails to provide an appropriately stable foundation of a system for incentivising and rewarding tissue providers (Devaney, 2013)

The tissue providers' motivations, the use to which the tissues might be put, whether the recipient will benefit sooner rather than later from use of the tissues, and whether the results of the tissue provision are definable, are factors which the Nuffield Council on Bioethics considers ethically meaningful, that they should impact upon the level and types of rewards and incentives that should be made available for the provider of human tissue (Devaney, 2013). However, it must be noted that there may be a discrepancy between the respondents' standpoints based on hypothetical situations and their behavior in real life situations. The level of willingness noted in our study might be over-estimated due to the social desirability effect i.e. people might be reluctant to admit that they rather would not make a contribution to the common good (*Kettis-Lindblad et al, 2005).*

The findings from South Africa regarding the participants' willingness to have their samples stored and re-used are consistent with findings from other studies. In our study in Nigeria, various reasons were proffered for non-willingness to donate HBS for storage and future use in research. Respondents' unwillingness was explained mainly by feelings of uncertainty and discomfort related to the HBS being used for purposes other than research. Their views revealed a significant mistrust for fellow human beings especially strangers, with the underlying beliefs and attitudes being related to concerns about researchers' integrity, suspiciousness, fear and insecurity. Though most respondents were supportive of donating HBS for storage and future use in research, they tended to justify their lack of trust in the research enterprise in the light of their perceived distressing socio-economic and environmental influences in Nigeria. One reason that featured prominently among the

respondents who were unwilling to donate their HBS was their expressed concern that the HBS may get into the wrong hands and get used for rituals or witchcraft.

Respondents, though willing to donate most human tissues and fluids for storage and re-use in research, had some reservations over certain HBS (i.e. semen, vaginal swab, foetal products, hair, nail clippings and skin snips) depending on the socio-cultural significance attached to them. For instance, among the Ibo (Igbo) of Nigeria where the study was done, a man's claim to social fatherhood for a child born by his wife – even if the child has been biologically fathered by another man – is created when he buries the child's placenta. For a placenta-based research, it can only be imagined what the level of tissue accrual would be in such a setting. This belief may however not hold true for other Nigerians , and people from different cultural settings (Jenkins and Sugarman ,2005). With the increasing global demand for HBS in research, concerted efforts have to be made to recognize competing and diverse cultural meanings attached to HBS with a view to engaging appropriately with the potential donors and their communities, and as a means of promoting ethical research.

Among the 252 respondents in our study who indicated willingness to donate their HBS for storage and future use in research, majority (62%) were willing to grant one-time consent for future unspecified use research. This is consistent with the findings in a related Nigerian study (Igbe and Adebamowo, 2012), where a few stated that they would like to be re-consented. Most of the 401 respondents (including those not willing to donate HBS for research) objected to the idea of getting fresh consent for every new research conducted on stored HBS; major reason being that it would be a waste of resources as re-contacting donors may be problematic in Nigeria. In the words of a man in the FGD, ''once donated, the person should forget about his specimen'' The proponents of obtaining fresh consent are largely of the view that re-contacting for fresh consent would give the donor the opportunity to know to what use one's HBS is being employed. Similarly, in another survey conducted in five sites throughout the USA, it was shown that 42% of participants preferred that consent be obtained for each new research study that an individual's DNA is used for, thus precluding the use of an opt-out policy(Kaufman et al,2009). Results in 2006 Finnish and Swedish studies were similar, with 30% of the participants and 46% of the participants respectively, preferring to have consent obtained with each new research study involving their genetic material

Despite the encouraging high level of willingness to donate HBS for storage and future use in research, our study however demonstrated a low level of willingness among all the study respondents (38.9%) to grant one-time general consent for future unspecified use in research. This contrasts greatly with the Ugandan study (81%) and the study among African-

Americans(75%) but relatively similar to Egyptian findings (<50%) with blood samples (Wendler et al , 2005;Chen et al,2005; Abou-Zeid et al, 2010). The Ugandan study particularly showed that these donors were willing to have their samples used for future research on any disease condition, if an institutional review board was involved with the approval of such future research.

In the Egyptian study, less than a majority of the patients (44.3%) thought that informed consent forms should provide research participants with an option to donate a linked blood sample for research, though more than 80% would participate in a study that only involved blood sampling. This may be a pointer to the fact that reluctance to donate a blood sample for future unspecified research is not probably related to tissues involved in blood sampling itself but rather to tissues involving in the storage of samples. In the U.S.A. as in most developed countries, most research participants authorize the unlimited future research use of their biological samples when given opportunity to do so. These findings suggest that providing research participants with a simple binary choice to authorize or refuse all future research might allow individuals to control use of their samples, simplify consent forms, and allow important research to be done (Chen et al, 2005). This may not be totally acceptable since it can be argued that this line of action will be an abuse of respect for autonomy. The South African study, however, indicates that the majority of participants were supportive of giving one-time consent for the storage and re-use of their samples (Van Schalkwyk et al,2012). The challenge, however, with the general consent model that offers only the options either not to donate or to donate a sample for unrestricted future research is that participants might not have realized that future research might include diseases associated with stigma (Abou-Zeid, 2010).

There are so many consent models and each subject should be given the opportunity of granting consent for any fresh research, by using any of the consent models. In our study, the most preferred model after one-time general consent is the need for re-consent for every new research. The least preferred consent model is obtaining only HREC approval, though it can be contested that the respondents fully understood the concept of HREC. In our study, they were not presented with the option of giving one-time consent for future unspecified use coupled with HREC approval when necessary. In the six studies which examined this option, most people (79 – 95%) were willing to provide one-time general consent and rely on ethics committees to determine the studies for which their samples would be used (Wendler, 2006).

The finding that most people endorse one-time general consent is consistent across more than a decade for many population groups. One-time consent respects the wishes of people to control the use of their samples without mandating that they decide the specific research to be

done with their samples. One-time general consent has practical advantages. It increases the scientific and social value of donated samples and lowers the costs of conducting research on them, eliminating the need to track the choices for each sample. It also allows people to avoid being repeatedly contacted and asked for consent, possibly for decades. With respect to addressing some central challenges which arise in the context of obtaining and storing human biological samples for future research, some commentators argue that one-time general consent is better than a gift model (Wendler, 2012).

For proponents of re-consenting or re-contacting the person for every new research, it may be considered necessary when the original consent was invalid or there has been a major change to the research or the subjects condition at the time of the original consent, such that research participation may no longer be consistent with the subjects preferences and interests and the subject may need to reconsider the decision (Resnick, 2009). It is well-established in the research community that re-consent is an action in which a subject makes the decision to participate in research once again. Because the body of knowledge impacting a study often changes, subjects should receive information from researchers after they have enrolled in a study, such as significant new findings or test results that may affect their decision to participate in research (Resnik, 2009).

Because informed consent is a key component of ethical research, it may be imperative for the IRBS/HRECS to help determine when it is necessary to re-consent or re-contact subjects. The IRBS may help provide researchers with guidance for these procedures, especially if they are empowered to provide appropriate oversight functions. It is being suggested in so many quarters that the most appropriate way of resting the consent conundrum is to propagate the concept of a 'broad consent' for future unspecified use research which would be strictly subject to the safeguards of human research ethics review, and a feasible 'opt-out' option for future research use. In this respect there should exist a mechanism to encourage and sustain an adequate flow of appropriate information/communication between the HRECs/IRBs, researchers, sponsors of research, communities and participants.

Ranking high among the greatest concerns our study respondents had over donating their HBS for storage and future unspecified use research are the fear of rituals and unknown consequences; fear of exploitation by researchers /sponsors, fear of bodily harm following collection of certain body tissues/fluids and the perception that researchers seldom provide adequate information to potential research participants. The general consensus among them about promoting and encouraging participation in researches requiring stored HBS for future unspecified use is the dire need for massive public enlightenment, intensive health

education/information campaign and for sincere, sustainable community engagement coupled with the institution of accountable, open, transparent security and oversight mechanisms. .

The crucial need for socio-culturally appropriate and adequate public education on research use of stored HBS is further brought to the fore, by the finding that a very significant majority of all the respondents indicated their desire for provision of all relevant information about the research at the point of requesting consent for research participation. In contrast, only 2.5% indicated their need for payment before granting consent for future use of stored HBS in research. This is consistent with the findings in another Nigerian study that the participants rarely mentioned money as an expected benefit from research (Igbe and Adebamowo,2012).It is widely held that research participants should never be offered any financial inducements to donate samples ,though payment of reasonable expenses is acceptable .In this sense ,it may constitute an 'undue inducement' to take part in research. The issue of payment for research participation still remains a thorny, controversial issue among researchers, sponsors and bioethicists(Wilkinson,2005).

Against the backdrop of ethical issues involved in the consenting process for future unspecified use research, the overriding consideration still seems to be the need to promote respect for research subjects and protect their interests, especially since by nature, for many of them, their participation in research is largely altruistic.

With respect to granting consent for HBS collected from their bodies during surgery to be stored and re-used for research purposes, majority in this study were willing to grant consent. The relatively high level of willingness to consent to having body tissues/fluids removed during surgery to be stored and re-used in research(59.9%) was shown to be significantly associated with only occupation (p-value=0.012). Most of the respondents believed that these samples were generally of no use to them; either being diseased, malfunctional, non-functional or leftover materials. However, our work failed to specify and/or identify the preferred timing of eliciting the consent. Some commentators argue that in some circumstances, it is a clear advantage to obtain research consent post-operatively(*Hewitt et al, 2009)*.Studies in various settings have reported relatively high consent rates for the use of residual tissue in medical research (Vermeulen et al, 2009; Furness and Nicholson, 2004; Chen et al, 2005;Stegmayr and Asplund, 2002). These results show that patients prefer to be informed about proposed research with tissue, contradicting the position of some researchers that patients do not need to be informed and do not need to be provided with the opportunity to opt-out or withhold consent for future research with residual tissues (Keulartz et al, 2004). Though majority in our study felt that actually granting consent was of secondary importance, they still felt it was

proper to be informed about any proposed research with their biological materials. The majority in favour of research on these residual materials suggests that an ideal system should be based on an opt-out rather than an opt-in basis. Literature available also suggests that there is still a significant proportion of patients who are unclear about what happens to tissue that has been removed at operations and also, a great deal of uncertainty about the ownership of human tissue among in-patients who have had an operation.

The three other related studies conducted in Africa(Uganda ,Egypt and South Africa) did not set out to determine the perspective of individuals to using tissues removed from their bodies following surgery, for research. In a related study in the United Kingdom, 96.3% of surgical in-patients indicated that they would not object to their tissues being used in research (*Bryant et al, 2008*). The retention and use of human tissue for research and other purposes had received media attention in the UK following the incidents at Brown Royal infirmary and Adler Hey Hospital. In the case of surgical procedures for treatment of an ailment, the patient is deemed to have a social agreement with the surgeon, which marks the operation as a transition between the disease and anticipated good health post-operatively. In many cases, this involves the removal of some diseased body tissues /fluids and as such, the majority of patients would not really mind for such specimens to be used in research, though the possibility may exist that a significant percentage of people may be unclear about what really happens to tissues removed during surgery. Since these tissues /fluids removed for therapeutic purposes could serve as a key source of research material, there may be a need for better explanations to be made to surgical patients prior to the surgery and at the time of consent; especially in a developing country like Nigeria where literacy levels may be low in some places and many of the health practitioners tend to be paternalistic in their relationships with their patients.

Emerging ethical concerns have forced a separation between 'surgical consent' by patients to have surgery performed and 'research consent' for the research use of residual surgically-derived tissues. Though general consent rates for the research use of surgically removed tissues are high, there does not seem to be any strong universal consensus as to the optimal or appropriate time during hospitalization (pre or post) at which to obtain research consent for such surgically-derived specimens.

For those respondents who may object to research use of their surgically –derived samples, it is possible that they might hold religious, cultural or superstitious beliefs which dictate that the whole of a person's body should be available /intact for burial when they die. In the light of all these considerations, it is not always reasonable to assume that a patient's consent to the

removal of body tissues/fluids implied consent to its subsequent use for any ethically acceptable purpose. Such assumptions may not command universal public support.

For those who propose that no consent is needed for using leftover body materials for research purposes, they argue that less material will be available for research if consent is asked for; bureaucratic bottlenecks will be more; the right to self determination is relative, especially for left-over material; the principle of solidarity (helping others) is more important; lack of consent never caused problems in the past; patients' privacy and interests can still be safeguarded without a consent system; and that the practical alternative for leftover material is to discard it, a situation which will help no one. They argue that every day we excrete stools and urine and rarely show any signs of wanting to keep these body elements under our control (Van Diest, 2002).

For the advocates of seeking consent for leftover body materials, the arguments put forward include research on tissue can harm patients by disclosing health or other information resulting in discrimination in employment or insurance (breath of confidentiality); patients may have values regarding research, especially commercial or genetic research; it may benefit patients by allowing the identity of participants to be known and results with implications for the health of the participants to be reported to them (and their families), may benefit researchers by allowing further information and samples to be gathered from participants and to link databases; it allows sensitivity to be shown towards cultural values; it empowers research participants and may enable them to share in the profits of research; and it promotes public confidence in medicine and research, prevents exploitation, and regulates the behaviour of researchers (Savulescu, 2002). The utilitarian school of thought, aiming to safeguard scientific integrity of data, maintains that an implicit consent should be adequate, while the rights approach emphasising autonomy and confidentiality demands an explicit consent (Al-Quadire et al, 2010).

A significant majority of the respondents in this study objected to the research use of HBS from their dead relatives. Among those who did not have any previous research experience, a significantly greater proportion were expectedly not willing to allow research use of HBS from dead relatives than those who were willing. Along the same line, though, among those with previous research experience, slightly more persons were willing to allow such research, in comparison to those not willing for such research use of HBS from their dead relatives.

On multivariate analysis, willingness to allow FUUR on HBS derived from the bodies of dead relatives was found to be significantly associated with only gender (p-value=0.002). A much greater proportion of females than males are more reluctant to grant consent for research

use of HBS from dead relatives, in comparison to those who are willing to grant consent. This may be a reflection of the power dynamics which come into play in decision making in the typical Igbo household, especially with respect to decisions affecting the entire household. In a situation where a decision has to be taken regarding a dead relative, the males in the family are usually the ones expected by the traditional Igbo society to handle such matters. For instance, in the traditional Igbo setting, at the time of condolence / visitation during the funeral ceremonies, it is usually only the males in the household /family who are mandated to sit at the head of the table and receive such visitors.

The reluctance of a greater proportion of females over granting consent for research use of HBS from their dead relatives is in recognition of the position of womenfolk in Igbo land, with respect to issues bordering on deceased relatives. This scenario may also hold true for most other parts of Nigeria. For those willing to donate HBS from their relatives, the consensus is that these body materials are no longer useful to the dead, and may as well be utilized for the good of those who are alive. Religious and cultural beliefs also have a significant role to play, in their willingness to allow research use of HBS from their dead relatives. With the predominant notion in the study area that corpses ought to be accorded great respect and should not be desecrated, more light is shed on the trend observed; in which a significant majority were not willing to allow research use of HBS obtained from their dead relatives. Almost all the respondents were Christians, and the influence of their doctrine may play some role in this issue.

This stance, no doubt, will have an impact on acquisition of cadaver for medical research and education in Nigeria. The revised Anatomy Acts in Nigeria does not provide ethical principles (Ewonu Bari et al, 2012), for cadaver acquisition. The purposes of the act are to ensure a licensed practice of anatomy and an adequate supply of cadavers for research and education. It ordinarily establishes a voluntary system of donation of dead bodies for anatomical examination. The deceased, while alive could either in writing or verbally in the presence of two or more witnesses during the illness that caused his death, donate his dead body to any school of anatomy. For anatomical examination. however, the Nigerian Act does not define ‘anatomical exam’ though the meaning could be deduced from the English Anatomy Act of 1984 as examination by dissection of a body for purposes of teaching or studying, or researching into morphology; and where parts of the body are separated in the course of its anatomical examination, such examination includes the examination by dissection of the parts for those purposes (Nwabueze, 2007).

In most cultures globally, permission from the next of kin or legally authorized representative is usually obtained for cadaver tissue sampling in research, as this concerns an additional intrusion to the body beyond regular procedures such as post mortem examination. However, it is pertinent to emphasise that under the Nigerian Act, the deceased's surviving spouse, and in fact, any known relative can override the deceased's decision to have his body submitted for anatomical examination. This is in conformity with the Nigeria customary law which vests ownership of a person and the dead body in his or her family. This may be an inhibiton to medical research flowing from traditional practices and religious beliefs. Since this philosophy that animates the Nigerian perspective on dead bodies potentially ensures an inadequate supply of cadavers for anatomical examination, one wonders how the various medical schools and teaching hospitals have managed to source cadavers for research and training. It is thus likely that the supply of cadavers may be coming from unclaimed dead bodies with unknown relatives.

The concept of voluntary body donation is alien to the Nigerian Society, unlike some other regions of the world where it is relatively accepted (Akinola, 2011). Moreover, the Nigerian populace seems not to be aware of the need for whole body bequests, and even at that, religious, socio-economic and cultural factors may hinder willing donors from signing up for bequest programs. There is probably a need for formal body bequest programs in Nigerian medical schools and Teaching hospitals and these should be supported by the appropriate education, awareness creation and legislation. The church and other religious organizations, as well as the traditional leadership institutions may also be involved in these interventions. Without such legal backing, it would be practically impossible to establish public body donation centers in Nigeria to facilitate easy collection of willed bodies after the death of the donors.

With respect to their views on whether research participants should be allowed to withdraw their consent /specimens at any time, multivariate analysis showed that only education (p-value=0.002) was found to be significantly associated with this. Advocates of such withdrawals to be permitted were of the view that it was the fundamental right of the participants as situations surrounding the research may change. The other group of respondents opposing this view suggested that allowing such withdrawals may jeopardize the research, and cause waste of resources. In a study among Egyptians, majority did not believe there should be a right for them to withdraw their donated blood samples. Only less than a third of the respondents believed there should be right to withdraw the donated blood samples; with the rural residents being more likely to believe this. Interestingly though, the respondents were unwilling to share their blood samples with other countries, especially those from the western

world. The reasons for this situation included issues of confidentiality, commodification of the samples, religious values, and a concern that once blood samples leave the country it might be more difficult to provide oversight on the types of research performed on them (Abou-Zeid, 2010).

However, it is a well established part of ethical guidelines that research participants must have the freedom to withdraw their consent /samples in the research. These terms of withdrawal ought to be clearly negotiated at the time the HBS is being collected. In view of the numerous variables which come into play in the course of a research, it is necessary that potential donors understand what their withdrawal of participation will mean for that research, in particular, whether it confers on them the right to have the sample returned, destroyed, or simply 'de-identified' (Otlowski, 2007).

Findings from our study indicate that majority of the respondents (42.2%) were of the opinion that stored HBS belong to the researcher, and a slightly less proportion(38.8%) felt that such stored HBS belong to the donor. Though the Ugandan study did not specifically explore the issue of ownership of HBS, it can be deduced from their findings that the parents were willing to cede ownership or custody of their HBS to the researchers or the IRB. The vast majority of these Ugandan correspondents were willing to share the sample with the investigators in the U.K., U.S.A. and ready to accept that future research with the stored sample would require IRB approval, not their own additional consent (Wendler et al, 2005). Similarly, a greater proportion of the participants in the South African study felt that the samples became the property of the researchers, once donated (Van Schalkwyk et al, 2012). A sizeable majority (38%) of respondents in a study conducted in the Netherlands considered themselves to be the owners of residual tissues (Vermeulen et al, 2009). In another study in 1996, only 10% of the patients stated that they believed they retained ownership over tissue removed at surgery (Start et al, 1996). In a related study conducted among surgical inpatients, 29.1% believed that the hospital had ownership of tissue once it had been removed, followed closely by the beliefs that ownership belonged to patients (23.2%), pathology department (19.7%)and nobody(15.3%) respectively in that order (*Bryant ,2008*). However, these respondents may not actually have interpreted ''ownership'' legally. They may consider the tissue to be theirs, but they may not feel they should derive rights from research with their tissue. Typically, when informed consent to a surgical or diagnostic procedure is obtained in most medical facilities, the consent forms include buried language conveying the permission to use any remaining portions of the excised specimens for unspecified future research, educational purposes or be disposed of as deemed fit. Because these consent forms typically

do not address the issue of ownership directly, this area is left open to various interpretations and applications. Some would argue that while people should have an autonomy right to permit or prohibit their bodies and body parts being used for research, teaching, or therapy, they should not have proprietary rights of ownership and control in relation to the parts removed with their consent. That, they argue, should reside with the person or institution holding them, who in turn, should use them for appropriate medical or scientific purposes under proper ethical scrutiny (Jones, 2003).It is still unclear to what extent participants should be and are able to retain rights to their donated samples. The problem becomes compounded here because future usage includes research that has the potential to generate profit.

There was some divergence of opinion when asked their views about stored HBS being regarded as property. Majority of the participants in our study felt that the donated samples were no longer their property and did not feel that surrendering ownership meant that they had lost all their rights and interests. Interestingly, majority of the participants did not have interest and any concern over storage of their HBS outside Nigeria for any period of time. This is consistent with findings that lay persons in Nigeria support shipment of their samples to other countries, preferably in collaboration with competent, ethical, trustworthy researchers (Igbe and Adebamowo, 2012). Similar attitude was shown among the South African and Kenyan patients (Van Schalkwyk et al, 2012; Wendler et al, 2005). While the contrary was the case in the Egyptian study (Abou-Zeid, 2010), when the participants expressed less of a desire to share their samples with the USA and European countries compared with Arab countries.

For the research industry to thrive and for ethical research (both local and collaborative) to be conducted in our society, different stakeholders including members of the public have to be consulted and carried along. With the advances being recorded in biotechnology, genomics and genetic medicine/research globally, great impetus has been given to the development of bio-banking facilities. Nigeria, with her large and heterogeneous population comprising over 250 ethnic groups, and the huge burden of infectious/metabolic conditions coupled with a large pool of skilled medical and para-medical manpower, provides a very viable option for gathering information on issues related to tissue banking practices, as well as other issues. Bio-banks, if developed in Nigeria, will depend on people's willingness to contribute samples for both storage and research. People would act based on what they know, believe, feel and accept .Thus, public support is very prominent to ensuring and securing the viability of research activity and bio-banking practices, and this rests squarely on the assumption that the complex issues surrounding tissue/fluid donation for storage and future use in research are handled appropriately and ethically by the various stakeholders in the research industry

(Kettis-Lindblad et al, 2005). Against the backdrop of all the afore-mentioned issues, more empirical research may, however, be required to determine if participants in research actually and fully appreciate the implications and multi-factorial dimensions of all the choices they make in research, especially now that some commentators are arguing for the inclusion of some of these issues in informed consent forms (Abou-Zeid et al, 2010).

5.4- Strength of the study

We adopted a mixed method approach of data collection. The response rate of 94% for the quantitative arm of the study was encouraging, this probably being a reflection of the effectiveness of the methodology adopted. In some western countries with response rates ranging from 25% - 90%, such study methods adopted included self administered postal questionnaires, analysis of consent forms signed by research participants, telephone surveys, and the study of bio-banks register data (Kettis-Lindblad et al, 2005; Chen et al, 2005; Wendler and Emmanuel,2002; Johnsson et al, 2008).

5.5- Limitations of the study

1) The results may not be generalizable to individuals in other parts of Nigeria, as the study was conducted in a predominantly Igbo-speaking area.

2) More emphasis was placed on issues concerning the consenting procedure than on other ethical issues.

3) It was beyond the scope of resources of the study to recruit larger and more diverse population groups.

4) Limited enquiries were made into the socio-cultural meanings assigned to human biological specimens by the respondents.

5) The study did not set out to establish cause-effect relationships between variables under investigation.

6) Limited qualitative research methods were applied

5.6- Conclusion

There is a low level of awareness among respondents about use of stored HBS in research. There is also a guarded attitude of the respondents to the use of stored HBS in future research, obviously as a result of lack of trust for researchers requiring HBS for their studies. There does not seem to be any concern over the use of identifiers on HBS for most respondents. There is a strong desire by research subjects to have results of the research to be disclosed to them, especially the ones relating to their health. Majority of the study respondents willing to donate

human tissues and fluid specimens for storage and future use in research are also willing to grant one-time general consent for future unspecified use in research.

5.7- Recommendations

- There is great need for intensive mass education and information campaigns to address issues relating to use of stored HBS in research and the implications for individuals and communities. There is need to ensure adequate levels of accountability and transparency among researchers. With respect to resolving the consent dilemma in future unspecified use of stored HBS in research ,the concept of a "one-time/blanket/broad/general' consent which would be strictly subject to HREC/IRB review or oversight and a feasible, practical ''opt-out'' option for interested research participants may be the way forward.
- Dissemination of research findings both to the individuals and study communities should be promoted.
- Policies to ensure sharing of benefits from research should be initiated and implemented.
- Further empirical and qualitative research needed to probe into all the dimensions of issues related to storage and use of HBS in research.

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APPENDIX 1: RELEVANT TABLES RELATED TO BIVARIATE ANALYSES REPORTED IN CHAPTER FOUR (RESULTS SECTION)

OUTCOME 1: RESPONDENTS' WILLINGNESS TO DONATE HBS FOR FUUR (related to figure 4.1) n = 401

Table (i) gender versus respondents' willingness to donate HBS for FUUR

GENDER	WILLINGNESS TO DONATE HBS FOR FUUR		
	YES (%)	NO (%)	TOTAL
MALE	141(70.15	60 (29.85)	201
FEMALE	111 (55.50)	89 (44.50)	200
TOTAL	252 (100)	149 (100)	401

(p-value = 0.003)

Table (ii) Education versus respondents' willingness to donate HBS for FUUR

EDUCATION	WILLINGNESS TO DONATE HBS FOR FUUR		
	YES	NO	TOTAL
PRIMARY	25	26	51
SECONDARY	111	50	161
TERITARY	114	68	182
COMMERCIAL	2	4	6
OTHERS	0	1	1
TOTAL	252	149	401

(p-value = 0.002)

Table (iii) Marital status versus respondents' willingness to donate HBS for FUUR

MARITAL STATUS	WILLINGNESS TO DONATE HBS FOR FUUR	
	YES	NO
TOTAL		

SINGLE	16	71	
232			
MARRIED MONOGA	82	71	
153			
MARRIED POLYGAMOUS		3	
5			
DIVORCED/SEPARATED		2	
4			
WIDOWED	4	3	
7			
TOTAL	252	149	
401			

(p-value = 0.018)

Table (iv) participation in previous research requiring HBS versus respondents' willingness to donate HBS for FUUR

PARTICIPATION IN PREVIOUS RESEARCH REQUIRING HBS	WILLINGNESS TO DONATE HBS FOR FUUR		
	YES	NO	TOTAL
YES	35	4	39
NO	216	144	360
CAN'T REMEMBER	1	1	2
TOTAL	252	149	401

(p-value<0.001)

Table (v) knowledge of HBS storage for research versus respondents' willingness to donate HBS for FUUR

KNOWLEDGE OF HBS STORAGE FOR RESEARCH	WILLINGNESS TO DONATE HBS FOR FUUR		
	YES	NO	TOTAL
YES	111	46	157
NO	135	97	232
NOT SURE	6	6	12
TOTAL	252	149	401

(p-value = 0.025)

Table (vi) knowledge of HBS reuse in research versus respondents' willingness to donate HBS for FUUR

KNOWLEDGE OF HBS RE-USE IN RESEARCH	WILLINGNESS TO DONATE HBS FOR FUUR		
	YES	NO	TOTAL
YES	85	31	116
NO	153	108	261
NOT SURE	14	10	24
TOTAL	252	149	401

(p-value = 0.02)

Table (vii) knowledge of risks in reuse of HBS versus respondents' willingness to donate HBS for FUUR

KNOWLEDGE OF RISKS IN RE-USE OF HBS	WILLINGNESS TO DONATE HBS FOR FUUR		
	YES	NO	TOTAL
YES	68	21	89
NO	172	119	291
NOT SURE	12	9	21
TOTAL	252	149	401

(p-value = 0.008)

Table (viii) knowledge of benefits in reuse of HBS versus respondents' willingness to donate HBS for FUUR

KNOWLEDGE OF BENEFITS IN RE-USE OF HBS	WILLINGNESS TO DONATE HBS FOR FUUR		
	YES	NO	TOTAL
YES	84	30	114
NO	157	114	271

NOT SURE	11	5	16
TOTAL	252	149	401

(p-value=0.011)

OCCUPATION	WILLINGNESS TO GRANT ONE-TIME CONSENT FOR FUUR		
	YES	NO	TOTAL
CIVIL SERVANT	24	8	32
PROFESSIONAL	31	12	43
HOUSEWIFE	415		
ARTISAN	10	4	14
		10	
		4	
		14	
FARMER	1	0	1
BUSINESSMAN/ TRADER	32	16	48
		48	

STUDENT	45	5 96	96
UNEMPLOYED	9	4	13
TOTAL	156	96	252

OUTCOME 2: WILLINGNESS TO GRANT ONE- TIME CONSENT FOR FUUR (related to figure 4.2) n = 252 Table (i) occupation versus willingness to grant one-time consent for (p-value = 0.022)

Table(ii) awareness of benefit in HBS reuse for research versus respondents willingness to

AWARENESS OF BENEFITS IN HBS REUSE FOR RESEARCH	WILLINGNESS TO GRANT ONE-TIME CONSENT FOR FUUR		
	YES	NO	TOTAL
YES	49	35	84
NO	104	53	157
NOT SURE	3	8	11
TOTAL	156	96	252

donate HBS for FUUR

(p- value = 0.026)

able (ii) awareness of benefits in HBS reuse for research versus respondents' willingness to donate HBS for FUUR (p-value = 0.026)

OUTCOME 3: NEED FOR FRESH CONSENT FOR EVERY NEW RESEARCH (related to fig.4.4) n=401

Table (i) MARITAL STATUS VERSUS NEED FOR FRESH CONSENT FOR EVERY NEW RESEARCH

MARITAL STATUS	**NEED FOR FRESH CONSENT FOR EVERY NEW RESEARCH**			
	YES	NO	NOT SURE	TOTAL
SINGLE	106	119	7	252
MARRIED MONOG	55	96	2	153
MARRIED POLYG	2	3	0	5
DIVORCED/SEPAR	2	2	0	4
WIDOWED	6	0	1	7
TOTAL	171	220	10	401

(P-value = 0.014)

Table (ii) occupation versus need for fresh consent for every new research

OCCUPATION	**NEED FOR FRESH CONSENT FOR EVERY NEW RESEARCH**			
	YES	NO	NOT SURE	TOTAL
CIVIL SERVANT	21	27	0	48
PROFESSIONAL	25	38	0	63
HOUSEWIFE	5	6	1	12
ARTISAN	5	16	0	21
FARMER	1	2	1	4
BUSINESS/TRADER	32	57	1	90
STUDENT	74	62	7	143

UNEMPLOYED	6	12	0	18
OTHERS	2	0	0	2
TOTAL	171	220	10	401

(P -value = 0-006)

Table (iii) KNOWLEDGE OF HBS REUSE IN RESEARCH VERSUS NEED FOR FRESH CONSENT FOR EVERY NEW RESARCH

(P –value = 0.001)

KNOWLEDGE OF HBS	**NEED FOR FRESH CONSENT FOR EVERY NEW RESEARCH**			
REUSE IN RESEARCH	YES	NO	NOT SURE	TOTAL
YES	53	59	4	116
NO	101	156	4	261
NOT SURE	17	5	2	24
TOTAL	171	220	10	401

Table (iv)

Previous laboratory test versus need for fresh consent for every new research

PREVIOUS LABORATORY	**NEED FOR FRESH CONSENT EVERY NEW RESEARCH TEST**			
	YES	NO	NOT SURE	TOTAL
YES	139	191	6	336
NO	32	29	4	65
TOTAL	171	220	10	401

(p - value = 0.04)

Table (v)

Knowledge of HBS storage in research versus need for fresh consent for every new resear

KNOWLEDGE OF HBS STORAGE IN RESEARCH	NEED FOR FRESH CONSENT FOR EVERY NEW RESEARCH			
	YES	NO	NOT SURE	TOTAL
YES	74	80	3	157
NO	87	138	7	232
NOT SURE	10	2	0	12
TOTAL	171	220	10	401

(p - value = 0.017)

OUTCOME 4: WILLINGNESS TO GIVE CONSENT FOR RESEARCH ON HBS REMOVED DURING SURGERY (Related to fig. 4.5) n=401

Table (i): occupation versus willingness to give consent to research on HBS removed during surgery

(P-value = 0.03)

OCCUPATION	WILLINGNESS TO GIVE CONSENT FOR RESEARCH ON HBS REMOVED DURING SURGERY			
KNOWLEDGE OF HBS	YES	NO	NOT SURE	TOTAL
REUSE IN RESEARCH	DURING SURGERY			
CIVIL SERVANT	36	12	0	48
PROFESSIONAL	42	19	2	63
HOUSEWIFE	5	6	1	12
ARTISAN	1	5	0	6
FARMER	3	0	1	4
BUSINESS	50	37	3	90
STUDENT	78	56	9	143
UNMPLOYED	11	6	1	18
OTHERS	1	0	1	2
TOTAL	240	144	17	401

	YES	NO	NOT SURE	TOTAL
YES	74	39	3	116
NO	157	94	10	261
NOT SURE	9	11	4	24
TOTAL	240	144	17	401

p- value = 0.033

Table (ii) Knowledge of HBS reuse in research versus willingness to give consent on HBS removed during surg

OUTCOME 5:WILLINGNESS TO GIVE CONSENT FOR RESEARCH ON HBS REMOVED FROM DEAD RELATIVES (Related to fig. 4.6) n=401

OUTCOME 5: WILLINGNESS TO GIVE CONSENT FOR RESEARCH ON HBS REMOVE FROM DEAD RELATES (related to fig.4.6) n=401#

Table (i) Gender versus willingness to give consent for research on HBS removed from dead relatives

p-value = 0.006

table (ii) PREVIOUS PARTICIPATION IN RESEARCH VERSUS WILLINGNESS TO GIVE CONSENT FOR RESEARCH ON HBS REMOVED FROM DEAD RELATIVES

PREVIOUS PARTICIPATION IN RESEARCH	**GENDER**	**WILLINGNESS TO GIVE CONSENT FOR RESEARCH ON HBS REMOVED FROM DEAD RELATIVES**			
		YES	NO	NOT SURE	TOTAL
YES	MALE	86	106	9	201
	FEMALE	56	136	8	200
	TOTAL	142	242	17	401
NO		121	223	16	360
NOT SURE		1	0	1	2
TOTAL		142	242	17	401

(p-value = 0.011)

OUTCOME 6:RESEARCH PARTICIPANTS TO BE ALLOWED TO WITHDRAW CONSENT/HBS AT ANYTIME (Related to fig. 4.8) n=401

Table (i)

marital status versus research participants to be allowed to withdraw consent/HBS at anytime

(p-value<0.001)

MARITAL STATUS	RESEARCH PARTICIPANTS TO BE ALLOWED TO WITHDRAW CONSENT/HBS AT ANYTIME			
	YES	NO	NOT SURE	TOTAL
SINGLE	137	78	17	232
MARRIED MONOGAMOUS	59	87	7	153
MARRIED POLYGAMOUS	2	3	0	5
DIVORCED/SEPARATED	1	2	1	4
WIDOWED	5	1	1	7
TOTAL	204	171	26	401

Table (ii): occupation versus research participants to be allowed to withdraw consent/ HBS at anytime

OCCUPATION	RESEARCH PARTICIPANTS TO BE ALLOWED TO WITHDRAW CONSENT/HBS AT ANYTIME			
	YES	NO	NOT SURE	TOTAL
CIVIL SERVANT	27	19	2	48
PROFESSIONAL	33	27	3	63
HOUSEWIFE	4	8	0	12
ARTISAN	6	14	1	21
FARMER	1	1	4	4
BUSINESS/TRADER	35	51	4	90
STUDENT	86	45	12	143
UNEMPLOYED	11	5	2	18
OTHERS	1	0	1	2
TOTAL	204	171	26	401

(p-value=0.004)

Table (iii)

Previous laboratory test versus research participants to be allowed to withdraw consent/ HBS at anytime

PREVIOUS LABORATORY TESTS	RESEARCH PARTICIPANTS TO BE ALLOWED TO WITHDRAW CONSENT/HBS AT ANYTIME			
	YES	NO	NOT SURE	TOTAL
YES	177	143	16	336
NO	27	28	10	65
TOTAL	204	171	26	401

(p-value = 0.009)

Table (iv) Education versus research participants to be allowed to withdraw consent/ HBS at anytime

EDUCATION	RESEARCH PARTICIPANTS TO BE ALLOWED TO WITHDRAW CONSENT/HBS AT ANYTIME			
	YES	NO	NOT SURE	TOTAL
PRIMARY	14	33	4	51
SECONDARY	80	70	11	161
TERTIARY	107	64	11	182
COMMERCIAL	3	3	0	6
OTHERS	0	1	0	1
TOTAL	204	171	26	401

(p-value=0.008)

Table (v)

Knowledge of HBS storage in research versus research participants to be allowed to withdraw consent/ HBS at anytime

KNOWLEDGE **OF HBS STORAGE IN RESEARCH**	RESEARCH PARTICIPANTS TO BE ALLOWED TO WITHDRAW CONSENT/HBS AT ANYTIME			
	YES	NO	NOT SURE	TOTAL
YES	90	52	15	157
NO	104	119	9	232
NOT SURE	10	0	2	12
TOTAL	204	171	26	401

(p-value<0.001)

Table (vi) Knowledge of HBS reuse in research versus research participants to be allowed to withdraw consent/ HBS at anytime

KNOWLEDGE OF HBS REUSE IN RESEARCH	RESEARCH PARTICIPANTS TO BE ALLOWED TO WITHDRAW CONSENT/HBS AT ANYTIME			
	YES	NO	NOT SURE	TOTAL
YES	58	47	11	116
NO	131	119	11	261
NOT SURE	15	5	4	24
TOTAL	204	171	26	401

(p-value=0.018)

Table (vii)

Risks of HBS reuse in research versus research participants to be allowed to withdraw consent/ HBS at anytime

RISKS OF HBS REUSE IN RESEARCH	PARTICIPANTS TO BE ALLOWED TO WITHDRAW CONSENT/HBS AT ANYTIME			
	YES	NO	NOT SURE	TOTAL
YES	48	34	7	89
NO	143	133	15	291
NOT SURE	13	4	4	21
TOTAL	204	171	26	401

(p-value=0.029)

Table (viii)

Benefits of HBS reuse in research versus research participants to be allowed to withdraw consent/ HBS at anytime

BENEFITS OF HBS REUSE IN RESEARCH	RESEARCH PARTICIPANTS TO BE ALLOWED TO WITHDRAW CONSENT/HBSAT ANYTIME			
	YES	NO	NOT SURE	TOTAL
YES	62	40	12	114
NO	130	128	13	271
NOT SURE	12	3	1	16
TOTAL	204	171	26	401

(p-value=0.017)

OUTCOME 7:WILLINGNESS FOR DISCLOSURE OF FINDINGS (Related to table 4.6 in the result section

table (i) marital status versus willingness for disclosure of findings

MARITAL STATUS	WILLINGNESS FOR DISCLOSURE OF FINDINGS			
	YES	NO	NOT SURE	TOTAL
SINGLE	134	18	8	160
MARRIED MONOGAMOUS	66	17	0	83
MARRIED POLYGAMOUS	2	1	0	3
DIVORCED/SEPARATED	0	1	1	2
WIDOWED	3	0	1	4
TOTAL	205	37	10	252

(p-value=0.002)

Table (ii)

Previous laboratory test versus willingness for disclosure of findings

PREVIOUS LABORATORY	WILLINGNESS FORDISCLOSURE OF FINDINGS			
TEST	YES	NO	NOT SURE	TOTAL
YES	179	29	6	214
NO	26	8	4	38
TOTAL	205	37	10	252

(p-value=0.03)

Multi-variate analysis tables for two outcomes

Table 1. Logistic Regression Analysis Models for willingness to donate HBS for FUUR relating to socio-demographic factors (after adjusting for other co-variates)

Penultimate Model				Final Model		
variable	**Odd Ratio**	**P-value**	**95%C.I**	**Odd Ratio**	**P-value**	**95%C.I**
Gender	1.885	0.003	1.241-2.864	1.864	0.003	1.232-2.820
Marital status	1.384	0.023	1.045-1.834	1.390	0.021	1.050-1.840
Education	0.943	0.688	0.709-1.254	-	-	-

Table 2. Logistic Regression Analysis Models for willingness to donate HBS from bodies of dead relatives for FUUR (after adjusting for other co-variates)

Penultimate Model				Final Model		
variable	**Odd Ratio**	**P-value**	**95%C.I**	**Odd Ratio**	**P-value**	**95%C.I**
Gender	1.927	0.002	1.268-2.929	1.930	0.002	1.270-2.933
Previous research experience	1.953	0.046	1.011-3.772	1.948	0.047	1.009-3.7GF63
Religion	0.944	0.58	0.769-1.159	-	-	-

APPENDIX 2

STORAGE AND FUTURE USE OF HUMAN BIOLOGICAL SPECIMENS IN RESEARCH: KNOWLEDGE AND ATTITUDE OF POTENTIAL RESEARCH PARTICIPANTS IN NIGERIA

QUESTIONNAIRE FOR CROSS-SECTIONAL SURVEY

Serial Number _____

A) SOCIO-DEMOGRAPHIC INFORMATION

1) Name of respondent (optional)

2) Sex Male/Female

3) Age _____ (Specify) 18-35yrs[ ] 36-59yrs [ ] 60 and above [ ]

4) Marital Status: Single [ ]
Married monogamous [ ] Married Polygamous [ ]
Divorced/Separated [ ] Widowed [ ]

5) Occupation:
Housewife [ ] Professional [ ]
Artisan [ ] Farmer [ ]
Business/Trading [ ] Student [ ]
Unemployed [ ] Civil Servant [ ]
Others (specify)……..

6) Religion:
Roman Catholic [ ] Muslim [ ]
Protestant Christian [ ] Traditionalist [ ]
Apostolic/Pentecostal Christian [ ]

Other (Specify)……

7) Educational level completed:

Primary School [ ] Secondary School [ ]

Tertiary School [ ] Commercial School [ ]

None [ ] Others (Specify)…….

8) Have you ever given any body tissue/fluid specimen for research?

Yes/No/Can't remember

If No skip to Q10

9) If Yes, what types of specimen? _____

- What types of research?_____
- Did the researcher tell you that the specimens may be stored or re-used? (Yes/No/Can't remember)

10) Have you ever given any body tissue/fluid specimen for laboratory investigation? Yes/No/Can't remember

If Yes, What types of specimens?_____

B) KNOWLEDGE ABOUT STORAGE AND FUTURE USE OF BODY TISSUES/FLUID IN RESEARCH

11) Do you know that body tissues/fluids are sometimes stored for long periods in research? Yes/No/Uncertain

If Yes, why_____

12) Do you know that body tissues/fluids are sometimes re-used in research? Yes/No/Uncertain

If Yes, why_____

13) Are you aware of any risk associated with the storage and future use of these specimens in research? Yes/No/Uncertain

If Yes, specify_____

14) Are you aware of any benefit associated with the storage and future use of these specimens in research? Yes/No/Uncertain

If Yes, specify_____

15) Are you aware of any law, code or regulation in Nigeria guiding the storage and future use of these specimens in research? Yes/No/Uncertain

C) ATTITUDE TO STORAGE AND FUTURE USE OF BODY TISSUES/FLUIDS IN RESEARCH

16) What would you require before you consider donating your body tissue/fluids for storage and future use in research?

All relevant information [ ] Payment [ ]

Both [ ] Others (specify) _____

Will not consent [ ]

17) Are you willing to donate your body tissues/fluids or those of your children for storage and future use in research?

Yes/No

Give reasons _____

_____

If no skip to question 31

18) Which body tissues/fluids are you willing to donate for storage and future use in research?

Blood	[ ]	Ear, Nose, Throat swab	[ ]
Urine	[ ]	Eye swab	[ ]
Saliva	[ ]	Semen	[ ]
Skin Scraping	[ ]	Nail Scraping	[ ]
Hair	[ ]	Vaginal swab	[ ]
Stool	[ ]	Others (specify) _____	

19) Are you willing to give at the point of specimen collection one-time consent for storage and future unspecified use research of your body tissues/fluids?

Yes/No (If yes, skip to question 21)

Give reasons _____

_____

20) If no to Question 19, would you consent to:

Future research limited to some researches [ ]

Future research limited only to the same medical condition for which the specimen was collected [ ]

Re-contact for consent before any re-use [ ]

Only HREC approval for any re-use [ ]

(HREC- a special selected group of persons- experts and lay persons- who oversee health researches).

21) Do you have any concerns over privacy/confidentiality of data when donating specimens for research?

Yes/No/Don't know

Give reasons _____

_____

22) Would it matter to you if there are identifiers to your specimens collected for storage and re-use in research

Yes/No/Don't know

Give reasons _____

_____

23) Would you consent to:

Short-term storage (days, weeks) [ ]

Medium term storage (months) [ ]

Long-term storage (years) [ ]

All of the above [ ]

None [ ]

24) Would it matter to you if your body tissues/fluids are stored in another country outside Nigeria?
Yes/No/Don't know

25) After collection of your specimens, who has the ultimate ownership?

Tissue Donor [ ] Not sure [ ]

Researcher [ ] IRB/REC [ ]

Sponsor of research [ ]

26) Should such specimens be regarded as objects of property?
Yes/No/Don't know

Give reasons _____

_____

27) Should tissues donors have access to and control over the specimens and data collected?
Yes/No/Don't know

Give reasons _____

_____

28) Are you interested in being provided with results from any future study using your stored specimen, even if those results may have unpleasant implications for you or your community?
Yes/No/Don't know

Give reasons _____

_____

29) Would you consent to storage and future use of your specimens by commercial companies?

Yes/No/Don't know

30) If researchers obtain some financial gain from storing and re-using your specimens, should the benefits be shared with you?

Yes/No/Don't know

Give reasons _____

_____

31) Would you consent to having body tissues/fluids removed from your body during surgery to be stored and re-used for research?

Yes/No/Don't know

Give reasons _____

_____

32) Do you feel that fresh consent is necessary for every new research conducted on previously collected specimens?

Yes/No/Don't know

Give reasons _____

_____

33) Would you consent to a dead relative's tissues/fluids to be collected for storage and re-use for research?

Yes/No/Don't know

Give reasons _____

_____

34) Should research participants be allowed to withdraw their consent/specimens at any time?

Yes/No/Don't know

Give reasons _____

_____

35) Should parents/guardians serve as proxies for people unable to give consent (mentally or physically challenged persons, unconscious persons) for storage and re-use of their specimens? Yes/No/Don't know

Give reasons _____

_____

36) Whose consent would be sufficient in donating body tissues/fluids for storage and re-use in research?

Individual [ ]
Community [ ]
Both [ ]

Give reasons:_____

37) What is the greatest concern you have over giving your body tissues/fluids for storage and future use in research?

_____

_____

38) What should be done to promote and encourage donation of body tissues/fluids for storage and future use in research?

_____

_____

THANK YOU FOR YOUR TIME!

APPENDIX 3

FOCUS GROUP DISCUSSION GUIDE

Study Location _____

FGD group _____

Date_____

Discussion Guide:

. Introduction and warm-up

. Request for consent

. Assurances of confidentiality

. Permission to record discussion

. Opening remarks

We are here to hold discussion with you on issues concerning research on body tissues/fluids. It will be appreciated if you tell us all you know on these issues, as we shall be relying on you to learn more on them. Whatever we learn from you today will help in designing future health researches for this and other communities. To help in remembering what you say, there will be tape-recording of our discussion, if you permit. This will be compared with the notes to be taken by my colleague here. But before we kick off, we may need to know each other's name, where we come from and what we do.

General introduction of all present.

Topics to be covered:

1. Awareness and perception on the use of human biological specimens in research-storage and future use.
2. Consent issues
3. Ownership of specimen, property rights. control/access to tissues /data, benefit sharing, commercialization
4. Privacy, confidentiality, identifiers on specimens
5. Disclosure of research findings to participants /communities

Questions

1. Please tell us all you know /feel about giving or taking human body tissues/fluids for research. you may share your personal experiences or those of others, in this community or elsewhere.

- Probe about their awareness that HBS can be stored for long periods and re-used for different types of research.

2. Would you be willing to donate HBS for such researches? (probe about willingness to donate HBS from surgeries and HBS from dead relatives, the types of HBS they would donate, reasons for donating /not donating, concerns /fears about donating HBS for research)
3. Would you be willing to grant one-time consent for future unspecified use of your HBS in research (probe for reasons, conditions necessary for such consent to be granted, other preferred consent models, concerns/fears ,withdrawal of consent/samples, need for fresh consent for every new research)
4. What are your views about ownership of donated specimens; controlling and having access to the specimens and data derived; benefit sharing, commercialization, selling of human tissues/fluids? probe for reasons.
5. What are your views about privacy and confidentiality of data derived from research on HBS donated by you? Would it matter to you if researchers place identifiers on your samples? probe for reasons
6. Are you interested in being provided with results from future use of your samples even if such results may have negative implications? Probe for reasons
7. What should be done to promote donation of HBS for storage and future unspecified use research?

Thank you

APPENDIX 4

STORAGE AND FUTURE USE OF HUMAN BIOLOGICAL SPECIMENS IN RESEARCH: KNOWLEDGE AND ATTITUDES OF POTENTIAL RESEARCH PARTICIPANTS IN NIGERIA

RESEARCH CONSENT FORM

I am Dr. Onochie Ike Okoye, a consultant ophthalmologist/ lecturer with the University of Nigeria Teaching Hospital, Ituku -Ozalla and the College of Medicine, University of Nigeria. I am conducting this research in partial fulfillment of the dissertation requirements for a masters' degree in Bioethics. This is with the support of the West African Bioethics training program, Ibadan, Nigeria.

I would like to request your consent and cooperation in the conduct of a study of ethical & socio-cultural issues associated with storage and re-use of human biological specimens donated for research purposes. You are being requested to participate because you are a member of this community and a potential tissue donor. We hope to learn about the views you and other community members hold on such issues. This information will contribute to ethical conduct of future human research and protection of human participants. Nothing you say will be considered right or wrong. If you should decide to participate, you will be interviewed by me and the interview should last between 30 and 45 minutes. Possible risk factors from your participation are no greater than your normal daily activities. Any information obtained in connection with this study which can be identified with you will remain strictly confidential and will be disclosed only with your permission. If you decide to participate, you are completely free to withdraw consent and discontinue participation at any time. Your decision as to whether or not to participate is without any associated form of coercion, inducement, compensation or reprisal. Only the investigator and the project supervisor will have access to the information. Giving your names to the investigator will be optional. You are encouraged to ask questions at any stage of the interview, and we are bound to obtain new consent if the conditions or procedures involved in the study change. Your community will be notified at a later date of findings from this study, which may be of interest and relevance. If you decide to participate, you shall be required to sign 2 copies of the consent form, one of which you may keep in your custody. This will indicate that you have completely understood the information provided and have granted genuine consent.

If you have additional questions that I have not answered to your satisfaction, please contact me at the:-

Department of Ophthalmology university of Nigeria Teaching Hospital, Ituku-Ozalla, PMB 001129, Enugu

Tel: 234-803-313-3810 234-808-878-8802 E mail:-oicokoye@yahoo.com.

Participant's Signature Date

Investigator/Interviewer's Signature Date

APPENDIX 5: Ethics Committee Certificate Of Approval.

UNIVERSITY OF NIGERIA TEACHING HOSPITAL

ITUKU-OZALLA, P.M.B. 01129, ENUGU, NIGERIA,

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Dr. (Chief) Charles U. Amanze, MB. BS.(KSM)
Chairman, U.N.T.H. Management Board

Offiong Chukwujama (Mrs.) B.Sc. (Hons), AMC, CHMP, MIHSAN.
Director of Administration/Secretary
U.N.T.H. Management Board

Dr. A. U. Mbah, MD (LODZ) FNCP, FNIM, (KSJ)
Chief Medical Director

Dr. P. U. N. Nze, MB.BS, DA. FWACS
Chairman, Medical Advisory Committee

Our Ref. UNTH/CSA.329/VOL.5 Date.....

NHREC/05/01/2008B

ETHICAL CLEARANCE CERTIFICAE

TOPIC: STORAGE AND FUTURE USE OF HUMAN BIOLOGICAL SPECIMENS IN RESEARCH: A KNOWLEDGE AND ATITUDE OF PARTICIPANTS. IN NIGERIA.

BY: DR. ONOCHIE I. OKOYE

FOR: A RESEARCH IN MASTERS (MS.C) IN BIOETHICS DEGREE PROGRAMME OF THE UNIVERSITY OF IBADAN.

This research project on the above topic was reviewed and approved by the University of Nigeria Hospital Research Ethics Committee.

This certificate is valid for **one** year from date of issue.

Prof. R. E. Umeh
Chairman
Health Research Ethics Committee

Date: 31/07/08

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