REVIEW ARTICLE

Ethics in Biomedical Research

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ABSTRACT

"The first step in the evolution of ethics is a sense of solidarity with other human beings". Ethics involves four basic principles that include Non-maleficence, Beneficence, Autonomy, and Justice. The history of biomedical research ethics is dark and led to the formulation of a universal code of ethics. The community of oral health researchers is vested with the responsibility for conducting and translating the research for the betterment of oral and systematic health and this level of responsibility should be continually visible to the profession and the public.

KEYWORDS: Research, Ethics, Institutional Review Board, Consent

INTRODUCTION

Ethics is derived from a Greek word "*ETHOS*" which means moral. "Ethics" (moral philosophy).It is a branch of philosophy that addresses questions about morality, concepts such as good and evil, right and wrong, virtue and vice, justice and crime.[1]

Levels of moral response constitutes, Expressive level where the individual reacts with just a feeling of the conscience, second is the Pre- reflective Level in which the individual's reaction is justified via law and legislation, last is the Reflective level where the responses are the reasoned ethical arguments and defenses based on ethical principles.[2]

Bioethics is the study of the typically controversial ethical issues emerging from new situations and possibilities brought about by advances in biology and medicine.[3,4] It is also a kind of moral discernment as it relates to medical policy, practice and research. Bioethics helps to answer the following questions.

- Decide what should be done? That should be morally right or acceptable.
- Why it should be done? Helps to justify our decisions in moral terms.
- How it should be done? Methods and manners those are ethical.

This narrative will try to unify the various aspects of ethics in biomedical research.

Clinical ethics is a practical regimen that provides a scrupulous and a rigorous approach to assist physicians in identifying, analysing and resolving ethical issues in clinical medicine[3,4] i.e. a normative type of ethical decision that includes *MICROETHICS* (at personal level), *MACROETHICS* (at a group level), *MESOETHICS* (between micro and macro level) and *MEGAETHICS* (transcends national health issues).[5]

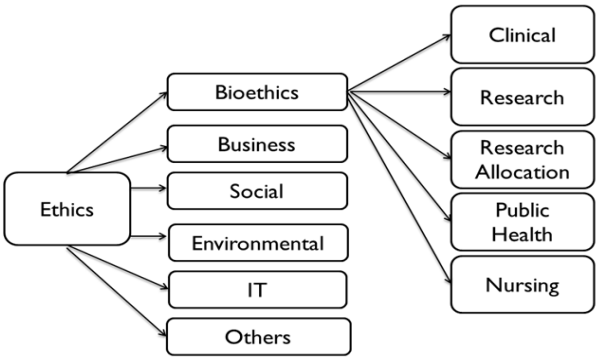

Figure 1: Branches Of Ethics

A common framework used in the analysis of medical ethics is the "four principles" approach postulated by *Tom Beauchamp* and *James Childress*.[6] It recognizes four basic moral principles, which are to be appraised and evaluated against each other, with attention given to the comprehensiveness of their application. The four principles are:

1. **Non-maleficence :** above all or first, do no harm (*PRIMUM NON NOCERE*)
2. **Beneficence:** this can be defined as "the principle of doing good and providing care to others" (Berglund, 2007:12), and promotion of well-being (Edwards, 2009). All the actions of a clinician should be for the prevention of harm, removal of harm and for the provision of benefits (risk-benefit analysis).
3. **Autonomy refers to** the ability to freely determine one's own course in life. A doctor should not prevent patients from carrying out decisions they make for themselves, about what they ought to do or what they will do or what should be done with information about them thus enabling the patients to make autonomous decisions.

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4. **Justice is** simply defined as "equal treatment of equal cases" (Hendrick. 2004:7). This means an avoidance of cultural, racial, social or other biases. Justice is about meeting everyone's individual needs fairly.

Other values that are sometimes discussed include:[6,7]

1. **Veracity** which is concerned with being open, honest and truthful with patients (Berglund, 2007). Accurate transfer of information should be delivered in a way that is suitable for the individual to understand (Edwards, 2009).
2. **Fidelity:** Latin "fides" means faithfulness. Being faithful to patient entails meeting patient's reasonable expectations.
3. **Confidentiality** defined as the principle of maintaining the security of information elicited from an individual in the privileged circumstances of a professional relationship. Information disclosed voluntarily should be protected from disclosure. Breach of confidentiality is considered the worse offense.

There have always been abstruse theories about three commonly used terms: privacy, confidentiality, and privilege as they often recondite the discussions of ethical issues faced in this arena. **Figure 2** attempts to illustrate the breadth of coverage for each of the concepts using a *Venn diagram*. The concepts of privilege and confidentiality often create confusion and the discernments between them have critical ramifications for understanding a variety of ethical problems. The concept of privilege (or privileged communication) describes certain specific types of relationships that enjoy protection from disclosure in legal proceedings.[8]

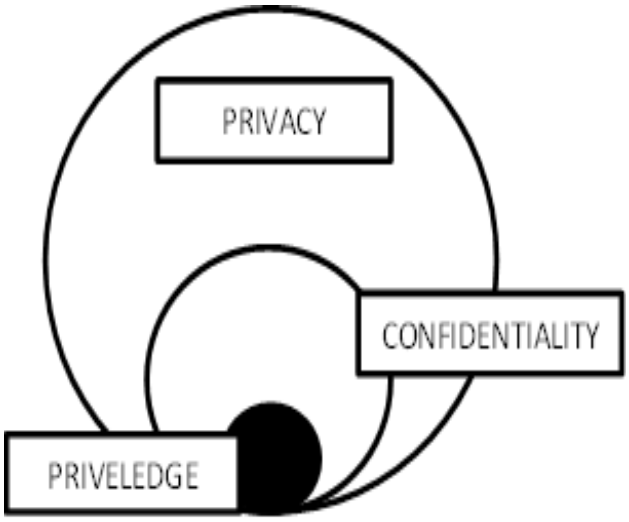

Figure 2: Concept Of Privilege, Confidentiality And Privacy Using Venn Diagram

Ethical Framework (F.A.I.R.) by Rowson (2006)[10]

- **F**airness
- Respect for **A**utonomy
- **I**ntegrity
- Seeking the most beneficial and least harmful consequences, or **R**esults.

THEORIES OF ETHICS

Most traditional moral theories rest on principles that determine whether an action is right or wrong. Classical theories in this vein include **DEONTOLOGY** that states that rightness or wrongness of any act depends on whether the person has followed his duty regardless of the consequences; this philosophy is more concerned with motive than results where actions are good or bad in advance of their performance. In contrast, another theory of **CONSEQUENTIALISM** states that the rightness or wrongness of any act is judged in relation to its consequences this philosophy is only concerned with results where the same act may be good or bad in different circumstances. Next theory is the theory of **UTILITARIANISM** which aims is to produce the greatest good for the greatest number.[11-13]

HISTORICAL BACKGROUND

Edward Jenner (1700) tested small pox vaccines on his own son and on neighborhood children.

In (1721) condemned prisoners in England were offered reduced sentence if they took part in inoculation trials.

Claude Bernard, 1865 justified experiments on condemned criminals in Egypt. "It is not cruel to inflict on a few criminals, suffering which may benefit multitudes of innocent people through all centuries."

Ethics violation in research[14-17]

1. Medical experiments of Nazi doctors (1939-1945)
There was a forced involvement of prisoners of war and civilians in the experiments that resulted in death, trauma, disfigurement or permanent disability. The research was sanctioned and promoted by government and conducted by researchers and physicians. The type of experiments conducted includes exposing the individuals to warm bath, freezing temperatures (hypothermia) and pharmacological agents. Subjects were tested for infectious diseases as well as genetic experiments were also conducts. Traumatic injury experimentation was performed on study subjects by often amputation of their limbs.

2. Mengele experiments (1946)
It was done by Joseph Mengele. He was called "*Angel of Death.*" He did brutal experiments on twins during Second World War. One of the twins was considered as the control and other as the guinea pig.

3. The massacre of Nanjing (1937)
The Japanese doctors in unit 731 conducted inhuman experimentations in wartime china. All Japanese doctors were let off though they were involved in wartime in human experimentations. Unit 731 was a covert biological and chemical warfare research.

4. Tuskegee syphilis study (1932-1972)

In 1932, a forty-year study was carried out by the Public Health Service in Macon County, Alabama, to examine cases of the bacterium *Treponema Palladium* (syphilis) among a group of carefully selected *African-American* males. In total, 600 patients were selected, 399 were infected with syphilis and 201 were not. All of the men in the study were poor, uneducated and were desperate to receive hot meals which was provided by the public health services in exchange for the treatment. Ironically, they were also offered burial insurance.

5. Vipeholm dental caries study (1954)

The most significant human study done at Vipeholm Hospital, Lund, in Sweden, reported in 1954, by Gustafson et al. More than 400 mentally retarded patients were placed on controlled diets and observed for five years. The subjects were divided into various groups. Some ate complex and simple carbohydrates at mealtimes only, while other supplemented mealtime food with between-meal-snacks, sweetened with sucrose, chocolate, caramel, or toffee.

6. Willow brook mental hospital (1956)

In 1950's, a study was done to understand issues related to the transmission of the hepatitis virus in retarded children who were residents in the Willow Brook State School, New York. The study design involved intentionally infecting healthy children with hepatitis by feeding them a solution made from the feces of children with active hepatitis.

7. Jewish chronic disease hospital (1965)

1960s: experiments were performed on chronically ill, most of the patients were mentally retarded, the study was conducted in the Jewish Chronic Disease hospital. The purpose of the research was to determine how a weakened immune system influenced the spread of cancer. To evaluate this, live cancer cells were injected into the bloodstream of the subjects.

These inhumane experiments by health care professionals led to formulation of guidelines for human subject research for various kinds of research involving human subjects that includes:

1. Nuremberg Code, 1947
2. Declaration of Helsinki, 1964
3. Belmont Report, 1979.
4. International Ethical Guidelines for Biomedical Research Involving Human Subjects, 1982.
5. Report of National Bioethics Advisory Committee, USA, In 2000.
6. Guidelines by Nuffield Council of Bioethics, UK.
7. CIOMS, Geneva by 2002.
8. The Helsinki Declaration in 2008.
9. UNESCO's "The Universal Declaration on Human Genome and Human Rights" (1997).
10. "The International Declaration on Human Gene Data" (2003).
11. "Universal Declaration on Bioethics and Human Rights" (2005).

	Year	Key points
Nuremberg code	**1947**	• Judicial decision condemning the atrocities of the Nazi physicians • Obtaining consent and favorable risk-benefit ratio
The declaration of Helsinki	**1964**	• To remedy the lacunae in the Nuremberg Code • Independent review, distinction between therapeutic and non-therapeutic research.
Belmont report	**1979**	• In response to US research scandals such as Tuskegee trial and willow brook hepatitis study • Informed consent, favorable risk benefit ratio, protection of vulnerable populations
Council for international organizations of medical sciences (CIOMS)	**1982**	• Intended to apply declaration of Helsinki in developing countries. • Compensation for research injuries, avoiding dissection.
Guidelines for good clinical practice - World health organization 1995,1996	**1995, 1996**	• A standard for the design, conduct, performance, monitoring, auditing, recording, analyses and reporting of clinical trials that provides assurance that the data and reported results are credible are accurate and that the rights, integrity and confidentiality of trial subjects are protected.

Table 1: Key Points From Declarations

THE NUREMBERG CODE

In 1947, the Nuremberg military tribunal developed a code of standards to be used in judging physicians accused of conducting research atrocities in Nazi concentration camps. It resulted from prosecution of 23 German physicians and administrators for allowing / performing 'experiments' like injecting prisoners with gasoline. The code defines 10 conditions for ethically permissible experiments and obtaining informed/ voluntary consent was the cornerstone for all the guidance, regulations required in human research.[18,19]

Nuremberg code – ten points

I. Consent must be voluntary, where the participant has a legal capacity to give consent without the element of force, fraud and deceit. Participants should be enlightened with sufficient knowledge of nature, duration and purpose, inconveniences and hazards reasonably expected from the study.

II. Experiments should yield fruitful results for the good of the society.

III. Design should be based on results of animal experiments and knowledge of natural history of the disease.

IV. Avoid all unnecessary physical and mental suffering and injury.

V. No experiment should be conducted where there is a prior reason to believe that death or disabling injury will occur.

VI. The degree of risk should not exceed as determined by humanitarian principles.

VII. Proper preparations should be made and adequate facilities provided to protect the experimental

subject against even remote possibilities of injury, disability or death.

VIII. The experiment should be conducted only by scientifically qualified persons with the highest degree of skill and care.

IX. During the course of the experiment the human subject should be at liberty to bring the experiment to an end.

X. 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, that a continuation of the experiment is likely to result in injury, disability, or death to the experimental subject.

DECLARATION OF HELSINKI (1964) [20]

It was developed to remedy the lacunae in the Nuremberg code. It focused on favorable risk benefits ratio and independent review. It is the only document to emphasize a distinction between therapeutic and non-therapeutic research. The declaration was adopted by the 18th **WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI** (WMA) General Assembly, Helsinki, Finland, June 1964.

Amendments:

I. 29th WMA General Assembly, Tokyo, Japan, October 1975

II. 35th WMA General Assembly, Venice, Italy, October 1983

III. 41st WMA General Assembly, Hong Kong, September 1989

IV. 48th WMA General Assembly, Somerset West, Republic Of South Africa, October 1996

V. 52nd WMA General Assembly, Edinburgh, Scotland, October 2000

VI. 55th WMA General Assembly, Tokyo Japan, October 2004.

VII. 59th WMA General Assembly, Seoul Korea, October 2008

The World Medical Association has developed the declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. The declaration states that medical research involving human subjects includes research on identifiable human material or identifiable data and it is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience should be dedicated to the fulfilment of this duty.

THE BELMONT REPORT (1979)

The **Belmont report** is a report created by the national commission for the protection of human subjects of biomedical and behavioural research. The report was issued on 30 September 1978 and published in the federal register on 18 April 1979. Rules derived from Belmont principles includes *beneficence, respect for persons, justice and risk benefits management* i.e**.** Benefit maximization and risk minimization for the participants is the corner stone of the report.[21]

Risk / benefit assessment can be achieved by the qualitative or quantitative estimation of the likelihood of adverse effects that may result from exposure to specified health hazards or from the absence of beneficial influences by considering all types of potential harms and benefits to participants and/or to society. Risk assessment involves three elements that include:

- Risk identification is to determine risks or hazards that exist or anticipates their characteristics, remoteness in time, duration period and possible outcomes.
- Risk estimation is to express the duration, intensity, magnitude and reach of the potential consequences of a risk in quantifiable or dollar value (monetary) terms.
- Risk evaluation is to determination of risk management priorities through establishment of qualitative and/or quantitative relationship between benefits and associated risks.[22]

GOOD CLINICAL PRACTICE

Good clinical practice is a set of guidelines for biomedical studies which encompasses the design, conduct, termination, audit, analysis, reporting and documentation of the studies involving human subjects. The fundamental tenet of GCP is that in research on man, the interest of science and society should never take precedence over considerations related to the well-being of the study subject. . It aims to ensure that the studies are scientifically and ethically sound and that the clinical properties of the pharmaceutical substances under investigation are properly documented. The guidelines seek to establish two cardinal principles: [23]

1. Protection of the rights of human subjects and
2. Authenticity of biomedical data generated.

It ensures that the studies are implemented and reported in such a manner that there is public assurance that the data are credible, accurate and that the rights, integrity and confidentiality of the subjects are protected. These guidelines have been evolved with consideration of WHO, International Conference of Harmonization, USFDA (*United States Food And Drug Administration)* and European GCP guidelines as well as the ethical guidelines for biomedical research on human subjects issued by the Indian Council of Medical Research .GCP aims to ensure that the studies are scientifically authentic and that the clinical properties of the "investigational product" are properly documented. In India, they should be followed for carrying out all biomedical research at all stages of drug development, whether prior or subsequent to product registration.[24]

RESEARCH ETHICS

Research ethics involves the application of fundamental ethical principles to a variety of topics involving research, including scientific research. These include the design and implementation of research involving human experimentation, animal

experimentation and various aspects of scientific misconduct.

Animal Research: It includes the three r's (3Rs) described by W.M.S. Russell and R.L. Burch in 1959, as stated bellow: [25]

- **Replacement** which refers to the preferred use of non-animal methods over animal methods whenever it is possible to achieve the same scientific aims. These methods include computer modelling.
- **Reduction which** refers to methods that enables researchers to obtain comparable levels of information from fewer animals, or to obtain more information from the same number of animals.
- **Refinement** refers to methods that alleviate or minimize potential pain, suffering or distress, and enhance animal welfare for the animals used. These methods include non-invasive techniques.

Human Experiments: In 2010, the ***National Institute of Justice*** in the ***United States*** published recommended rights of human subjects that include obtaining voluntary/ informed consent from the subjects. Participants should have full access to information regarding research. Participants should be treated as autonomous agents and they should be given the privilege to end participation in research at any time. Protection from physical, mental and emotional harm and safeguarding the integrity is a mandatory requirement in human experiments, thus the benefits should outweigh the cost.

INSTITUTIONAL REVIEW BOARD

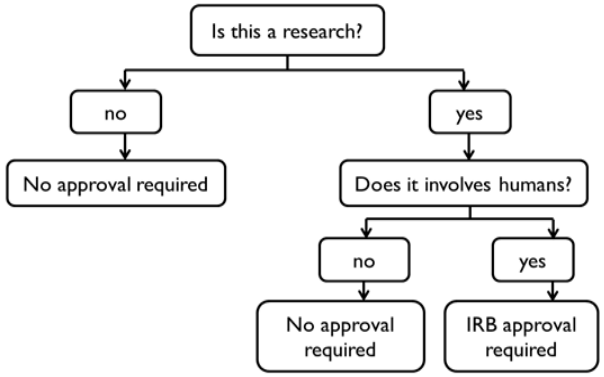

Figure 2: ILLUSTRATES THE SITUATIONAL NEED OF I.R.B.

The purpose of the review process is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating as subjects in a research study. A key goal of IRBs is to protect human subjects from physical or psychological harm, which they attempt to do by reviewing research protocols and related materials. The protocol review assesses the ethics of the research and its methods, promotes fully informed and voluntary participation by prospective subjects capable of making such choices (or, if that is not possible, informed permission given by a suitable proxy and seeks to maximize the safety of subjects. The regulations set out the board's membership and composition requirements, with provisions for diversity in experience, expertise and institutional affiliation. For example, the minimum number of members is five, and they must include men and women, at least one scientist, and at least one non-scientist. The full requirements are set out in 21 CFR 56.107.[26]

Decision of IRB: Unless a research proposal is determined to be exempt (see below), the IRB undertakes its work either in a convened meeting (a "full" review) or by using an expedited review procedure. When a full review is required, a majority of the IRB members must be present at the meeting, at least one of whom has primary concern for the non-scientific aspects of the research. The research can be approved if a majority of those present are in favour.

An expedited review may be carried out if the research involves no more than minimal risk to subjects, or where minor changes are being made to previously approved research. The regulations provide a list of research categories that may be reviewed in this manner. An expedited review is carried out by the IRB chair, or by their designee(s) from the board membership. Research activity cannot be disapproved by expedited review. [26-29]

Informed and voluntary consent: Informed consent is a process for getting permission before conducting a healthcare intervention on a person. A clinical researcher may ask a research participant before enrolling that person into a clinical trial, it is completely subjected to the willingness to participate in a particular study and in its documentation. The confirmation is sought only after information about the trial including an explanation of its status as research, objectives, potential benefits, risks and inconveniences associated with the research. It also provides information regarding alternative treatment that may be available and are of the subject's rights.[30]

Often research participants think that the research intervention is designed to provide them a personal benefit which in scientific terminology this is referred as "***THERAPEUTIC MISCONCEPTION***" the crucial issue is whether the participants understand the risks and benefits of the research project.[31-32] Thus in discussions and consent form technical jargon and complicated sentences should be avoided. When participants are not capable of giving informed consent then **Proxy Consent** is obtained from the subjects legally authorized representatives. The investigator in the protocol should ensure that research question could not be answered without involving such subjects.[30] There has been significant international debate about the standard of care that should be provided to the participants of the control group in research. Much debate has been focused on whether the participants in the control group of the research should be provided with universal standards regardless where the research is conducted or non-universal treatment available in a defined region.[33,34]

Once the research study is completed the sponsors and the researchers are confronted with issues of providing further health care to the study participants and the

community as whole. With regard to the provision of an intervention shown to be successful and once the research is complete there are three groups of people to be considered members of the control group in the trial, all the participants in the research project and the wider community in which the research took place. [30]

Clinical equipoise: Clinical research that compares therapies or interventions must have – "an honest null hypothesis" or what Friedman called **Clinical Equipoise.**it is also referred as to a genuine doubt over which treatment under comparison is superior, research that compares therapies are unlikely to be of value without clinical equipoise.[32]

Payments for the participants: Participants in clinical research deserve payment for sparing their time, effort and spending for transportation and other contingencies. They should be compensated only for actual expenses and the time, at an hourly rate for unskilled labor but offering higher payment or incentives amounts to inducements.[30]

Stopping the trial: Predefining the end points helps in stopping the research. Independent data surveillance and monitoring board can determine when a trial should be terminated prematurely as the body should keep a check on the data and when a significance difference is obtained the trial can be stopped. In case of low enrolment, few outcome events or high dropout rates or in the event of fatal incidents and severe adverse effects the study needs to be stopped and reviewed, thus examining interim data and statistical stopping rules should be specified in the protocol.

Conflict of interest: It is a set of conditions in which professional judgment concerning **a primary interest** (such as patient's welfare or validity of research) tends to be unduly influenced by a **secondary interest** (such as financial gain). Conflict of interest may arise among patients due to **Dual Roles for Clinical Investigators** where an investigator may be the personal physician of an eligible research participant, such a participant might fear that his future care will be jeopardized if he declines to participate or sometimes the subjects are not able to distinguish between research and treatment. **Ideological conflict of interest** may arise among the investigators if they are carrying an ideological position that views the study negatively / positively such position may be political, academic, and religious. Pharmaceutical companies or biotechnology firms usually fund the drug trials. This may lead to bias in the design and conduct of the study sometimes it may promote over-interpretation of positive results or funding pressures may impose a failure to publish negative results by the investigator which is usually referred as **financial conflicts of interest.**[35]

Special considerations: Some participants may be at greater risk for being used in ethically inappropriate ways in research. They might be unable to give voluntary and informed consent or are more susceptible to adverse events like children, prisoners, slum dwellers, institutionalized, migrants, and people with cognitive deficiency pregnant women, fetuses and embryos.

SCIENTIFIC MISCONDUCT

Scientific misconduct is the violation of the standard codes of scholarly conduct and ethical behaviour in professional research. The consequences of scientific misconduct can be damaging for both perpetrators and any individual who exposes it. In addition there are public health implications attached to the promotion of medical or other interventions based on dubious research findings.[36,37]

Forms of scientific misconduct includes **Plagiarism** which means claiming the ideas or data of another as one's own then using those ideas or data without appropriate credit or compensation thus presenting the research results of another as one's own (in whole or in part). A subset is **Citation Plagiarism** where the author fails to appropriately credit other or prior discoverers, so as to give an improper impression of priority.[37]

Fabrication refers to making up (inventing) data or results by inflating respondent or subject numbers a minor form of fabrication is padding reference list in a publication to give arguments the appearance of widespread acceptance, but are actually fake.[36]

Falsification refers to changing or wrongly reporting data or results such that the research is not accurately represented in the research record. Sometimes repeating an experiment until the "expected results" are obtained is also a form of falsification.[36]

Ghost-writing is the phenomenon where someone other than the named author(s) makes a major contribution. Typically, this is done to mask contributions from drug companies. It incorporates plagiarism and has an additional element of financial fraud.[38]

Suppression is the failure to publish significant findings due to the results being adverse to the interests of the researcher or his/her sponsor(s)—to be a form of misconduct as well.

Salami slicing: is the process of reporting the results of one research study in several papers. The negative aspects of salami slicing include that the research literature is distorted if readers believe they came from a different subject sample. In systematic reviews and meta-analyses some data could be over-represented.[39]

Fraudulent designs are where research can be deliberately designed to provide misleading results. It involves data concoction, data manipulation, data dredging, deliberate selection of favorable subjects and deception.

ETHICS IN BIOMEDICAL RESEARCH IN INDIAN SCENARIO

The Indian Council of Medical Research brought out the 'policy statement on ethical considerations involved in research on human subjects' in 1980 and revised these

guidelines in 2000 as the 'ethical guidelines for biomedical research on human subjects'. Statement of ethical guidelines for biomedical research on human participants is known as the ICMR Code

It consists of the following:-

a) Statement of general principles on research using human participants in biomedical research.
b) Statement of specific principles on research using human participants in specific areas of biomedical research.

General statement of ICMR relating to biomedical research in medical and related research using human beings as research participants must necessarily ensure that:[40]

I. The **purpose**, of such research is that it should be directed towards the increase of knowledge about the human condition in relation to its social and natural environment and research is for the betterment of all, especially the least advantaged.
II. Research is **conducted** under conditions that no person or persons become a mere means for the betterment of others and that human beings who are subject to any medical research or scientific experimentation are dealt with in a manner conducive to and consistent with their dignity and well-being, under conditions of professional fair treatment and transparency.
III. Such research must be subjected to a regime of **evaluation** at all stages of the proposal and such evaluation shall bear in mind the objects to be achieved, the means by which they are sought to be achieved, the anticipated benefits and dangers.

Principles recommended by ICMR for biomedical research[40]

- *Principle of essentiality:* The research entailing the use of human participants is considered to be absolutely essential after a due consideration of all alternatives in the light of the existing knowledge in the proposed area of research
- *Principles of voluntariness, informed consent and community agreement:* Research participants are fully apprised of the research and the impact and risk of such research on the research participant and others. They have the right to abstain from further participation in the research irrespective of any legal or other obligation.
- *Principle of non-exploitation:* Research participants are remunerated for their involvement in the research or experiment. Irrespective of the social and economic condition or status, or literacy or educational levels attained by the research participants kept fully apprised of all the dangers arising in and out of the research so that they can appreciate all the physical and psychological risks as well as moral implications of the research whether to themselves or others, including those yet to be born.
- *Principles of privacy and confidentiality:* The identity and records of the human participants of the research or experiment are as far as possible kept confidential; and that no details about identity of said human participants, which would result in the disclosure of their identity, are disclosed without valid scientific and legal reasons which may be essential for the purposes of therapeutics or other interventions
- *Principles of precaution and risk minimization:* Due care and caution is taken at all stages of the research and experiment to ensure that the research participant and those affected by it including community are put to the minimum risk, suffer from no known irreversible adverse effects.
- *Principles of professional competence:* The research is conducted at all times by competent and qualified persons who act with total integrity and impartiality and who have been made aware of and are mindful of, preferably through training.
- *Principles of accountability and transparency:* Research or experiment will be conducted in a fair, honest, impartial and transparent manner after full disclosure is made by those associated with the research or experiment of each aspect of their interest in the research.
- *Principle of the maximization of the public interest and of distributive Justice:* Research or experiment and its subsequent applicative use are conducted and used to benefit all human kind and not just those who are socially better off but also the least advantaged.
- *Principle of institutional arrangements:* Duty of persons connected with the research to ensure that all the procedures required to be complied with and all institutional arrangements required to be made in respect of the research and its subsequent use or application are duly made in a transparent manner.
- *Principle of public domain:* Research and any further research, experimentation or evaluation in response to, and emanating from such research is brought into the public domain so that its results are generally made known through scientific and other publications.
- *Principle of totality of responsibility:* It is a professional and moral responsibility, for the due observance of all the principles, guidelines or prescriptions lay down generally or in respect of the research or experiment in question, devolve on all those directly or indirectly connected with the research or experiment.
- *Principle of compliance:* Is a general and positive duty on all persons, conducting, associated or connected with any research entailing the use of a human participant to ensure that both the letter and the spirit of these guidelines, as well as any other norms, directions and guidelines which have been specifically laid down or prescribed.

Public health significance: Medical progress is based on research, which ultimately must rest in part on experimentation involving human subjects. In medical research on human subjects, considerations related to the

well-being of the human subject should take precedence over the interests of science and society. In current medical practice and in medical research; most prophylactic, diagnostic and therapeutic procedures involve risks and burdens. Research investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth by the respective professional organisations.

CONCLUSION

Oral health professionals have an obligation to promote research. For investigators this requires rules, regulation and guidelines for conducting ethical research. The community of oral health researchers is vested with responsibility in conduct and translation of research for betterment of oral and systematic health and this level of responsibility should be continually visible to the profession and the public .only in this way an investigator can earn and maintain required trust needed to advance the human experimentation enterprise.

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