

# Legal and Ethical Laws Governing Human Medical Research and Experimentation

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## Abstract

Human Medical research and experimentation is important to the development of life science and helpful to the health of human beings. Ethics is an essential dimension of human research as it can be considered as both a discipline and practice. The need for human medical research cannot be over emphasized; it ensures a progression in the curative as well as scientific aspect of medicine which is beneficial to all mankind. In view of desire of humans to live and not die notwithstanding new diseases emerging, scientific research must be encouraged to remain on top of all forms of health challenges. The purpose of this work is to further the arguments on the relevance of human medical research and experimentation as well as the necessity to ensure that adequate regulations are put in place to checkmate the excesses of researchers particularly when conducting experiments with developing countries like Nigeria, such that requisite ethical values are sustained. It reviews widely accepted ethical principles that govern the conduct of research with human participants. Application of research ethics committees to monitor and approve prior review of proposed research that involves human participants in research has been elucidated along with the legal and practical implications. There are so many challenges brought about by human experimentation, which should be paid more attention to by law in order to protect the right of the subject. International as well as domestic laws are enacted in order to beat the illegitimate human experiment, while criminal countermeasures should be taken to redeem the failure of medical researchers in adhering to these ethical issues which are internationally recognized. Legal measures are recommended to emphasize the need to protect right to life notwithstanding the burning urge to enhance science and medicine, in Nigeria and globally.

## Introduction

The conduct of human medical research involving human participants raises a host of ethical and legal issues that have concerned philosophers, lawyers, policy makers, scientists, and clinicians for many years.<sup>1</sup> Human medical research is conducted for the purpose of systematically collecting and analysing data from which general conclusions may be drawn that may aid in improving the care of currently unknown beneficiaries in the future.<sup>2</sup> The chief role of human participants in research is to serve as sources of needed data. This is a different situation than ordinarily occurs in clinical medicine, in which diagnostic or therapeutic interventions are suggested or carried out solely to benefit the current patient.<sup>3</sup> If medical progress were to depend solely upon the scientific by product of experimentation conducted incidental to therapy, medical science and human health care might, figuratively, still be in the dark ages. Human experimentation has achieved many spectacular successes, such as the control of polio<sup>4</sup> and the reported worldwide eradication of smallpox.<sup>5</sup> It has, on occasion, been an incentive to subjects to attain important benefits and avoid death or severe harm.

There are three distinguishable types of cases involving the treatment of human subjects. The first is traditional treatment which uses normal and approved methods and techniques for therapeutic purposes. The second is research treatment, which means that a sick person is treated with new methods and techniques primarily for therapeutic purposes. This is sometimes called therapeutic experimentation. The third is research which consists of treating individuals with new procedures and drugs for purely scientific purposes. This may be labelled "research experimentation."<sup>6</sup> If medical progress were to depend solely upon the scientific by product of experimentation conducted incidental to therapy, medical science and human health care might, figuratively, still be in the dark ages. Throughout medical history, research experimentation has played a central role in the development of knowledge which is beneficial to human health. The influence of human experimentation permeates not only medicine and the other biological sciences but also behavioural, sociological, political,

<sup>1</sup> Coleman C.H, Menikoff J.A, Goldner J.A, et al. *The Ethics and Regulation of Research with Human Subjects*. Newark: Matthew Bender Co, 2005:3–50.

<sup>2</sup> Code of Federal Regulations, Part 46.102(d) U.S.A

<sup>3</sup> Sankar P. *Communication and Miscommunication in Informed Consent to Research*. *Med Anthropol Q* 2004; 18:429–46.

<sup>4</sup> See C. Fried, *Medical Experimentation: Personal Integrity and Social Policy* 147-48 (1974). 16 Bollett, supra note 6, at 47

<sup>5</sup> Henderson, *Smallpox-Epitaph for a Killer?* 154 NAT'L Geographic 796 (1978).

<sup>6</sup> Giesen, *Civil Liability of Physicians for New Methods of Treatment and Experimentation*, 25 INT'L & Comp. L. Q. 180, 188 (1976), M. Cheriff Bassiouni, Thomas G. Baffes, John T. Evrard, *An Appraisal of Human Experimentation in International Law and Practice: The Need for International Regulation of Human Experimentation*, *Journal of Criminal Law and Criminology* vol.72, issue 4, Article 20 (1981)

economic, and military endeavours. Because human experimentation deals with effects upon large numbers of people, experimenters possess the potential to enhance or diminish the welfare of mankind.<sup>1</sup> Since this potential may result in wilful, reckless or inadvertent acts harmful to human beings, human experimentation is also a proper concern for the international regulations. These ethical concerns are addressed by an extensive regulatory structure pertaining to human subjects' research in several countries of the world such as United States of America where human medical research has gained grounds.<sup>2</sup>

One of the arguments discussed, is whether and to what extent individuals or groups have a 'right' to experimental treatment, or at least to have access to it without undue government interference. Also, could it be said that such claims call into question the principles and practices that underlie biomedical research with human subjects? The principal 'access' to medicine problem, worldwide, is the inability of so many people, in both rich countries and poor countries, to secure medicines and treatments that are known to work well, and that are available to the rich at a moment's notice.<sup>3</sup> The need for protection was particularly great if the subjects were members of groups that historically were disadvantaged<sup>4</sup>. The AIDS epidemic taught a different lesson: persons facing near certain death from a deadly disease may welcome risk-taking in the name of possible therapy<sup>5</sup>. The failure to provide a reasonable level of health care to all persons that need it is principally blamed on the costs involved, but also on medical infrastructure and the absence of services in many areas, and sometimes to patients' ignorance. It is a tragedy nonetheless when someone dies for want of medical attention that could easily save him or her. Whether this failure violates international human rights obligations is a topic with its own huge literature. A large number of international and regional documents solidly ground a right to basic health care and the principle of access to health care without discrimination. Presently, the rules seem to assume that the risks of clinical research more commonly outweigh the therapeutic rewards<sup>6</sup>.

One major issue law needs to regulate, is the governments need to balance the 'right' to access to experimental treatment without necessarily accepting to take part in a trial against the public's 'right' to be protected against the risk of harm from inadequately evaluated drugs. Yet, clearly lots of patients are denied clinical research opportunities they would accept in a moment because of the investigators' desire to follow required ethical research practices.<sup>7</sup> However, it strikes at the heart of the whole system the need to be protected from research risk. Thus, the need for institutional and regulatory review processes the international research community has created, in the name of research ethics, are intended to deny patients access to some experimental treatments, i.e. those that an independent committee believes it imprudent to begin studying in humans, despite the sponsoring physician's readiness to proceed. This then means death for the patient when nothing is done, unlike the experimental approach which offers some slim hope.

The essence of the extensive ethical and legal protections for human subjects is that the subjects, especially vulnerable populations such as prisoners, must be treated with the dignity befitting human beings and not simply as experimental guinea pigs. The Nuremberg Code and other guidance's also call on the medical professional to treat persons with their best interests in mind and to minimize pain or other risks and harms in the service of a research goal. Doctors are required to use treatments that are expected to be effective and not to engage in speculative medicine at the expense of a human research subject.

### Definition of Terms

According to Black's Law dictionary<sup>8</sup>, *legal ethics* means a lawyer's practical observance of or conformity to

<sup>1</sup> M. Cheriff Bassiouni, Thomas G. Baffes, John T. Evrard, *An Appraisal of Human Experimentation in International Law and Practice: The Need for International Regulation of Human Experimentation*, *Journal of Criminal Law and Criminology* vol.72, issue 4, Article 20 (1981)

<sup>2</sup> M.B Kapp, *Ethical and legal issues in research involving human subjects: do you want a piece of me?* *J Clin Pathol*; 59:335-339. (2006)

<sup>3</sup> For instance, AIDS focused new attention on the need for scientific and medical innovation, and the necessity of taking risks to get it. With AIDS came a gradual cultural transformation in the image of participating in research. When research principles crystallized into international legal and ethical norms, in the 1960's and 70's, the dominant intellectual paradigm - whatever the attitudes of real patients with real diseases - stressed the risks inherent in medical research, and the need to protect research subjects from them.

<sup>4</sup> Harold Edgar and Ricardo Cruz-Coke, *Ethical Considerations Regarding Access to Experimental Treatment and Experimentation on Human Subjects*, United Nations Educational, Scientific and Cultural Organization (UNESCO) CIP/BIO.501/96/4 Paris, 22 December 1996

<sup>5</sup> Edgar and Rothman, 1990 *ibid*

<sup>6</sup> *Ibid* n. 5 p.4

<sup>7</sup> These ethical issues such as informed consent, confidentiality, research misconduct, respect and responsibility, data protection Act 1998, Declaration of Helsinki, Nuremberg code etc. will be discussed in the course of the work. See also Veatch R.M. *The Patient as Partner: A Theory of Human Experimentation Ethics*. Bloomington: Indiana University Press, 1987:16-76

<sup>8</sup> B.A. Garner, *Black's Law Dictionary*, 9<sup>th</sup> edition, 2004 p. 976

established standards of professional conduct.

Ethical codes or principles are an expression of how we should behave as individuals and as a society. They are moral judgments that can be applied to particular situations to help us make decisions and guide our behaviour. Inevitably, they are linked to cultural values at a particular time in our history and are subject to change as attitudes and values evolve. What was normative just a half century ago, may be considered insensitive today.

### Human Medical Research

Some medical interventions "are designed solely to enhance the well-being of an individual patient or client" and "have a reasonable expectation of success."<sup>1</sup> In contrast, *medical research* "designates an activity designed to test a hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge, expressed, for example, in theories, principles, and statements of relationships."<sup>2</sup>

### Human Medical Experimentation

Similarly, *medical experimentation* "refers to relatively untested and usually more innovative medical and surgical procedures which are applied primarily as a means of contributing to the common good in the interests of humanity through anticipated progress in medical science."<sup>3</sup> A procedure is deemed experimental "because it has not been accepted by the medical community as a standard treatment for a specific disease or disorder, or for a subclass of patients, e.g., infants, the elderly."<sup>4</sup>

Human experimentation can also be broadly defined as 'anything done to an individual to learn how it will affect him.'<sup>5</sup> Its main objective is the acquisition of new scientific knowledge rather than therapy. If an experiment is ultimately beneficial to others or even to the subject himself, this does not mean that therapy served an important purpose.<sup>6</sup>

U.S. Federal regulations for protection of human research subjects define a 'human subject' as 'a living individual about whom an investigator obtains: data through intervention or interaction with the individual or identifiable private information'<sup>7</sup>.

### Historical Background

The history of human experimentation dates to some of the oldest writings on earth. The effects of inoculation were studied by the Chinese of the Sung Dynasty in 590 B.C. and were recorded in a Sanskrit text; studied in India in the second and third centuries A.D.<sup>8</sup> The practice in ancient Persia was for the king to consign condemned criminals to scientific experimentation. The Ptolemaist permitted this practice in Egypt, and it existed in Renaissance Pisa.<sup>9</sup> When Hippocrates asserted that epilepsy is not an act of divine intervention but an ordinary disease, he set the stage for the study of neurology and mental disease.<sup>10</sup> Galen stressed experimentation in conjunction with observation, formalizing medical experimentation in Western society about 1800 years ago.<sup>11</sup> Harvey's dominance in the seventeenth century supplanted the earlier dominance of Galen. In particular, Harvey carried out controlled experiments on animals and man in order to demonstrate that blood circulates through the heart and lungs.<sup>12</sup>

In the early 1960s, most notably are the United States instances of unethical medical research was reported

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<sup>1</sup>National Commission for the Protection of Human Subjects of Biomedical and Behavioural Research, *The Belmont Report* (Washington, DC: Government Printing Office, 1978), p. 2, cited in A.M. Capron, "Human Experimentation" in Robert M. Veatch (ed.), *Medical Ethics* (Boston: Jones & Bartlett, 1989), p. 132 Ronald Munson. *Intervention and Reflection Basic Issues in Medical Ethics*, 4th ed. (Belmont, CA: Wadsworth Publishing, 1992), p. 320. A.M. Capron, "Human Experimentation" in Robert M. Veatch (ed.), *Medical Ethics* (Boston: Jones & Bartlett, 1989), pp. 137-8.

Munson, *Intervention and Reflection*, p. 331. See also Orville N. Griese, *Catholic Identity in Health Care: Principles and Practice* (Braintree, MA: Pope John Center, 1987), p. 321.

<sup>4</sup>Capron, "Human Experimentation", pp. 138-139.

<sup>5</sup> Bowker, *Experimentation on Humans and Tissue: Article 20-23 of the Civil Code*, 19 McGill L.J. 161, 164 (1973).

<sup>6</sup> M. Cheriff Bassiouni, Thomas G. Baffes, John T. Evrard, *An Appraisal of Human Experimentation In International Law and Practice: The Need For International Regulation Of Human Experimentation*, *The Journal Of Criminal Law & Criminology* Vol. 72, No. 4 p.2

<sup>7</sup> Levine, C. Faden R, Grady C, Hammerschmidt D, Eckenwiler L, Sugarman J. *The Limitations of Vulnerability as a protection for Human Research Participants*. A.M. J. Bioeth 2004; 4(3): 44-49

<sup>8</sup> Bollet, Smalox: *The Biography of a Disease-I, Resident and Staff Physician* Aug. 1978, at 47, 48.

<sup>9</sup> H. Beecher. *Research and the Individual: Human Studies* 5 (1970). P. 8

<sup>10</sup> Ibid

<sup>11</sup> Ibid at 6

<sup>12</sup> Ibid

over the volunteers, especially those who were vulnerable or terminally sick, were treated with obvious disrespect and exposed to significant risk of harm<sup>1</sup>. Among these were the infamous project conducted at the Brooklyn Jewish Chronic Disease hospital in which elderly patients who had some disability were injected with live cancer cells in circumstances in which it was unclear whether consent was sought.<sup>2</sup> A study of infectious hepatitis C at the Willow brook home for children with Mental retardation, who were deliberately infected with hepatitis C, not only raised serious concerns in public, but also jeopardised the reputation of noble medical profession. In 1966, Henry Beecher's article, 'Ethics and Clinical Research' in the new England Journal of Medicine reported 22 examples of medicinal research that involved suboptimal ethical treatment of human subjects<sup>3</sup> For nearly 40 years (1932-1972), the U.S. National Health service conducted a research titled the Tuskegee study of untreated syphilis in the negro male<sup>4</sup>. The study was done on about 600 black men of whom 399 had syphilis. The participants were never informed that they were involved in a research study, and their informed consent was not obtained<sup>5</sup>. Such unethical incidents necessitated the dire of informed consent from participants and researchers' responsibility to be satisfied that the gain anticipated in any research project was commensurate to the risk involved. Notwithstanding the progress made with regulations on human experimentation, there are advanced levels of unethical practices of experimentation still taking place in the United States which needs to be addressed before it relates into war crimes.<sup>6</sup>

### Development of Regulations

It was the trial of Karl Brandt and others (now called the Medical Case) between 1946 and 1947 by the Nuremberg Military Tribunal that shook the confidence of the international community in the propriety of leaving research subject protection and welfare to the sole judgment and conscience of an investigator.<sup>7</sup> The Karl Brandt trial revealed horrendous experiments conducted by some Nazi scientists and physicians on prisoners in concentration camps without their consent or any form of ethics or institutional review.<sup>8</sup> Though the defendants at the Nuremberg Military Tribunal claimed that their actions were justifiable under the existing domestic law and were not condemned by then prevailing international law, the Tribunal presented ten basic principles of ethical, moral, and legal complexion that provided the measure of the defendants' actions.<sup>9</sup> These principles crystallized into what is known as the Nuremberg Code,<sup>10</sup> and they set minimum standards for the ethical conduct of biomedical research. Normatively, the Nuremberg Code is at least part of customary international law<sup>11</sup> and binds member states of the United Nations.<sup>1</sup> However, its existence has not prevented subsequent

<sup>1</sup> Thomson C.J.H, *Research Ethics Committees*, 2012, see also Salman Y. Guraya, N.J.M London, Shaista S. Guraya, 'Ethics in Medical Research' *Journal of Microscopy and Ultrastructure*. 2 (2014) 121-126

<sup>2</sup> Wisely J. *Research Ethics Committee*, *Brit J. Gen. Pract.* 2008; 58 (553):580

<sup>3</sup> Beecher H.K. *Ethics and Clinical Research*. *Bull World Health Organization* 2001;79 (4): pp.367-372

<sup>4</sup> Salman Y. Guraya, N.J.M London, Shaista S. Guraya, 'Ethics in Medical Research' *Journal of Microscopy and Ultrastructure* 2 (2014) 121-126

<sup>5</sup> Thomas S.B. Quinn SC. The Tuskegee Syphilis study, 1932-1972: Implications for HIV education and Aids

<sup>6</sup> Report identifies evidence of unethical and illegal human subject experimentation conducted by US health professionals on detainees. Human experimentation, in the form of systematic medical monitoring and subsequent transformation of the data obtained into generalizable knowledge. Physicians for Human Rights (PHR) has identified evidence that in the months and years following the Sept. 11, 2001 attacks, the Bush administration violated essential standards that prohibited human experimentation on detainees. For further reading. See Nathaniel Raymond, *Experiments In Torture: Evidence of Human Subject Research and Experimentation in the "Enhanced" Interrogation Program, A White Paper by Physicians for Human Rights*, (2010)

<sup>7</sup> M. Grodin, *Historical Origins of the Nuremberg Code, in the Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation*. 121-44 (G.J. Annas & M. Grodin eds., 1992); Matthew Lippman, *The Nazi Doctors Trial and the International Prohibition on Medical Involvement in Torture*, 15 *Loy. L.A. INT'L Comp. L.J.* 410 (1993).

<sup>8</sup> Such unethical experiments have been discussed above except these cases where non consenting subjects were locked in low pressure chambers that mimicked the atmospheric conditions and pressures prevailing at high altitude up to 68,000 feet; freezing experiments in which victims were denuded and exposed for long hours to temperatures below freezing point or placed inside a tank of ice water; deliberate infliction of battle-like wounds and aggravated infection thereof to test the efficacy of sulfanilamide and other drugs; deliberate poisoning of the food of victims to determine the effects of certain poisons and bullets on human beings; sexual sterilization experiments using surgery, high-dose x-rays, and pharmacological techniques; and the deliberate killing of some Jewish prisoners to provide skulls and skeletons for cranial and racial research at the Reich University of Strasbourg. **United States v. Karl Brandt**, reprinted at Jay Katz, *Experimentation with Human Beings: The Authority of the Investigator, Subject, Professions and State in the Human Experimentation Process at 292-94* (1972).

<sup>9</sup> Excerpt of the judgement of the Nuremberg Military Tribunal is reproduced in *Clinical Investigation in Medicine: Legal, Ethical, and Moral Aspects* 116-19 (Irving Ladimer & Roger W. Newman eds., 1963).

<sup>10</sup> For the early attempts at the international level to codify the principles enunciated by the Nuremberg Military Tribunal, see Robert K. Woetzel, *The Nuremberg Trials in International Law* 232-44 (1962).

<sup>11</sup> Pascal Arnold & Dominique Sprumont, *The 'Nuremberg Code': Rules of Public International Law*, in *Ethics Codes in*

research scandals.<sup>2</sup>

A major issue at Nuremberg was defining the criteria for ethical human experimentation. Consequently, the Articles of the Nuremberg Tribunal developed as the first formal attempt to create a legal framework governing human experimentation. These Articles provide:

1. The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision. This latter element requires that before the acceptance of an affirmative decision by the experimental subject there should be made known to him the nature, duration, and purpose of the experiment; the method and means by which it is to be conducted; all inconveniences and hazards to be expected; and the effects upon his health or person which may possibly come from his participation in the experiment. The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs, or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.
2. The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.
3. The experiment should be so designed and based on results of animal experimentation and knowledge of the natural history of the disease or other problems under study that the anticipated results will justify the performance of the experiment.
4. The experiment should be so conducted as to avoid all unnecessary physical and mental suffering and injury.
5. No experiment should be conducted where there is an a priori reason to believe that death or disabling injury will occur; except, perhaps, in those experiments where the experimental physicians also serve as subjects.
6. The degree of risk to be taken should never exceed that determined by the humanitarian importance of the problem to be solved by the experiment.
7. Proper preparations should be made and adequate facilities provided to protect the experimental subject against even remote possibilities of injury, disability or death.
8. The experiment should be conducted only by scientifically qualified persons. The highest degree of skill and care should be required through all stages of the experiment of those who conduct or engage in the experiment.
9. During the course of the experiment the human subject should be at liberty to bring the experiment to an end if he has reached the physical or mental state where continuation of the experiment seems to him to be impossible.
10. During the course of the experiment the scientist in charge must be prepared to terminate the experiment at any stage, if he has probable cause to believe, in the exercise of the good faith, superior skill, and careful judgment required of him, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.<sup>3</sup>

The concepts of Nuremberg were re-evaluated at the meeting of the World Medical Association in Helsinki, in June of 1964, and were incorporated into the Code of Ethics on Human Experimentation of the World Medical Association.<sup>4</sup> Helsinki was the second formal attempt to place human experimentation within a legal framework.<sup>5</sup> This code also allowed for experimentation on human subjects including the very young, the unconscious and those who lacked legal capacity such as the mentally ill<sup>6</sup>.

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Medicine: Foundations and Achievements of Codificationsince 1947 90 (Ulrich Tröhler & Stella Reiter-Theil eds., 1998). Due to the Nuremberg Code's continuing and uniformed applications (usus) by a majority of countries, as well as the general recognition of its binding nature (opinio juris), these basic principles have become rules of customary international law. In fact, they are applied in the common interest of all nations and are so deeply rooted in the international legal consciousness that they constitute peremptory public international law (ius cogens). This means that they cannot be modified by any State or professional organization, either by statute or ethical guidelines.

<sup>1</sup> Christine V. D. Wyngaert & Guy Stessens, *International Criminal Law: A Collection of International and European Instruments* 50 (1996).

<sup>2</sup> For instance, in 1963, twenty-two chronically ill and debilitated patients at the Jewish Chronic Disease Hospital (JCDH) in Brooklyn were given injections of liver cancer cells to study their immunologic status, or their rejection responses. The study was a non-therapeutic clinical research project and was funded by the United States Public Health Service and the American Cancer Society.

<sup>3</sup> J. Appleman, *Military Tribunals and International Crimes* 142-43 (1954), at 147-48; Beeson, Bondy, Donnelly, & Smith, *Panel Discussion: Moral Issues in Clinical Research*, 36 *Yale J. Biology & Med.* 455-56 (1964), see also *ibid* n.19 p.11

<sup>4</sup> World Medical Association, *Human Experimentation: Code of Ethics of the World Medical Association*, 2 *Brit. Med. J.* 177 (1964); Declaration of Helsinki, adopted first by the World Medical Association in 1964, Declaration of Helsinki: Recommendations Guiding Doctors in Clinical Research, 197 *J.A.M.A.* 32 (1966).

<sup>5</sup> Bryant, *the Burgeoning Law of Medical Experimentation Involving Human Subjects*, *John Marshall J. Prac. & Proc.* 19, 20 (1974).

<sup>6</sup> While some have criticised the Helsinki Declaration (for watering down the consent provisions of the Nuremberg Code) it

Those meeting at Helsinki emphasized that the Declaration of Geneva by the World Medical Association,<sup>1</sup> include the words: "The health of my patient will be my first consideration," and be binding upon the physician. They also pointed out that the International Code of Medical Ethics<sup>2</sup> declares that "any act or advice which could weaken physical or mental resistance of a human being may be used only in his interest." Based upon those underlying concepts the final Code embodied the following basic principles:

1. Clinical research must conform to the moral and scientific principles that justify medical research and should be based on laboratory and animal experiments or other scientifically established facts.
2. Clinical research should be conducted only by scientifically qualified persons and under the supervision of a qualified medical man.
3. Clinical research cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
4. Every clinical research project should be preceded by careful assessment of inherent risks in comparison to foreseeable benefits to the subject or to others.
5. Special caution should be exercised by the doctor in performing clinical research in which the personality of the subject is liable to be altered by drugs or experimental procedure.<sup>3</sup>

The World Medical Association also defined, for the first time, a fundamental distinction between clinical research, which is essentially therapeutic, and "pure" clinical research, which is primarily for the purpose of acquiring scientific information with little anticipated therapeutic value to the subject.<sup>4</sup> Different guidelines were formulated for each situation:

#### **A. Clinical Research Combined with Professional Care**

1. In the treatment of the sick person the doctor must be free to use a new therapeutic measure if in his judgment it offers hope of saving life, re-establishing health or alleviating suffering. If at all possible, consistent with patient psychology, the doctor should obtain the patient's freely-given consent after the patient has been given a full explanation. In case of legal incapacity, consent should also be procured from the legal guardian; in case of physical incapacity, the permission of the legal guardian replaces that of the patient.
2. The doctor can combine clinical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that clinical research is justified by its therapeutic value for the patient.

#### **B. Non-therapeutic Clinical Research**

1. In the purely scientific application of clinical research carried out on a human being, it is the duty of the investigator to remain the protector of the life, health, and privacy of that person on whom clinical research is being carried out.
2. The nature, the purpose, and the risk of clinical research must be explained to the subject by the investigator.
- 3a. Clinical research on a human being cannot be undertaken without his free consent, after he has been fully informed; if he is legally incompetent, the consent of the legal guardian should be procured.
- 3b. The subject of clinical research should be in such a mental, physical, and legal state as to be able to exercise fully his power of choice.
- 3c. Consent should as a rule be obtained in writing. However, the responsibility for clinical research always remains with the research workers; it never falls on the subject, even after the consent is obtained.
- 4a. The investigator must respect the right of each individual to safeguard his personal integrity and privacy, especially if the subject is in a dependent relationship to the investigator.
- 4b. At any time during the course of clinical research, the subject or his guardian should be free to withdraw permission for research to be continued. The investigator or the investigation team should discontinue the research if in his or their judgment it may, if continued, be harmful to the individual.<sup>5</sup>

Clearly, the scientists who met at Helsinki could not condemn all human experimentation. They recognized that medical science had advanced beyond the point where simple observation and accumulation of random clinical data could satisfy the requirements for effective inquiry into the causes and treatment of human disease. It was also apparent that the Helsinki Code would serve only as a broad guideline, against which the investigator must compare his conduct in relation to the subject-patient.<sup>6</sup> The Code of Ethics on Human Experimentation of

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gained more publicity than the Nuremberg Code and was more influential within the medical profession. see Kuhse H, Singer P, Paul M. McNeill, *Experimentation on Human Beings: A History, and Discussion of Current Regulations a Companion to Bioethics*. Blackwell: Companions to Philosophy, Blackwell Publishers: 369-378. (1998)

<sup>1</sup> The Declaration of Geneva, 1948: A 1971 Reappraisal, 2 MED. J. AUSTL. 735 (1971).

<sup>2</sup> Adopted by the Third General Assembly of the World Medical Association at London, October, 1949.

<sup>3</sup> Adopted by the Third General Assembly of the World Medical Association at London, October, 1949.

<sup>4</sup> See n.31

<sup>5</sup> Ibid n.31

<sup>6</sup> Ibid Beecher, @ 279

the World Medical Association has been adopted by the American Medical Association and, in modified but similar forms, by most professional medical organizations throughout the world.<sup>1</sup>

Paradoxically it was Germany that had first developed codes of ethics for experimenting on human subjects. In 1900 a directive from the Prussian Minister of Religious, Educational and Medical Affairs was issued to the Directors of Clinics. By that directive medical experiments could only be conducted on competent adults who had consented after a proper explanation of the adverse consequences that might result. Subsequently there were accusations in the German press of the abuse of subjects of experiments including children. As a consequence, the German Minister of the Interior published Richtlinien that is regulations or guidelines. The 1931 that included the requirements for testing on animals, consent based on the provision of appropriate information, and the exclusion of any experiments which might endanger children even in 'the slightest degree'. These regulations were in force during the period of the Third Reich but they were obviously flouted.

Although the trial of the Nazi doctors and bio scientists condemned, in the strongest possible way, inhumane experiments on human beings, the Nuremberg Code contained in the Court's judgment, was not itself very influential. The attitude in the Anglo-American World was that the Code was the result of an extreme abuse of human subjects which could only occur in the peculiar circumstances of Nazi Germany during the War.

Medical specialist colleges and international medical groups were also reluctant to accept the Nuremberg Code because it included an absolute requirement for consent prior to any experimentation on human subjects.

### **Development of Research Ethics Committee Review**

One of the early responses to publicity given to those unethical experiments was a requirement in 1966, by the Surgeon-General of the United States, for committee review of applications for Public Health Service grants. Each applicant was required to state that a committee had considered the risks of the research for any human subjects and had satisfied itself of the adequacy of protection of their rights. Subsequently the American Senate insisted on a national commission to consider human experimentation. The resulting Commission published a number of reports including the Belmont Report<sup>2</sup> identifying basic ethical principles and the Institutional Review Board Report which included a survey of the committees known as Institutional Review Boards (IRBs) that were created following the Surgeon-General's request of 1966. The Senate also insisted on the promulgation of regulations covering research on human beings and those regulations incorporated and strengthened the National Institutes of Health policy require that all publicly funded research be approved by a committee.

In 1966 Canada followed the United States' lead and adopted the requirement for review by committee, and the following year the Royal College of Physicians of London recommended committee review of research proposals within its guidelines for research with human subjects. New Zealand introduced a requirement for committee review in 1972 and a policy of committee review was adopted by the National Health and Medical Research Council in Australia in 1973. Other countries also followed this lead and international codes<sup>3</sup>, such as the Council for International Organizations of Medical Science<sup>4</sup> guidelines have adopted committee review of

<sup>1</sup> Shaffer, Medical Ethics, 1 Editorial Research Rep. 461, 470 (1972).

<sup>2</sup> The Belmont Report and The US Code of Federal Regulations: The Common Rule the Belmont Report, published in 1974, is a statement of ethical principles governing research with humans developed by the US Congressionally appointed Commission for the Protection of Human Subjects of Biomedical and Behavioural Research. It identifies three ethical principles: respect for persons, beneficence, and distributive justice. The Belmont principles have been codified into Regulations and the Common Rule and have been adopted in whole or part by nineteen US federal agencies to regulate research with humans conducted or supported by the US government. Revisions to the Common Rule were proposed in July 2011. The proposed changes, responses to public comments, and the final revision will be available on the website of the Office Human Research Protections.

<sup>3</sup> International Conference for Harmonization Guidelines for Good Clinical Practice (GCP) Good Clinical Practice Guidelines were developed by the International Conference on Harmonization (ICH). Governments can use them to develop regulations governing clinical trials with humans. They include protection of human rights, standards for conduct of trials, and responsibilities and roles of sponsors, investigators, monitors and clinical research associates. When adhered to, the results of trials conducted multi-nationally should be acceptable for safety and efficacy decisions by all participating governments. In 2005, a Handbook for Good Clinical Practice was published and in 2009 an on-line course became available. Standards and Operational Guidance for Health Related Research The "*Standards and Operational Guidance for Health-Related Research*" is a draft document released for comment in 2011 by the WHO. This document is more specific than general ethical guidelines and is intended to govern the establishment and operation of research ethics committees that review research with human subjects.

<sup>4</sup> The Council for International Organization of Medical Sciences the Council for International Organizations of Medical Sciences (CIOMS) was founded by the World Health Organization (WHO) and the United Nations Educational, Scientific and Cultural Organization (UNESCO) in 1949. In the 1970s CIOMS and WHO worked on guidelines to indicate how the ethical principles articulated in the Declaration of Helsinki could be applied to research with humans, especially in developing countries. As new research methods and practices emerged, particularly the expansion of clinical trials in developing countries, conferences were held to address issues that were not covered in the original guidelines. In 2002, CIOMS published ethical principles (they adopted the principles in The Belmont Report) and 21 guidelines that are broadly

research proposals as a major protection for human subjects of experimentation.<sup>1</sup>

Internationally there is very little legislation specifically addressing experimentation on human subjects<sup>2</sup>. The United States was exceptional in issuing governmental regulations covering human experimentation. As indicated above, both the Netherlands and Belgium governments have issued decrees. Requirements in other countries are usually issued as guidelines<sup>3</sup>. These guidelines have been issued by funding bodies such as the Canadian Medical Research Council, the Australian National Health and Medical Research Council; and governmental departments such as the Departments of Health in New Zealand the United Kingdom and by professional bodies such as the Royal College of Physicians of London.

- There are a number of common features of all of these guidelines standards and regulations: All of them rely on review by a committee of proposals for research on human subjects.
- The committees are required to consider proposals and decide whether or not they are ethical.
- Committees have the power to approve a proposal in the form in which it is presented, request modification by the researcher, or reject the proposal.
- Membership of the committees is specified to include some members with expertise in research and one or two community (or lay) members.

There are some differences between countries in the other members of committees recommended. Typically the guidelines state the matters that the committee should take into account in deciding whether or not to approve the proposal: for example the requirement to consider whether the potential benefits of the research justify any risks of harm to the human participants. However a rejection by an ethics committee, or failure to present a proposal for approval by a committee, will often have implications for funding and may lead to the refusal of a journal to publish any results from research programs that have not been approved.

In essence, the purpose of prior ethical review of medical research employed is to protect the rights and welfare of human participants ensuring the legal and ethical application of codes of practice of medical research conduct. An institutions Research Ethics Committee<sup>4</sup> aims to safeguard the welfare, dignity and safety of the

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applicable, including in low resource countries. They cover • ethical justification of the research, • scientific validity, • ethics committee review, • informed consent and situations when consent is not attainable, • inducements to participate in research, • risks and benefits, • research with low resource populations, • choice of control groups in clinical trials, • research with vulnerable groups, • confidentiality, • compensation for injury in research, • strengthening infrastructure in developing countries, and • ethical obligation to provide health services. Each Guideline is accompanied by commentary. In 2009, an update issued Guidelines for epidemiological research was published. For updates see <http://www.cioms.ch>.

<sup>1</sup>Within Scandinavia, Sweden has had ethics committee review since the late 1960s, Denmark since the late 1970s and Finland since the early 1980s. In 1984 the Swiss Academy of Sciences recommended advisory bodies on experimentation and, in the same year, both the Netherlands and Belgium governments issued decrees required ethics committee review. While there are review committees in France, reports indicate that in practice few research proposals are considered. Germany and Japan, the two countries in which there were flagrant abuses of the ethics of experimentation on humans (as discussed above), have been conspicuous in having relatively undeveloped review systems for considering human experimentation although in the last five years Japan has developed a system of committee review for drug trials. Reports from other countries in Europe, India, the East generally, Africa and Latin America are either non-existent or sketchy and this may indicate the lack of developed systems of review. McNeill (1993)

<sup>2</sup> Third Geneva Convention, Article 13, which states: No prisoner of war may be subjected to physical mutilation or to medical or scientific experiments of any kind which are not justified by the medical, dental, or hospital treatment of the prisoner concerned and carried out in his interest. **Convention (III) relative to the Treatment of Prisoners of War**, Article 13. Geneva, 12 August 1949. Web. 01 Jun 2010. <<http://www.icrc.org/ihl.nsf/7c4d08d9b287a42141256739003e63bb/6fef854a3517b75ac125641e004a9e68>>. While this language maintains the existing prohibition on biological experiments. The WCA in America during president Bush tenure added two qualifications that appear to have lowered the bar on biological experimentation on prisoners. That language requires that the experiment have a “legitimate” purpose, but does not require that it be carried out in the interest of the subject. It also adds the requirement that the experiment not “endanger” the subject, which appears to raise the threshold for what will be considered illegal biological experimentation. Bush administration revisions to the WCA remain in effect. As long as weakened statutory language exists that may permit experimentation on detainees in US custody, the risk remains that current and future detainees could be subjected to serious violations of human rights.; **the United Nations Conventions Against Torture** Convention Against Torture and Other Cruel, Inhuman, or Degrading Treatment or Punishment. G.A. Res. 39/46. U.N. GAOR. 39th Sess. Supp. No. 51. 1984:197. Entered into force June 26, 1987. U.N. Doc. A/Res/39/46. Web. 17 May 2010. <http://www.un.org/documents/ga/res/39/a39r046.htm>; **the International Covenant on Civil and Political Rights**, International Covenant on Civil and Political Rights, opened for signature December 16, 1966. Article 7. 999 U.N.T.S. 171. Entered into force March 23, 1976. Web. 17 May 2010. <http://www.un.org/millennium/law/iv-4.htm>; **the Universal Declaration of Human Rights** Article 5 of UDHR states: “No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment.” Universal Declaration of Human Rights, G.A. res. 217A (III), U.N. Doc A/810, at 71. (1948). Web. 17 May 2010. <<http://www.un.org/en/documents/udhr/>>. Accessed on 11<sup>th</sup> March 2017.

<sup>3</sup>Variously called 'codes', 'guidelines', 'statements', or 'standards'



participants, ensures that ethically approved research is conducted in line with the approved protocol, and promoted public confidence in the conduct of human research. Research Ethics committees play a key role in promoting ethical practices in biomedical research and in identifying solutions to ensure that the interests of researchers and society do not take precedence over the rights of the participants<sup>1</sup> The Association of Accreditation of Human Research Protection Programs (AAHRPP) accredits research ethics committees and human protection programs nationally and internationally in an effort to achieve high quality and continuing education.

#### **Functions of the Research Ethics Committee:**

- a.) Prior review of human research ethics proposals, scrutinizing the ethical standards for research conduct in legal framework
- b.) Observation to the investigators, to modify the research proposal to meet the required ethical standards
- c.) Decision to reject or approve the research proposal
- d.) Monitoring the conduct of approved research proposals ensuring that their conduct continues to conform to approved protocol.
- e.) Resolution or referral for resolution, of complaints in relation to the conduct of approved research projects or the conduct of the ethical review of those projects.
- f.) Premature termination and/or suspension of the conduct of a research proposal whenever it becomes evident that continuing conduct will expose participants to greater level of risks than those approved.
- g.) Accountability and quality assurance by reporting to the relevant institutions about its performance.

#### **Key Issues on Research Ethics**

##### **Informed Consent**

Informed consent refers to an ethical and legal doctrine based on the understanding that all interventions (diagnostic, therapeutic, preventive or related to scientific studies) in the medical field should only be performed after a participant has been informed about the purpose, nature, consequences and risks of the intervention and has freely consented to it<sup>2</sup>. The primary focus of consent should be on informing and protecting research subjects, through disclosure and discussion of relevant information, meaningful efforts to promote participants' understanding, and by ensuring that decisions to participate, or to continue participating, are always made voluntarily.

Informed consent is the ethical cornerstone of randomized clinical trials (RCT), where volunteers are given the option to participate in a trial that includes randomization or to remain outside the trial and receive traditional medical treatment. Mandatory condition for an informed consent include; provision of detailed information to a subject; adequate understanding of the information provided; expression of consent and/or authorization of the intervention.<sup>3</sup> The researcher's primary moral responsibility is to design a clinical trial that will answer a research question without exposing human subjects to undue risks in the process<sup>4</sup>. When fully informed subjects give their consent, acknowledge their role as research participants and take responsibility for their designated roles. Assuming that the research question is significant, the trial is well structured, and the risks to the individual patient are justified, the tension between collective ethics and individual ethics is obviated when individual subjects give their informed consent. This holds true if the primary intent of the investigator is to compare two treatments, not to provide better overall care to the subject<sup>5</sup>. Implementation of informed consent can be considered as a sign of the growing patients' welfare and rights movement, protecting various dimensions of their integrity, safety, and confidentiality.

Obtaining consent does not necessarily employ disclosing the information; rather it demands comprehension of the information ensuring that the subject is, in fact, amicably informed. However the problems in attaining fully informed consent are well documented<sup>6</sup>. In some situations, despite researcher's sincere efforts, subjects often fail to understand the nature or rationale for the research and hence are incapable of providing an informed consent. In two separate studies that assessed bio bank participants' understanding, more than one-

<sup>1</sup> Martin-Arribas MC, Rodriguez-Lozano I, Arias-Diaz J, *Ethical Review of Research Protocols: Experience of a Research Ethics Committee*. *Rev. Esp Cardiol* (English Edition) 2012; 65 (6): 525-529

<sup>2</sup> Glickman S.W, McHutchison JG, Peterson ED, Cairns CB, Harrington RA, Califf RM, et al. *Ethical and scientific implications of the globalization of clinical research*. *N Engl. J Med* 2009;360(8): 816-23.

<sup>3</sup> Agre P, Campbell F.A, Goldman B.D, Boccia M.L, Kass N, McCullough L. B, et al. *Improving informed Consent: The Medium is Not the Message*. *IRB: Ethics Hum Res* 2003;25(5): S9-11

<sup>4</sup> Pullman D, Wang X. *Adaptive Designs, Informed Consent, and the Ethics of Research Control Clin Trials* 2001;22(3):203-10

<sup>5</sup> Lilford R. J, Jackson J. *Equipose and the Ethics of Randomization*. *J R Soc Med* 1995;88(10):552.

<sup>6</sup> Pullman D. *Conflicting Interests, Social Justice and Proxy Consent to Research*. *J Med Philos* 2002;27(5):523-45. Emanuel, E.J, Wendler, D. Grady, C. *What Makes Clinical Research Ethical?* *J Am Med Assoc* 2000;283(20):2701-11

third of participants answered questions incorrectly regarding the objective of the research, limitations to confidentiality protections, that their DNA would be stored as part of the research, that the research involved some risks, and whether they would receive individual genetic results<sup>1</sup>. This reflects an important understanding that genomic research presents challenges for traditional models of informed consent, and provides opportunities for new models of consent and communication<sup>2</sup>.

### **Confidentiality**

Confidentiality means the nondisclosure of certain information except to another authorized person. The concept of confidentiality applies that the information a person reveals to a professional is private and has limits on how and when it can be disclosed to a third party<sup>3</sup>. Various dimensions of confidentiality described in the literature include human rights, confidentiality in young persons, domestic violence, true anonymisation of data, validity of consent for disclosure, cancer and genetic registers, fertility, involuntary disclosure, and safeguards<sup>4</sup>.

There is no breach of confidentiality if the following recordings for any purpose were used, as long as they were effectively anonymised<sup>5</sup>:

- a. Conventional X-rays
- b. Images taken from pathology slides
- c. Laparoscopic images of the inside of abdominal cavity
- d. Images of internal organs
- e. Ultrasound images

To maintain the subject confidentiality, the researcher should collect only the data that is really required, should collect anonymous data, store name and data separately by using identification numbers instead of names, use pass-word to protect the data files, and secure the office and computer.

### **Privacy**

Privacy is the quality of being secluded from the presence or view of others. Privacy in research refers to the right of an individual to make decisions concerning how much information about their physical status, health, social network, and thoughts and feelings will be shared with investigators<sup>6</sup>. To protect the privacy rights of family members, researchers must be careful in determining whether family members should be considered as research participants.

### **Privileged communication**

This includes, conversations within the context of a protected relationship, such as that between doctor and patient, a therapist and client, an attorney and client, a husband and wife, or a priest and penitent; under common law, privilege involves a number of rules excluding evidence that would be adverse to a fundamental principle or relationship if it were disclosed<sup>7</sup>. Such communications are secure, reliable, and meant to be kept among the directly involved parties.

### **Respect and responsibility**

Respect in research refers to respect for people and respect for truth. People have the right to dignity and privacy (informed consent and confidentiality). Respect for truth implies probity and respect for the intellectual rights of others. All possible efforts should be directed to avoid plagiarism and clinching false conclusions by over and under emphasizing the results<sup>8</sup>.

<sup>1</sup>Ormond K, Cirino. A, Helenowski I, Chisholm R, Wolf W. *Assessing the understanding of biobank participants*. Am J Med Genet A 2009;149(2):188–98. McCarty CA, Nair A, Austin DM, Giampietro P. Informed consent and subject motivation to participate in a large, population- based genomics study: the Marshfield Clinic Personalized Medicine Research Project. Public Health Genomics 2006;10(1):2–9

<sup>2</sup>Mascalzoni D, Hicks A, Pramstaller P, Wjst M. Informed consent in the genomics era. Plos Med 2008;5(9): e192

<sup>3</sup>Mielke HW. Research ethics in paediatric environmental health: lessons from lead. Neurotoxicol Teratol 2002;24(4):467–9.

<sup>4</sup>Woodward Z, Argent VP. Patient confidentiality. Curr Obstet Gynaecol 2005;15(3):211–4

<sup>5</sup>Mandl KD, Szolovits P, Kohane I.S, Markwell D, MacDonald R. *Public standards and patients' control: How to Keep Electronic Medical Records Accessible but Private. Medical Information: Access and Privacy. Doctrines for Developing Electronic Medical Records. Desirable Characteristics of Electronic Medical Records. Challenges and Limitations for Electronic Medical Records. Conclusions Commentary: Open Approaches to Electronic Patient Records. Commentary: A Patient's Viewpoint*. Brit MedJ 2001;322(7281):283–7.

<sup>6</sup>Miller R.A; Schaffner K.F; Meisel A. *Ethical and Legal Issues Related to the Use of Computer Programs in Clinical Medicine*. Ann Intern Med 1985;102(4):529–36.

<sup>7</sup>Salman Y. Guraya, N.J.M London, Shaista S. Guraya, 'Ethics in Medical Research' *Journal of Microscopy and Ultrastructure 2 (2014) 121-126*

<sup>8</sup>Ibid n.55 p.124

Responsibility of the human subject involves voluntary informed consent, avoiding deception, rewards and incentives, privacy, and disclosure. Also the researchers are responsible for maintaining the reputation of educational research by adhering to the highest standards of quality research. When publishing the research, investigators should disclose any competing or financial interests.

## **Impact of Medical research and Experimentation in Africa**

### **The AZT trials in Africa**

The AIDS Clinical Trial Group (ACTG) in 1994 reported the findings of their study 076 in which the use of Zidovudine (AZT) during pregnancy, in labour and to the newborn reduced the mother to child transmission (MTCT) of HIV by two-thirds.<sup>1</sup> With this finding, use of oral AZT during pregnancy and intravenous AZT during labour and oral AZT to the neonate became the standard of care for HIV-positive mothers in the United States and Europe. However in Africa, where the burden of HIV was high, this regimen was considered unaffordable. The World Health Organisation summoned a meeting to discuss the conduct of research into finding less expensive and affordable interventions to prevent (MTCT) of HIV in developing countries. Subsequently a series of placebo-controlled trials were conducted in Africa and Asia. Many bioethicists have questioned the morality of using a placebo-controlled design in these studies. They argued, that with the results of the ACTG 076 study, the appropriate research question should be - 'Can we have a cheaper intervention compared with the standard ACTG 076 without compromising on the demonstrated efficacy of ACTG 076'.<sup>2</sup>

Thus the study design would be an equivalence study with ACTG 076 being given as the control arm. But by using placebo-controlled design, the research question became, 'are these cheaper interventions better than nothing' or 'Is the short course of AZT better than nothing'.<sup>3</sup> Ethicists argued that since a placebo-controlled trial would not be acceptable in developed countries (as AZT had become the standard of care), it smacked of moral imperialism and double standard to offer such to developing countries.<sup>4</sup> By conducting placebo-controlled trials of AZT in developing countries many neonates who would have been saved from contracting HIV infection if their mothers had been given the AZT rather than placebo were not saved.

### **Pfizer and Cerebral-Spinal Meningitis in Nigeria<sup>5</sup>**

In 1996, there was an outbreak of cerebral-spinal meningitis in Tudun Wada in Kano State. Children were predominantly affected by the outbreak. The state government mobilised resources to combat the meningitis epidemic. Also, international organisations like the Medicines Sans Frontiers (MSF) were there to assist in treating patients. Pfizer brought in a team to conduct a research on its test drug TROVAFLOXACIN (TROVAN) - a quinolone antibiotic. Pfizer recruited a total of 200 children into the study in two arms- one arm had the test drug Trovan orally and the control arm was given Ceftriaxone or Chloramphenicol. Within 3 weeks of commencing the study the required numbers of participants were recruited and the study concluded.<sup>6</sup> The study was, however, criticised severely for falling short of ethical standards.<sup>7</sup> The allegations were that:

1. Pfizer never obtained ethical clearance before conducting the study;
2. Pfizer did not obtain informed consent before recruiting participant and did not inform the study participants that the drug was an experimental drug;
3. Pfizer capitalised on the poor, illiterate and desperate situation of the people; and,

<sup>1</sup> Lancet, Zidovudine for mother, foetus, and child: Hope or poison? Nigerian Medical Journal 1994; 344:207-209.

<sup>2</sup> Lurie P, Wolfe SM. Unethical trials of interventions to reduce perinatal transmission of the human immunodeficiency virus in developing countries. Nigerian Medical Journal 1997; 337:853-6.

<sup>3</sup> Patrick I. Okonta. *Ethics of clinical trials in Nigeria* Nigerian Medical Journal. 2014 May-Jun; 55(3): 188-194.

<sup>4</sup> Merson MH. Ethics of placebo-controlled trials of zidovudine to prevent the perinatal transmission of HIV in the Third World. Nigerian Journal of Medicine. 1998; 338:836. Varmus H, Satcher D. *Ethical Complexities of Conducting Research in Developing Countries*. N J Med. 1997; 337:1003-5. Phanuphak P. *Ethical Issues in Studies in Thailand of the Vertical Transmission of HIV*. N.J Med. 1998; 338:834-5. Stoddert DM, Brennan TA. *Clinical Trials in Developing Countries: Scientific and Ethical Issues*. Med J Aust. 1998; 169:545-548 Crouch RA, Arras JD. *AZT Trials and Tribulations*. Hastings Cent Rep. 1998; 28:26-34.

<sup>5</sup> In *Zango v. Pfizer International Inc*, Case No. FHC/K/CS/204/2001 while the case filed in Nigeria was pending, another suit was filed by thirty families in a District Court in the United States, seeking punitive damages against Pfizer under the United States Alien Tort Claims Act and alleging that Pfizer had violated the law of nations in its alleged non-conformity with international ethical standards for research. The suit was later dismissed on grounds of *non forum conveniens*. They appealed and it was remanded to the District Court of Appeal. The court dismissed on similar grounds, stating that Nigeria was the proper forum for action and it was restated in the later case of *Abdullahi v. Pfizer Inc*. (2002) WL 31082956 (S.D.N.Y.); (2003) WL 22317923 (C.A.2(N.Y.)); (2005) WL 187081 (S.D.N.Y.).

<sup>6</sup> Nyika A. Trovan trial case study: After profits or to save lives? Accessed on march 20 2017. Available from: <http://www.amanet-trust.org/discuss/viewtopic.php>.

<sup>7</sup> Ahmad K. Drug company sued over research trial in Nigeria. Lancet. 2001; 358:815. Nigerian Medical Journal

4. Pfizer left the town after conducting the study despite the fact that the epidemic was still ongoing.<sup>1</sup> The Government panel set up to investigate the study reached these conclusions:
1. Pfizer never obtained authorisation from the necessary authorising agencies including ethical clearance and that Pfizer's experiment was "...an illegal trial of an unregistered drug" and "a clear case of exploitation of the ignorant."<sup>2</sup>
  2. Pfizer later agreed to a \$75 million out of court settlement.<sup>3</sup>

### **Human Medical Research in Nigeria.**

As a political entity, Nigeria attained statehood on October 1, 1960. However, biomedical research started in the colonial era, long before Nigeria gained its political independence from Great Britain. In 1920, the Rockefeller Foundation initiated a colonial research enterprise in the west coast of Africa known as the "Rockefeller Foundation Yellow Fever Commission to the West Coast of Africa."<sup>4</sup> In 1925, the Yellow Fever Commission, as it was generally called, built a Research Unit in Yaba, Lagos.<sup>5</sup> Few details are known about any clinical trial or other activities by the Yellow Fever Commission, but, considering that ethics review was developed in the 1960s,<sup>6</sup> yellow fever research would probably raise only issues of informed consent. In 1954, the British colonial government established the West African Council for Medical Research for its West African territories of Nigeria, Ghana, Gambia, and Sierra Leone.<sup>7</sup> The main function of the Council was to arrange for the conduct of medical research in those West African territories and to provide medical research information concerning West Africa to the British government.<sup>8</sup> Legislation establishing the Council was not specific on the type of medical research to be conducted or sponsored by the Council, nor did it contain any provision relating to the ethics review of research protocols conducted under the auspices of the Council. In 1952, the Nigerian colonial government established the University College Hospital, Ibadan (UCH).<sup>9</sup> UCH was established as a teaching hospital of the University of Ibadan (then University College, Ibadan). Part of the mandate of the UCH was to carry out clinical research or other medical experimentation<sup>10</sup>, though no research guideline was specifically mentioned.<sup>11</sup> Following the UCH research mandate, subsequent teaching hospitals established in Nigeria were given the same clinical research jurisdiction.<sup>12</sup> In 1972, the then Nigerian Military government established the Medical Research Council of Nigeria (MRC).<sup>13</sup> The federal agency was responsible for the conduct of medical research in Nigeria. However, in 1977, the National Science and Technology Development Agency<sup>14</sup> (NSTDA) was statutorily established in Nigeria to advise the federal government on matters relating to scientific research and development. The NSTDA Decree repealed the Medical Research Council of Nigeria Decree 1972.<sup>15</sup> Pursuant to the NSTDA Decree, the Research Institute's Order of 1977<sup>16</sup> established the National Institute of Medical Research in Yaba Lagos (NIMR). The assets and rights of the MRC were transferred to the NIMR.<sup>17</sup> The NIMR is authorized to conduct medical research related to health problems in Nigeria and to cooperate with Nigerian medical schools and universities to provide the necessary facilities for training medical researchers in Nigeria. Though the NIMR is a major Nigerian institute concerned with human medicine and research in Nigeria, it has not promulgated any formal guideline for the conduct of research involving human subjects

<sup>1</sup> Ahmd K. Drug company sued over research trial in Nigeria. *Lancet*. 2001; 358:815, Stephens J. Panel faults Pfizer in '96 clinical trials in Nigeria. Accessed on 2017 March 20.

<sup>2</sup> *Ibid* n.57

<sup>3</sup> MacDonald G. Pfizer settles Nigerian Trovan trial case out of court. Accessed on 2017 March 20. Available from: <http://www.inpharmatechnologist.com/industry-drivers/pfizer-settles-nigerian-trovan-trial-caseout-of-court>.

<sup>4</sup> The National Institute of Medical Research, Yaba Lagos, Nigeria, available at <http://www.nimr-ng.org/NIMR-nav.htm> accessed on march 15, 2017

<sup>5</sup> *Ibid*

<sup>6</sup> The first ethical review committee was established in the United Kingdom in 1966. See P. Ferguson, Do Researchers Feel an LREC Hinders Research? 165 *Bull. of Med. Ethics* 17, 19 (2001). In the United States the policy that made it mandatory for a review of federal-funded research by an Institutional Review Board began in 1966.

<sup>7</sup> West African Council for Medical Research Ordinance, Laws of the Federation of Nigeria and Lagos, Cap. 215 (1958).

<sup>8</sup> *Ibid* p.3

<sup>9</sup> University College Hospital Act, Laws of the Federation of Nigeria and Lagos, Cap 205, p. 3 (1958).

<sup>10</sup> *Ibid*

<sup>11</sup> At that period the main international medical research guideline was the Nuremberg Code, which I shall discuss later.

<sup>12</sup> Such as the University of Nigerian Teaching Hospital; University of Lagos Teaching Hospital; University of Benin Teaching Hospital, and Obafemi Awolowo University Teaching Hospital.

<sup>13</sup> Decree No. 1, Medical Research Council of Nigeria (1972).

<sup>14</sup> Decree No. 5, National Science and Technology Development Agency Decree (1977).

<sup>15</sup> *Ibid* 11, Schedule 3.

<sup>16</sup> Research Institutes (Establishment, etc.) Order 1977, Annual Volume of the Laws of the Federal Republic of Nigeria (1977).

<sup>17</sup> *Ibid* at 8 (c)

## **Review of National Health Act 2014 on Human research and Experimentation**

Prior to this Act, there was no regulation in Nigeria which dealt with medical research and experimentation as such, the National Health Act 2014 is a great step in the growth and regulation of ethics in the exercise of medical research and experimentation.

**Section 31** of the National Health Act, provides for the establishment of the National Health Research Committee. This committee, by virtue of **Section 31(6)(a)-(d)**, is saddled with the following responsibilities:

- Promoting health research to be carried out by public and private health authorities;
- Ensure that health research agenda and research resources focus on priority health problems;
- Develop and advise the Minister on the application and implementation of an integrated national strategy for health research; and
- Collate and document information on the research activities of public and private health establishments.

**Section 32** of the Act, provides for research or experimentation with human subjects. This provides that notwithstanding anything to the contrary in any other law, experimentation or research on a living person or living persons, must comply with 2 requirements:

- It must be in the manner prescribed by the relevant authority and
- It must be with written consent of the person after he shall have been informed of the objects of the research or experimentation and any possible effect on his health.

It further provides for minors in two ways, being when the research is for a therapeutic purpose and when it is for a non-therapeutic purpose.

If it is for a therapeutic purpose, by virtue of **Section 32(2)**, it must:

- Be in the best interest of the minor;
- Must be in such a manner and on such conditions as prescribed by the National Health Research Ethics Committee; and
- With the informed written consent of the parent or the minor

If it is for a non-therapeutic purpose,

- Must be in such a manner and on such conditions as prescribed by the National Health Research Ethics Committee;
- With the informed written consent of the parent or the minor

It is right to say that perhaps the reason for the necessity of the experiment being in the best interest of the minor when it is for a therapeutic purpose, is because such an experiment aims at healing or curing the minor and restoring him to good health.

The Act in **Section 33**, further provides for the establishment of the National Health Research Ethics Committee. The Act again, by virtue of Section 33(6) shall have the power to determine the guidelines to be followed for the functioning of institutional health research ethics committee, as well as:

- Set norms and standards for conducting research on humans and animals, including clinical trials;
- Determine the extent of health research to be carried out by public and private health authorities;
- Adjudicate on complaints about the functioning of health research ethics committees and hear any complaint by a researcher who believes he has been discriminated against by any of the research ethics committee;
- Register and audit the activities of health research ethics committees;
- Refer to the relevant body, matters involving the violation or potential violation of an ethical or professional rule by a health care provider;
- Recommend to the appropriate regulatory body, disciplinary action that should be taken against anyone who violates and standard or guideline set for the conduct of research under the Act;
- Advise the Federal and State Ministries of Health, on any ethical issue concerning research on health.

The requirement of a research ethics committee, is no strange to the international community as it has been earlier stated in this paper that other countries such as the United States and Canada, have provisions in their laws with regards to the research ethics committees.

## **Challenges of Human Medical Research and Experimentation**

### **Lack of regulation and Sanctions in developing countries such as Nigeria**

The conduct of human medical research and experimentation in developing countries<sup>1</sup> could be said to have been motivated by altruistic concerns to help developing countries confront particular health care problems, thereby

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<sup>1</sup> The expressions "developing" and "developed" countries have contested meanings and are not used here in any technical sense. The term "developing" is used to describe non-industrialized countries like Nigeria that are still caught in the throes of poverty and economic underdevelopment. Similarly, "developed" is used to describe industrialized and wealthy countries in North Africa.

reducing the inequality in global health research expenditures.<sup>1</sup> However, this conduct (i.e. human medical research) has also exploited and taken advantage of the abundant research subjects, illiteracy, poverty and disease, low level of regulation, and comparatively cheaper cost of experimentation in developing countries.<sup>2</sup> For instance, a developed country's pharmaceutical corporation may undertake experimentation in a developing country simply out of convenience and to quickly generate clinical data that would support drug registration application in the developed country.<sup>3</sup> A myriad of factors contribute to public sensitivity to trials in developing countries. These includes the placebo-controlled trials that took place in various developing countries" that tested the efficacy of a short course zidovudine (AZT) in the reduction of prenatal transmission of HIV/AIDS. These trials raised the ethical issue of whether ethically unacceptable research in a developed country for instance, the United States could be ethically appropriate in a developing country; Another factor that drew public attention to international clinical trials concerned the ethical propriety of Pfizer's 1996 clinical trial in Nigeria that tested the efficacy of trovan in the treatment of epidemic meningitis.<sup>4</sup> In other words, one will ask whether the standard of care in research is universal or dependent on local circumstances.<sup>5</sup> On this note there is need for a more robust guideline or regulations in Nigeria the provisions in the National Health Act is not adequate enough in view of all the International laws which have been discussed. With regard to sanctions, none of the guidelines include sanctions against researchers, or their institutions, for failure to comply with ethical rules. It is a known fact that where there is no law, there is no sin. Upon this background the writer is of the opinion that one major reason why scientist can get carried away with their research is due to the fact that the law with regards to sanctions is

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<sup>1</sup> See Ad Hoc Committee on Health Research Relating to Future Intervention Options, Investing in Health Research and Development: Report of the Ad Hoc Committee on Health Research Relating to Future Intervention Options (World Health Organization) (1996). The World Health Organization estimated that 90% of health care research money in the world is applied to diseases representing less than 10% of the global burden of disease. See *id.* In other words, only 10% of the global health research budget is devoted to diseases afflicting about 90% of the world's population; these are mainly people in the developing countries. See *id.* See also Commission on Health Research for Development, *Health Research: Essential Link to Equity in Development* (Oxford University Press 1990); Global Forum for Health Research, *The 10/90 Report on Health Research* (Global Forum for Health Research 1999).

<sup>2</sup> Rebecca A. Finkenbinder, *New Recommendations on International Human Research: Can Minimum Standards Prevent the Exploitation of Vulnerable Human Subjects in Developing Countries*, 21 PENN ST. INT'L. REV. 363, 364 (2003).

<sup>3</sup> This was part of the motivation for the proposal sent in 2001 to the U.S. Food and Drug Administration by a Pennsylvania biotechnology company to conduct clinical trials of a drug for the treatment of infant's lung disease in Latin America. The trial used a placebo-arm (inert) considered unethical in the United States because of the availability of established surfactant drugs. Similar trials proposed in Europe would not use a placebo. See Mary Pat Flaherty & Joe Stephens, Pa. Firm Asks FDA To Back Experiment Forbidden in U.S., WASH. POST, Feb. 23, 2001, at A3. The president of the Pennsylvania company estimated that the trial could shave eighteen months off of the development of the experimental drug. See *id.* The NBAC considers this proposed study to be unethical: In studies of this kind-in which the disease is life threatening, an established effective treatment is available, patients in developed countries will be the primary beneficiaries of the results of the clinical trial, and it is not clear that the clinical trial is responsive to the health needs of the host country-a placebo control would not be permissible under the rules recommended in this report. National Bioethics Advisory Commission, *Ethical Issues in International Research: Clinical Trials in Developing Countries: Report and Recommendations of the National Bioethics Advisory Commission* (2001) (NBAC), at 25.

<sup>4</sup> Joe Stephens, *Doctors Say Drug Trial's Approval Was Backdated*, WASH. POST, Jan. 16, 2001, at A1; Sonia Shah, *Globalizing Clinical Research: Big Pharma Tries Out First World Drugs on Unsuspecting Third World Patients*, *The Nation*, July 1, 2002, at 23.

<sup>5</sup> This has been discussed briefly in this article at p. 19. For more information about the AZT trials and ethical debates, see generally P. Fidler, "Geographical Morality" Revisited: International Relations, International Law, and the Controversy Over Placebo-Controlled HIV Clinical Trials in Developing Countries, 42 HARV. INT'L L.J. 299 (2001); Leonard H. Glantz, et al., *Research in Developing Countries: Taking 'Benefit' Seriously*, *Hastings Center Rep.*, at 38 (Nov.-Dec. 1998); Jonathan Todres, *Can Research Subjects of Clinical Trials in Developing Countries Sue Physician-Investigators for Human Rights Violations?* 16 N.Y.L. SCH. J. HUM. RTS. 737 (2000); Ronald Bayer, *The Debate Over Maternal-Fetal HIV Transmission Prevention Trials in Africa, Asia, and the Caribbean: Racist Exploitation or Exploitation of Racism?* 88 AM. J. Pub. Health 567 (1998); David Orentlicher, *Universality and its Limits: When Research Ethics Can Reflect Local Circumstances*, 30 J.L. Med. and Ethics 403 (2002); Eldryd Parry, *The Ethics of Clinical Research in Developing Countries*, 34 J. Royal C. Physicians Lon. 328 (2000); Joanne Roman, *U.S. Medical Research in the Developing World: Ignoring Nuremberg*, 11 Cornell J.L. & Pub. POL'Y 441 (2002); Robert Levine, *International Codes of Research Ethics: Current Controversies and the Future*, 35 IND. L. REV. 557 (2002); Harold Varms & David Satcher, *Ethical Complexities of Conducting Research in Developing Countries*, 337 New Eng. J. Med. 1003 (Oct. 2, 1997); Peter Lurie & Sidney M. Wolfe, *Unethical Trials of Interventions to Reduce Perinatal Transmission of the Human Immunodeficiency Virus in Developing Countries*, 337 New Eng. J. Med. 853 (Sept. 18, 1997); Marcia Angell, *The Ethics of Clinical Research in the Third World*, 337 New Eng. J. Med. 847 (Sept. 18, 1997); George Annas and Michael Grodin, *Human Rights and Maternal-Fetal HIV Transmission Prevention Trials in Africa*, 88 AM. J. Pub. Health 560 (1998); Robert A. Crouch and John D. Arras, *AZT Trials and Tribulations*, *Hastings Center Rep.*, at 26 (Nov.-Dec. 1998); Carol Levine, *Placebos and HIV: Lessons Learned*, *Hastings Center Rep.*, at 43 (Nov.-Dec. 1998).

quite open ended leaving room for individual excesses.

### **Research Misconduct**

Currently, majority of the research misconduct and irregularities are related to studies funded by the pharmaceutical industry and strongly linked with the financial interests of this industry. Technical faults in the research design, wrong recruitment process, insufficient sample size, and weak statistical analysis of the data often led to non-punishable research. Another form of research misconduct is the procedural irregularities by misinterpreting the trial data, attempting to draw favourable conclusions than those warranted by the available data<sup>1</sup>.

### **Conflict of interest**

In view of the fact that most of the researches are sponsored by different research groups or pharmaceutical companies, institutions several conflict of interest tend to arise. Some<sup>2</sup> claim that institutional committees have an inherent conflict of interest because external research funds that benefit the institution are contingent on IRB approval of the research. Review by free-standing committees to avoid this conflict is an alternative but is much less commonly used in the U.S., especially if the free-standing committee is a for-profit organization. Aside from institutional conflicts of interest, investigators may have individual financial conflicts of interest, personal conflicts of interest, and professional conflicts of interest that may affect their behaviour as reviewers of manuscripts and funding applications. IRBs may be assigned the task of identifying and managing conflicts, especially financial conflicts of interest, in addition to their other responsibilities.

**Cost and Burden:** There is no doubt that the present economic situation in Nigeria cannot adequately provide food for the populace not to talk about constituting a committee required to be paid monthly salary. In developed countries, for instance, there is general agreement that the U.S. ethics review system is expensive, weighed down by procedural requirements, and time-consuming for all involved. Yet, it cannot be ascertained how well human participants are protected or how consistent that protection is across institutions and research projects. This is not to say that a review committee is not important but there are seemingly more pressing needs the government seeks to address. This creates a form of hindrance to the protection of humans in the growth of human research experimentation.

### **Conclusion**

The conduct of human medical research and experimentation for the development and licensing of clinical treatments is a very important aspect of healthcare. The need to develop more effective and safer medical research to tackle existing disease and also new emerging diseases cannot be over-emphasised. Ethical principles, codes of ethics and oversight of research provide guidance to a continuous research without a breach of human rights laws. This article has considered the ethical issues involved in medical research and experimentation with emphasis on the Nigerian context in particular. The main objective has been to highlight potential ethical challenges in the conduct of clinical trials in Nigeria and outline legal ways in which these can be avoided. Current international and national regulatory and ethical guidelines are reviewed to illustrate the requirements for ethical conduct of human experimentation. Ultimately, there is no universally accepted position as to how research should proceed. Laws and codes are far too general for deciding such cases, which is where ethical judgements, committees, and arguments come in that allow agreement to be reached. These can delay research or draw on resources available for a trial, but they are essential if we are to maintain a high level of scrutiny in often complex situations and prevent further scandalous cases from arising.

### **Recommendation**

**Enforcement of the Medical oath:** Medical research ethics is anchored in the Hippocratic Oath, in doing no

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<sup>1</sup> Conseil C. De L'europe O.E. Convention for the Protection of Human rights and Dignity of the human being with regards to the application of biology and medicine: convention on human rights; 1997. Reporting of fabricated favourable results due to the comparison of the drug under study only against placebo or a non-gold standard drug also leads to research misconduct.

<sup>2</sup> Commercial interests have become deeply embedded in all aspects of biomedical science. Indeed, biomedical science has become a vast commercial activity. This may or may not be a good development, but for many researchers it certainly generates a new and expanded portfolio of actual or perceived conflicts of interest. As a result, the public no longer considers individual self-regulation adequate. In fact, however, it was always difficult to imagine that given the multitude of pressures that physician/scientists work under what they could adequately address the ethical implications of their own work. In my view it has always been unreasonable and unfair to leave all the ethical decision making to the moral sensitivities of the individual medical investigator. Given the various pressures investigators work under, we protect neither subject nor investigator by having a system devoid of meaningful third party oversight. Harold T. Shapiro Ethical Considerations in Research on Human Subjects: A Time for Change... Again, [www.Princeton.edu/hts/PDF](http://www.Princeton.edu/hts/PDF)

harm, and tends to take the protection of the individual as its main objective<sup>1</sup>. Therefore, according to the Declaration of Helsinki, studies should be designed in the safest manner possible and every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens weighed against foreseeable benefits to the subject or to others.

General principles governing the ethics in research demand that research involving humans has merit and is beneficial, that researchers have integrity, that the benefits and burdens of research participation are justly shared, that risks to participants are minimized and are justified by potential benefits, and that participants are respected as people and their informed consent is given. Recently, there is escalating attention to topics such as reasons for or against participants' satisfaction with informed consent procedures<sup>2</sup>, comprehension of risks<sup>3</sup>, views on compensation<sup>4</sup> and sources of trust or mistrust in the research enterprise<sup>5</sup>.

There should be a consensus on the right to withdraw by the researcher. Due to the danger of rapid dissemination, this right to withdraw becomes impractical and invalid in no time, and current recommendations do not have enough regulatory control in such situations.

**Adequate trainings:** Institutions need to organize workshops, seminars, and training courses for the academia and novice researchers for the education and knowledge about research ethics. Since ethics is something based on moral convictions, one could state that no two individuals will have the same moral views and considerations, in view of the fact that we are all of different environmental, social, cultural and religious background. Thus it becomes impediment for both international organizations and institutions to organize trainings elucidating the need for strict adherence to the spirit of these ethical provisions.

**Deer need for extensive Regulations:** This recommendation is particularly related to developing countries like Nigeria. Despite Nigeria's involvement in biomedical research since colonial times, the provision in the National Health Act is yet inadequate. Although the Nuremberg Code and the Declaration of Helsinki apply in Nigeria, it will be better to specifically state how these laws will be enforced and include some other International provisions which will deal with foreign companies using Nigeria for experimentation and still go unpunished. For instance the issue of conflict of interest can be dealt with through legal provisions. In 1996, Nigeria witnessed a biomedical research scandal that depicted lack of respect for the dignity and welfare of research participants. The research was not preceded by a competent ethics review of the protocol. The importance of including sanctions to the regulations cannot be overemphasized.

**Adequate Financing of Research Ethics Committees:** research ethics committee has been provided for by the 2014 National Health Act, however the rate of corruption in Nigeria cannot be ignored. In view of the fact that most companies sponsoring research and experimentation have the capacity to influence the ethics review committee, Nigeria must have a solid arrangement on ensuring that these review boards are not bought over or influenced at the detriment of the community<sup>6</sup>. It was mentioned by Remigius Nwabueze<sup>7</sup> in his work that due process was not followed before pfizer experience occurred. Going by the Trovan experience in Nigeria, it was reported<sup>8</sup> that the letter granting Pfizer Company the permission to carry out their research was written after the incidence and then backdated. I therefore recommend also that the International ethical regulations of whatsoever country a researcher seeking to conduct a research in a developing country, must be adequately adhered to, before it is allowed to perform its research in the said developing country.

<sup>1</sup> Hoeyer K, Dahlager L, Lynøe N. *Conflicting Notions of Research Ethics: The Mutually Challenging Traditions of Social Scientists and Medical Researchers*. Soc Sci Med 2005;61(8):1741–9.

<sup>2</sup> Corrigan O. *Empty Ethics: The Problem with Informed Consent*. Soc Health Illn 2003 ;25(7):768–92.

<sup>3</sup> Sachs GA, Hougham GW, Sugarman J, Agre P, Broome M.E, Geller G, *et al. Conducting Empirical Research on Informed Consent: Challenges and Questions*. IRB: Ethics Hum Res 2003;25(5): S4–10.

<sup>4</sup> Hampson LA, Agrawal M, Joffe S, Gross CP, Verter J, Emanuel EJ. *Patients' views on Financial Conflicts of Interest in Cancer Research Trials*. N Engl J Med 2006;355(22):2330–7.

<sup>5</sup> McDonald M, Townsend A, Cox SM, Paterson ND, Lafrenière D. *Trust in health research relationships: accounts of human subjects*.

<sup>6</sup> This could be achieved by ensuring that committee members are wealthy and successful people who have their reputation and carrier at stake.

<sup>7</sup> Remigius N. Nwabueze. *Ethical Review of Research Involving Human Subjects in Nigeria: Legal and Policy Issues Ind*. International and Company Law Review. Volume 14

<sup>8</sup> Ibid n.108 p.5