Ethics of Clinical Research: An Islamic Perspective

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Abstract

Medical progress depends on clinical research that at some point has to involve human subjects. The human rights of research subjects must be protected. Ethical principles and guidelines have been developed by international organizations such as the World Medical Association (WMA) and the Council for International Organizations of Medical Sciences (CIOMS). The Islamic Organization for Medical sciences (IOMS) in Kuwait convened a meeting in Cairo, Egypt, in 2004 and produced a document advancing an Islamic viewpoint on these principles and guidelines. In this paper I discuss all these documents. The guidelines developed by CIOMS are in general agreement with Islamic principles i.e. respect for the person, bringing benefit, avoiding harm, and justice. However some differences exist to which I alluded. I also added some personal opinions.

Muslim physicians and scientists should get involved in clinical as well as other medical research. It is *farḍ kifāya* (collective religious duty). They should be familiar with the ethical principles and guidelines and abide by them in their own research. Also, they should monitor externally sponsored research in their own countries to ensure that these guidelines are followed.

Key words: Clinical research, ethics, Islam, Declaration of Helsinki, Council for International Organizations of Medical Sciences, Islamic Organization of Medical Sciences

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Introduction

Academicians in faculty positions are traditionally involved in clinical research. Private practitioners can and should be involved in clinical research as well.[1] A requirement of clinical research is that it conforms to internationally recognized ethical guidelines. For Muslim physicians, conforming to Islamic ethical guidelines is an added requirement. In this article, I will discuss the international guidelines and Islamic viewpoints regarding these guidelines.

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Muslim Obligation to Conduct Research

Muslim countries are, in general, lagging behind in research, including medical research, despite their collective material and human potential. This is very ironic, noting that Muslim physicians of the past were the pioneers of scientific and medical research and were the first to employ scientific experimentation.[2-5]

It is worthwhile to emphasize the importance laid by Islam on the pursuit of learning. There are several Qur'anic verses and traditions of the Prophet ﷺ to this effect. The first revealed verses of the Qur'an state:

Recite in the name of your Lord, Who created. He created man from a leech-like structure. Recite, and your Lord is Most Generous, Who has taught by the pen. He taught Man that what he knew not.[6]

Allah ﷻ also says, addressing the Prophet ﷺ,

Say, "My Lord, increase my knowledge."[7]

Allah ﷻ asks us to look inside ourselves and at the universe to discover God's laws.

Let man consider from what he is created.[8]

And in another verse:

Will they not reflect on camels, how they are created; the sky, how it is raised; the mountains, how they are erected; and the earth, how it is leveled.[9]

Learning in Islam is not limited to religious studies. Early Muslim scholars used to acquire an extensive knowledge, not only in jurisprudence (*fiqh*), Qur'an, and linguistic studies, but also in medicine, chemistry, and natural sciences. Knowledge has to be based on evidence. Allah ﷻ says:

...Can there be another god besides Allah? Say bring forth your proof if you are telling the truth![10]

Based on the above, scientific research is considered by some scholars as *farḍ kifāya* (collective religious duty). The Prophet Muhammad ﷺ is reported to have said:

Allah created disease and its cure except senility (death). Children of Adam, seek the cure but use not *ḥarām* (forbidden) things.[11]

This hadith makes it incumbent on us to investigate the causes of disease and to try to find cures. This can only be achieved by undertaking both basic and clinical research.

International Ethical Guidelines for Clinical Research

Clinical research must rest in part on experimentation involving human subjects. Research involving human subjects creates a lot of potential pitfalls that unfortunately led to tragedies in the last century. The most well-known of these are the experimentation by Nazis on the prisoners and in the United States in the Tuskegee study of untreated syphilis.[12] This study was conducted by the U.S. Public Health Service (USPHS). Over the period of 40 years (1932-72), 399 syphilitic African Americans were followed to study the natural course of the disease without treatment.[13-6] The study patients were never informed of the availability of Penicillin, which in the late 1940s was found to be an effective treatment for their disease. The Nuremberg Code was promulgated in 1947 as a direct consequence of the trial of Nazi physicians who conducted research on the prisoners of World War II without their consent. The United Nations general Assembly adopted the Universal Declaration of Human Rights in 1948 and the International Convention on Civil and Political Rights in 1966. Its article seven states in part: "In particular, no one shall be subjected without his free consent to medical or scientific experimentation."

In parallel with these efforts, medical professionals worked on formulating principles of ethical use of human subjects in research. The first such document, the Declaration of Helsinki, was adopted by the World Medical Association (WMA) in 1964 in Helsinki, Finland. This was updated several times. The last was in Seoul, South Korea, in 2008 at the WMA 59th General Assembly meeting.[17] The central point of the declaration is that medical research should be subject to ethical standards that promote respect for all human beings and protect their health and rights.

The Declaration of Helsinki consists of 35 articles divided into three sections: the introduction, "Principles for All Medical Research," and "Additional Principles for Medical Research Combined with Medical Care." This document stresses that in the field of biomedical research, fundamental distinction should be recognized between medical research in which the aim is essentially diagnostic or therapeutic for a patient, and medical research, the essential object of which is purely scientific and without direct diagnostic or therapeutic value to the person subjected to research. Medical

research should be subject to ethical standards that promote respect for all human beings and protect their health and rights.

The Declaration of Helsinki also stresses that some research participants are vulnerable and need special protection. The research should be approved by especially appointed ethical review committees. Each potential research subject should be adequately informed of the aims, methods, sources of funding, and potential risks of the study. They should be informed about their right to abstain from participation or to withdraw from the study without any reprisal. For a research subject who is a minor or legally incompetent, the investigator must obtain informed consent from the legal guardian. These and other vulnerable groups should not be included in research unless it is necessary to promote the health of the particular group from which they are recruited.

In the United States, the U.S. National Commission for the Protection of Human Subjects of Biomedical Research was created in 1974 and produced the Belmont Report in 1979, which distilled principles of ethics related to research.[18] It addresses boundaries between medical practice and research; basic ethical principles such as respect for persons, beneficence, and justice; and informed consent, assessment of risks and benefits, and selection of subjects.

Another international organization, The Council for International Organizations of Medical Sciences (CIOMS), was founded in 1949 under the auspices of the World Health Organization (WHO) and the United Nations Educational Scientific Cultural Organization (UNESCO). CIOMS in association with WHO undertook its work on the ethics of biomedical research in the 1970s. It produced guidelines to enable the effective application of the ethical principles set forth in the Declaration of Helsinki, particularly in developing countries. Their first report was published in 1982. Following that, there were major developments, such as the outbreak of the HIV/AIDS pandemic and proposals to undergo large scale experiments with vaccines and medications. There were also rapid advances in biotechnology and an increase in multinational field trials involving vulnerable populations in developing countries. These developments raised new ethical issues, and in 1996 CIOMS updated its report and published International Ethical Guidelines for Biomedical Research involving Human Subjects, updating it in 2002. This consisted of a statement of general ethics, a preamble, and 21 guidelines.[19]

The Islamic Viewpoint on CIOMS Guidelines

The Islamic Organization of Medical Sciences (IOMS), based in Kuwait, translated this document into Arabic. It was then reviewed by a scholar of Islamic jurisprudence. The document and the latter's comments were discussed by a group of Muslim scholars, physicians, including myself, and other individuals with interest in ethics and the law. The Islamic viewpoint on each of these guidelines was studied in depth by this group and discussed in a three day conference held in Cairo, Egypt, in December 2004. The results of these deliberations were published as the International Ethical Guidelines for Biomedical Research involving Human Subjects: An Islamic Perspective.[20] In this paper I will summarize the CIOMS guidelines, the IOMS document, and add my personal opinions.

The CIOMS guidelines as well as the principles of the Declaration of Helsinki are based on the generally accepted ethical principles of respect of person, beneficence, nonmaleficence, and justice.[21]

These four principles are in agreement with Islamic rules. Allah ﷻ says:

> We have honored Adam's children.[22]

Respect of the person is a major aspect of human dignity. Respect of the person gives him the right to make his own choices and decisions. In the context of research, no one should be involved in a research project without his free and voluntary consent. The Islamic principle that applies here is "No one is entitled to dispose of the right of human being without his permission."[20]

A basic purpose of Islamic law is to "secure benefits for people and to protect them from harm."[20] This is termed beneficence in our lexicon at present. Another Islamic law states that "every action that leads to harm or that prevents a benefit is forbidden.[20] This is what is now called "nonmaleficence." In cases where benefit and harm are not absolute, which is the usual case in biomedical research, the rule that applies is that "if a less substantial instance of harm and an outweighing benefit are in conflict,

the harm is forgiven for the sake of the benefit."[20]

Justice is an established principle in Islamic law. Allah ﷻ says

> God enjoins justice and charity.[23]

Justice means equity and fairness, and charity is either the acquisition of benefit or the prevention of harm.

Now, I will discuss these guidelines individually.

Guideline 1: Ethical Justification and Scientific Validity of Biomedical Research involving Human Subjects

In agreement with this guideline, the performance of research on human subjects is Islamically acceptable. However, it should be useful and responsive to the five purposes of Islamic law (*maqāṣid al-sharī`a*), i.e. the safeguarding of one's religion, life (and health), intellect, progeny and property/resources, and that it should not cause harm. On the other hand, a person who pursues scientific knowledge to cause harm is subject to God's wrath. God says:

> And they learn what causes them harm and brings them no benefit, and they already know that whoever purchases it has no share in the hereafter.[24]

The Prophet ﷺ asked God's refuge from learning that brings no benefit.[25] The research should by no means lead to something prohibited. A researcher should comply with the framework of Islamic law in any research he undertakes. Moreover, a researcher should observe the rules and ethics of the profession, especially as they relate to the ethics of biomedical research. To be more specific, the research is Islamically acceptable under the following conditions:

1) The purpose of the study is to secure an absolute benefit i.e., enhancing human health, or to prevent an instance of absolute harm that impairs health or to give priority to securing an outweighing benefit over preventing a less substantial instance of harm.
2) The benefit does not violate a legal stipulation nor contradict any absolute ruling of Islamic jurisprudence.
3) The research itself should be legitimate i.e. both the means and end must be legally permissible.
4) The design of study should be scientifically sound so that it should be more likely to achieve the purpose it is expected to accomplish. This is based on the rule that "every action that ceases to pursue its objective is unacceptable."[20]
5) That the research team is qualified and competent to conduct the research as consistent with the Qur'anic guidance:

> God enjoins you to deliver your trusts to their rightful owners[26]

and the Prophetic saying:

> Allah loves the person who is performing a job to do it in the best possible way.[27]

Guideline 2: Ethical Review Committees

This guideline addresses the formation and role of the ethical review committees. A universally accepted standard is the establishment of ethical review committees to evaluate biomedical research and to ensure that its purpose and methodology are in accordance with the ethical guidelines. This concept is Islamically ordained. Medicine and biomedical research are so important that they need to be practiced under supervision. In that regard I like to point out that Muslims were the first to establish the practice of licensure to physicians and the system of *ḥisba* (inspection).[28] This was meant to ensure that all people in trades, including physicians, were behaving justly.

The ethical review committees, usually called institutional review boards (IRBs), consist of scientists, physicians, lay people, and legal personnel. In an Islamic country, it is recommended that the ethical review committee gets the opinion of an Islamic jurisprudence (*fiqh*) committee to be certain that the proposed study is within the guidelines of Islam. An Islamic rule is "A responsible adult is not to embark on any undertaking before he finds out how it is regarded by God."[20]

The guideline that ethical review committees should be independent of the research teams and sponsors is in agreement with Islamic principles. The ethical review committee is in effect giving testimony. For such to be Islamically acceptable, it must be

made by a neutral party. To satisfy the requirement of validity of testimony, any material or nonmaterial rewards for the committees should not be contingent upon the outcome of the review (testimony).

Guideline 3. Externally Sponsored Research

In case the research is externally sponsored, i.e. by an institution or an industrial or drug company from another country, the scientific and ethical review should be conducted objectively, independently, and honestly in the country of the sponsoring organization. This is to guarantee that the standard ethical controls are applied. These should not be less stringent when applied in another, possibly less-developed country than the controls normally applied in the country of the sponsoring organization, as all members of the human race should be treated equally. Equity for all people is a basic tenet of Islam. Allah ﷻ says:

> O mankind reverence your Guardian Lord who created you from a single person.[29]

In addition, another ethical review should be conducted in the host country to make sure that the proposed research meets the health needs and priorities of that country. One of the purposes of Islamic law is "To place everything in its right place [on the list of priorities.]"[20]

Guideline 4. Individual Informed Consent

This guideline stipulates that the investigator must obtain a voluntary informed consent from each prospective study subject. This is in conformity with Islamic law that calls for respect of the independence of every individual, his right to make his personal choices and arrive at decisions suitable for him without any trace of coercion or deception, and his right to be protected from injury, misleading inducement, or exploitation by others. The consent should be given willingly after the subject, if fully competent, receives and understands the necessary information. This is stipulated in *fiqh* rule: "No one is entitled to dispose of the rights of a human being without his permission" and "no right of a human being can be canceled without his consent."[20] The information should be given in a written format in a language easily understood by the individual, and the consent should be documented.

Guideline 5. Essential Information for Prospective Participants

This guideline details the necessary information that should be given to the potential subjects for the research. The informed consent should be given with full knowledge and correct understanding of the content of his consent on the part of the subject.

Guideline 6. Obligations of Sponsors/Investigators

This guideline details the duties of both the sponsors and investigators to give the subjects accurate information and neither withhold any information that may negatively influence the potential research subjects' decision to consent nor deceive them in any way. They should not include any explicit or implicit threats in their discussions with the potential subjects. Islamic jurisprudence stipulations support this guideline. These stipulations are: "mutual agreement cannot be reached under conditions of ignorance" and "consent to an unknown thing and acquittal from an unknown thing are not valid."[20]

Guideline 7. Inducement to Participate

There is no objection from the Islamic point of view to compensate research subjects for lost earnings, transport, and other expenses that might be incurred as a result of participating in the research. Actually, the rule of reparation and the principles of justice and fairness make it necessary to compensate the subjects adequately for their expenses. Additional financial or in-kind payments made to induce participation in research may imply undue inducement. If it pressures the subject to give consent not based on conviction, then it is legally prohibited. However, if such payment does not influence the subject's decision making, and he gives his consent, with his free will, his consent in Islamic jurisprudence is valid. Nevertheless there should be – in my view – some restriction. The additional payments given to a poor person, or the provision or even the promise of medical care to a person who does not have access to that care in less developed countries or uninsured individuals in Western societies, could be a significant inducement that may cloud the ability of the person to make a true informed decision. The person may consent to participate and expose himself to certain risks he would avoid were he not in need of such incentives.

Guideline 8. Benefits and Risks of Study Participation

The investigators must ensure that potential benefits and risks are reasonably balanced, and the risks are minimized. The need to strike a balance between potential benefits and risks in research involving human subjects, with the prospective benefits being more likely and the need to minimize risks, is included in a basic principle of Islamic Law. It says "if a less substantial instance of harm and an outweighing benefit are in conflict, the harm is forgiven for the sake of the benefit." If a benefit and an instance of harm are in conflict, priority should be given to the weightier of the two.[20]

It is acceptable from a religious perspective to use the expected, significant benefits to society as a justification of the risks interventions pose to an individual who has no possible direct diagnostic, therapeutic, or preventive benefit. This is based on a rule of jurisprudence, "Public interests take precedence over private ones."[20] This is different from the Helsinki Declaration and the CIOMS guidelines that emphasize that individual benefit precedes social benefits. This point needs further study by Islamic scholars to determine to what extent public interest supersedes individual interest as it relates to human clinical research.

Guideline 10. Research in Populations and Communities with Limited Resources

Before undertaking research in a population or a community with limited resources, the sponsor and investigator must make every effort to ensure that the research is responsive to the health needs and priorities of the community in which the research will be conducted. Also, any knowledge generated or any intervention or product developed as a result of that research must be made reasonably available for the benefit of that population or community.

This guideline is consistent with the Islamic principle of justice and charity.[23]

Guideline 11. Choice of Controls in Clinical Trials

This guideline can also be endorsed from an Islamic point of view as it requires researchers to observe, in dealing with human subjects, the obligation of trust when choosing the method of intervention to protect their human rights fully and ensure their safety.

> God enjoins you to deliver your trust to their rightful owners.[26]

Whether the use of a placebo arm in clinical trials is ethically acceptable has been vigorously debated.[30] Against objection by scientists, the 2000 version of the Helsinki Declaration specifically prohibits the use of placebos, except in limited situations. CIOMS recommends the use of equivalency trials or add-on studies. Equivalency trials compare an investigational intervention with an established effective treatment and produce scientifically reliable data. An add-on design may be employed when the investigational therapy and a standard therapy have different mechanisms of action. The treatment to be tested and the placebo are each added to the standard treatment to determine if the investigational therapy leads to a better outcome or to fewer side effects.

If the use of a placebo arm is essential for the clinical trial to produce useful information and there is no resulting harm to the subjects in the control arm, it will be Islamically acceptable. The rationale for that is that "although a sort of deception is practiced, the consequences are safe."[20] In my view, it may cause harm if the research subject in the control arm is deprived of a currently accepted treatment. I believe that the concerned ethics review committee has to carefully examine each specific case, evaluate the possibility of harm to the subjects in the placebo arm and try to work with the investigator to find an alternative study design.

Guideline 12. Equitable Distribution of Burdens and Benefits in the Selection of Groups of Subjects in Research

This guideline is again in harmony with Islamic law, which calls for justice in all affairs of life.[23] So it is unfair that participants in a study share in the burdens i.e. the potential side effects or other hardships but they do not share in the benefits when a successful intervention is achieved but is not made available to them.

Guideline 13. Research Involving Vulnerable Persons

These include persons with limited capacities or freedom to consent or decline to consent. They may be mentally incapacitated, elderly people who developed varying degrees of dementia, residents of nursing homes, people receiving welfare benefits, the

unemployed, patients in emergency rooms, some ethnic or racial minorities groups, homeless persons, nomads, refugees, prisoners, and patients with incurable diseases. Junior or subordinate members of hierarchical groups, for example medical and nursing students, employees of pharmaceutical companies and members of the armed forces or police, are all considered vulnerable groups. Their agreement to volunteer may be influenced by the expectation of preferential treatment if they agree and retaliation if they refuse.

Ethical justifications for the involvement of these vulnerable groups are:

1. The research could not be carried out equally well with less vulnerable persons.
2. The research will lead to improved treatment of health problems unique to the vulnerable class.
3. They are assured that they will have reasonable access to any product that comes out of the research
4. The risk is minimal.
5. The agreement to participate is supplanted by the permission of a legal guardian or other appropriate representative.

This CIOMS guideline is in conformity with Islamic law. These individuals need their rights and interests protected. They should not be forced, pressured, deceived, or subjected to exploitation of their psychological condition or financial difficulties in order to make them consent to be research subjects. Such coercion or exploitation involves injustice that is disapproved by Islamic law. In a divine tradition, Prophet Muhammad ﷺ quotes his Lord ﷻ, as saying:

يا عبادي إني حرمت الظلم على نفسي وجعلته بينكم محرما فلا تظالموا

> My worshippers, I have forbidden injustice on my part and made it forbidden among you, so do not be unjust to one another.[31]

Thus, a special justification of recruiting vulnerable individuals to serve as research subjects is required in Islamic Law, and, as stipulated in the CIOMS guideline, strict measures to protect their personal rights and interests should be taken.

Guideline 14. Research Involving Children

The participation of children is essential in research on childhood diseases and treatments given to children, including medications and vaccines. However, the researcher must ensure that the research could not be carried out equally well in adults and that the knowledge to be acquired is relevant to the health needs of children. Further, a parent or guardian must give permission, and the assent of the child should be obtained to the extent of that child's capabilities and a child's refusal to participate or to continue in the research should be respected.

Under Islamic rulings, a child under the age of puberty is incompetent and his "consent" to participate in biomedical research is not valid. Moreover, in variance with this CIOMS guideline, Islamically, the permission of the guardian is not legitimate except a) when there is an absolute or outweighing benefit or when the child's condition needs urgent participation, b) when there is general need to conduct research relevant to children's diseases, drugs,or vaccines, and c) if the risks involved do not exceed what is associated with a normal medical or psychological examination of the child or when the increase in risk level is slight and approved by an ethical review committee. These special circumstances are considered "necessities that render permissible what is usually prohibited" in Islamic law.[20]

In another variance from the CIOMS guideline, a child's objection to participate in the study is not taken in consideration. The authority to withdraw from a study is only given to the guardian. An exception would be if the child is perceptive i.e. is close to puberty and his perception skills have developed sufficiently even though he is still under guardianship.

Guideline 16. Women of Reproductive Age as Research Subjects

Investigators should not exclude women of reproductive age from biomedical research. If participation may be hazardous if a woman conceives, the investigator/sponsor should offer her pregnancy testing and provide her with access to effective contraception before the research.

In agreement with this guideline, Islamic jurisprudence considers the exclusion of women of reproductive age from biomedical research as unjust because it deprives them from potential benefit.

Their participation is conditional on voluntary informed consent, including information on the precautions taken to spare her and her fetus if she becomes pregnant from any hazards. In Islamic law, it is unacceptable for the permission of a husband to replace that of his wife. That would be an affront to her human rights. Although not a requirement, it is preferable for a married woman to obtain her husband's consent.[20] No such point is included in the CIOMS guidelines.

Guideline 17. Pregnant Women as Research Subjects

Research involving pregnant women is complicated by the fact that it may present potential benefits and risks to both the women and their fetuses. However, pregnant women should be presumed to be eligible for participation in biomedical research as long as they are adequately informed about the benefits and risks to themselves, their pregnancies, their fetuses, their subsequent pregnancies, and their fertility. The research should be relevant to the particular health needs of pregnant women in general. Investigators should include in their protocols a plan to monitor the outcome of the pregnancy with regard to both the health of the woman and the short- and long-term health of the newborn.

Islamically, there is no objection to the participation of pregnant women in biomedical research because of the potential benefit of the research to them and to their fetuses. Ideally, before enrolling pregnant women in biomedical research, the investigators should rule out any harm to the fetus. However, that is almost impossible to achieve. The safety of new medications can not be assumed from animal experiments or from the study of the pharmacology of the medication used. There will always be some risk. Islamically, accepting the possibility of such harm would nevertheless be permissible if the mother or the fetus is likely to gain an absolute or outweighing benefit. When there are potential risks for the fetus, even when they are minor or outweighed, the investigator should also obtain the consent of the father. This is not a requirement of the CIOMS guidelines. It states "...it is desirable in research directed at the health of the fetus to obtain the father's opinion also, when possible."[20]

In some instances, clinical trials are meant for the treatment of the fetus and not the mother. In these cases there are more risks to the mother without any benefit to her. In my opinion the most obvious example is in utero (prenatal) fetal surgery to correct a fetal birth defect. In these cases, the maternal instinct may unduly influence her to agree to such trials. Ethically and Islamically, the investigators should make an extra effort to explain the trial, the potential benefit to the fetus, and the potential complications in the neonatal management, the short- and long-term prognosis for the fetus/neonate/child and especially the short- and long-term complications for the mother before she agrees to participate in the trial. Safeguards should be established to prevent undue inducement to pregnant women to participate in the research for the sole benefit of the fetus. In these circumstances I recommend that the ethics review committee establishes a special counseling team independent of the investigator.

Guideline 18. Safeguarding Confidentiality

The subjects' research data should be held in strict confidentiality. However, the subjects should be told the limits, legal or otherwise, to the investigator's ability to absolutely safeguard confidentiality and the possible consequences of possible breeches of confidentiality.

Safeguarding confidentiality is a basic tenet of Islamic law. This is the "trust" between an individual and the physician/investigator. Exceptions from the requirement of safeguarding confidentiality are made in cases where concealing the confidential information causes greater harm for the person involved than that caused by revealing it or when revealing it brings a benefit that outweighs the harm of concealing it. This is based on the rule of the permissibility of commission of the lesser of two injuries to prevent the greater injury. Also, there are cases where revealing confidential information is permitted because it brings a social benefit or prevents public harm.[20]

Guideline 19. Right of Injured Subjects to Treatment and Reparation

Research subjects are entitled to free medical treatment when they incur any injury or any other harm as a result of their involvement in the

research. They are also entitled to equitable compensation for any impairment, disability, or handicap that result from their participation. In the case of death, dependents are entitled to compensation. Their entitlement is based on the principle of justice, the fourth principle of ethics. The same is true from the Islamic point of view. This is based on the Islamic legal rule of reparation, which makes it an obligation for a person who causes any damage to another to make equitable compensation for the loss. When a subject dies as a result of his participation in research, his heirs are entitled to monetary compensation, which is the blood money stipulated in Islamic legislation for accidental homicide. The implicit agreement between research sponsor(s) and involved subjects entails a religious responsibility on the part of the former party to make up for the damages suffered by a subject as a result of participation in the research. However, it was pointed out during the deliberations in the Cairo conference that it is permissible for the investigators or sponsors to obtain in advance the subjects' informed consent to waive the investigator's responsibility, including the research subjects' entitlement to compensation for disability and handicaps when they are not deliberately caused. This is based on the fact that Islamically, a competent individual is entitled to waive voluntarily any of his rights, provided that he does that completely voluntarily without any pressure, inducement, or deception.[20] While this is true, in my opinion, there is danger of it being abused as it will be impossible to prove that the waiver was given truly voluntarily. I would think that waiving of the right to reparation ought not to be permitted. In my view, allowing waivers will make the investigator less careful in avoiding harm to the research subject. Further, I believe there is a difference between harm resulting from accepted treatment versus that resulting from investigational treatment in the course of conducting a clinical trial. CIOMS Guideline 19 specifically prohibits such waivers.

Guideline 20. Strengthening Capacity for Ethical and Scientific Review and Biomedical Research

In externally sponsored research, sponsors and investigators have an ethical obligation to ensure that biomedical research projects for which they are responsible in the host countries contribute effectively to national or local capacity to design and conduct biomedical research and to provide scientific and ethical review and monitoring of such research.

Guideline 21. Ethical Obligations of External Sponsors to Provide Health Care Services

External sponsors are ethically obliged to ensure the availability of health care services that are essential to the safe conduct of the research and for the treatment of subjects who suffer injury as a consequence of the research. External sponsors should also ensure the availability of services to make a beneficial intervention developed as a result of the research reasonably available to the population.

Guidelines 20 and 21 both fall under the Islamic principles of justice and charity and that of reparation previously discussed.

Summary of the Differences between the Islamic Viewpoint and CIOMS Guidelines

Few differences exist between the two documents. A major difference is the importance that Islam puts on "public interest." It takes precedence over private interest in special cases. This contrasts with Guideline 8 as well as with the Declaration of Helsinki.

CIOMS Guideline 14 requires the consent of the guardian for a child to participate in research study. Under Islamic rulings this is also necessary, but the permission of the guardian is legitimate only under the strict conditions outlined above. Further, the CIOMS guideline stipulates that the assent of the child should be obtained if possible. Islamically, that is not required. At the same time, the child's objection to participation in the study is not to be accepted if the guardian believes that participation is beneficial. However, if the child's perceptive skills have developed sufficiently, the child's objection can be taken into consideration. On the other hand, the CIOMS guideline respects a child's objection to participate.

When recruiting a married woman for research, it is Islamically preferable to obtain the husband's consent. This is not included in CIOMS Guideline 16. When recruiting a pregnant woman for a research study if there is any potential risk to the fetus even when minimal or outweighed the husband's consent should be obtained according to Islamic rulings, but not according to CIOMS Guideline 17.

Islamic rulings allow revealing confidential

information if it brings social benefit or prevents public harm. This is not mentioned explicitly in CIOMS Guideline 18 but is implied in certain situations. The concept of public versus private interest is again invoked here as in the discussion about Guideline 8. It needs further elaboration by Islamic scholars.

Another difference relates to Guideline 19. Whereas Islamic rulings will allow waiving of liability against the investigator(s) under certain conditions, the guideline prohibits such waivers. I expressed my stand against the waiver.

Integrity in Clinical Research

It has been stressed in Guideline 1 and in the Islamic prerequisites for research that the investigators should be qualified and competent to conduct the study by virtue of their education and experience. I believe it is important to add that they need to be honest. Although honesty is implied in competency, it is better and more practical to have it as a separate trait. Integrity or honesty can be manifested in two aspects. The first is for an investigator, upon noting unexpected side effects or harm to the study subjects, to discontinue the study and notify the concerned IRB or ethics review committee. An example of this has been reported.[32] The second aspect is to never falsify research data. Unfortunately, there have been instances of "competent" researchers falsifying data.

Article 30 of The Declaration of Helsinki touches on the subject:

> Authors, editors and publishers all have ethical obligations with regard to the publication of the results of research. Authors have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. They should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results should be published or otherwise made publicly available. Sources of funding, institutional affiliations, and conflicts of interest should be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.[17]

These points can not be stressed enough. Islam stresses honesty and truthfulness. It abhors false testimony under which falsification of scientific data falls:

> O you believe! Be staunch in justice, witness for Allah even though it be against yourselves or your parents or your kindred ...[33]

> ...So shun the filth of idols, and shun lying speech.[34]

Conclusion

In this paper I presented the current ethical principles embodied in the Helsinki Declaration and the guidelines the CIOMS established for the application of these principles. They are mostly in conformity with Islamic law. I did point out some of the differences. Some of these are outlined in the "International Ethical Guidelines for Biomedical Research (An Islamic Perspective)."[20] Other differences represent my personal viewpoints.

It behooves Muslim researchers to fully abide by these principles and guidelines. Muslims who have *taqwā* (God consciousness) should be the first to promulgate those ideals as we are given the privilege by Allah ﷻ to care for His most honored creation, humans.

References

1. Khan FA. Clinicians as effective researchers. J Islam Med Assoc. 2010;42:9-14. http://dx.doi.org/10.5915/42-1-4846
2. Muazzam MG, Muazzam N. Important contributions of early Muslim period to medical science. I. Basic sciences. J Islam Med Assoc. 1989;21:8-13. http://dx.doi.org/10.5915/21-1-5513
3. Muazzam MG, Muazzam N. Important contributions of early Muslim period to medical Science. II. Clinical sciences. J Islam Med Assoc. 1989;21:64-70. http://dx.doi.org/10.5915/21-2-5514
4. Khan HR. Contributions of Muslims to medicine and science: up to the middle of thirteen century. J Islam Med Assoc. 1982;14:111-4. http://dx.doi.org/10.5915/14-4-5526
5. Haddad FS. Original contributions of physicians during the Islamic era. J Islam Med Assoc. 1996;28:103-12. http://dx.doi.org/10.5915/28-3-5530
6. The Glorious Qur'an Chapter 96, Verses 1-5.

7. The Glorious Qur'an Chapter 20, Verse 114.
8. The Glorious Qur'an Chapter 86, Verse 5.
9. The Glorious Qur'an Chapter 88, Verses 17-20.
10. The Glorious Qur'an Chapter 27, Verse 64.
11. Sunan Abī Dāwūd. Kitāb al-ṭibb.Bāb fī al-adwiya al-makrūha. Hadith no. 3874. muhaddith.org
12. Pressel DM. Nuremberg and Tuskegee: lessons for contemporary American medicine. J Natl Med Assoc. 2003;95:1216-25. PubMed Central PMCID: PMC2594827
13. Vonderlehr RA, Clark T, Wenger OC et al. Untreated syphilis in the male Negro: a comparative study of treated and untreated cases. JAMA. 1936;107:856-60. http://doi.org/hd6
14. Schuman SH, Olansky S, Rivers E et al. Untreated syphilis in the male Negro: background and current status of patients in the Tuskegee study. J Chronic Dis. 1955;2:543-58. http://doi.org/hd7
15. Olansky S, Schuman SH, Peters JJ et al. Untreated syphilis in the male Negro: X. Twenty years of clinical observation of untreated syphilitic and presumably nonsyphilitic groups. J Chronic Dis. 1956;4:177-85. http://dx.doi.org/10.1016/0021-9681(56)90019-4
16. Rockwell DH, Yobs AR, Moore MB. The Tuskegee study of untreated syphilis: the 30th year of observation. Arch Intern Med. 1964;114:792-8. http://doi.org/hd8
17. 59th World Medical Association General Assembly. Declaration of Helsinki: ethical principles for medical research involving human subjects. 2008. http://www.wma.net/en/30publications/10policies/b3/17c.pdf
18. The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Department of Health Education and Welfare. The Belmont Report. Ethical principles and guidelines for the protection of human subjects of research. April 18, 1979. http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.html
19. Council for International Organizations of Medical Sciences. International ethical guidelines for biomedical research involving human subjects. Geneva: World Health Organization; 2002. http://www.cioms.ch/publications/guidelines/guidelines_nov_2002_blurb.htm
20. Islamic Organization for Medical Sciences. International ethical guidelines for biomedical research involving human subjects "an Islamic perspective." In El-Gendy AR, Al-Awadi ARA, editors. The international Islamic code for medical and health ethics. Kuwait: Islamic Organization for Medical Sciences; 2005:Vol 2, 121-276.
21. Beauchamp TL, Childress JF. Principles of biomedical ethics. 5th ed, Oxford (UK) and New York: Oxford University Press; 2001.
22. The Glorious Qur'an, Chapter 17, Verse 70.
23. The Glorious Qur'an, Chapter 16, Verse 90.
24. The Glorious Qur'an, Chapter 2, Verse 102.
25. Sahih Muslim. Siddiq AH, translator. Lahore: Sh. Muhammad Ashraf; 1987: 1425, hadith no 6568.
26. The Glorious Qur'an, Chapter 4, Verse 58.
27. Jalāl al-dīn al-Suyūṭi. Al-Jāmi` al-ṣaghīr. Vol 2. Chapter of Alif. Hadith no 1861. http://muhaddith.org
28. Chiarelli LC. Muslim Sicily and the beginnings of medical licensing in Europe. J Islam Med Assoc. 1999;31:79-82. http://doi.org/hd9
29. The Glorious Qur'an, Chapter 4, Verse 1.
30. Vastag B. Helsinki discord? A controversial declaration. JAMA. 2000;284:2983-5. http://doi.org/hfb
31. Sahih Muslim. Siddiq AH, translator. Lahore: Sh. Muhammad Ashraf; 1987: 1365, hadith no. 6426.
32. Straus SE. Unanticipated risk in clinical research. In: Gallin JI, Ognibene FP, editors. Principles and practice of clinical research. 2nd ed. New York: Elsevier; 2007:78-94.
33. The Glorious Qur'an, Chapter 4, Verse 135.
34. The Glorious Qur'an, Chapter 22, Verse 30.