•General Ethical Principles:

- All research involving human subjects should be conducted in accordance with three basic ethical principles, namely respect for persons, beneficience and justice in varing circumstances that may be expressed differently and given different moral weight, and their application may lead to different decisions or courses of action. The present guidelines are directed at the application of these principles to research involving human subjects.

•Respect for the persons incorporated at least two fundamental ethical considerations namely:

a- Respect for autonomy, which requires that, those who are capable of deliberation about their personal choices.

b- Protection of persons with impaired or diminished autonomy.

•Beneficence refers to the ethical obligation to

maximize benefits and minimize harms. Beneficence further prescribes the deliberate infliction of harm on person; non-malfeasance (do not harm).

• Justice refers to the ethical obligation to treat each person in accordance with morally right and proper, to give each person what is due to him or her.

• The principle refers primarily to distributive justice, requires the equitable distribution of both the burdens and the benefits of participation in research.

□ The Guidelines:

Guideline 1: Ethical justification and scientific validity of biomedical research:
Ethical justification and scientific validity of biomedical research

Involving human being is the prospect of discovering new ways of benefiting people's health.
Such research can be ethically justifiable only if it carried out in ways that respect, protects and are fair to the subjects of that research and are morally acceptable within the communities in which the research is carried out.
Moreover, because scientifically invalid research is unethical in that it exposes research subject to risks without possible benefits.

Guideline 2: Ethical review committees

All proposals to conduct research involving human subjects must be submitted for review of their scientific merit and ethical acceptability to one or more scientific review and ethical review committees.
The review committees must be independent of the research team and any direct financial or other benefit they may derive from the

research should not be contingent on the outcome of their review.

- The investigator must obtain their approval or clearance before undertaking the research. The ethical review committee should conduct further reviews as necessary in the course of research.

- Guideline 3: Ethical review of externally sponsored research:

- An external sponsoring organization and individual investigators should submit the research protocol for ethical and scientific review in the country of sponsoring organization.

And the ethical standards applied should be on less stringent that they would be, for research carried out in that country.

- As well as a national or local review committee, should ensure that proposed research is responsive to the health needs and priorities of the

host country and meets the requisite ethical standards.

Guideline 4: Individual informed consent

For all biomedical research involving humans the investigator must obtain the voluntary informed consent of the prospective subject or in the case of an individual who is not capable of giving informed consent, the permission of legally authorized representative in accordance with applicable law.

Waiver of informed consent is being regarded as uncommon and exceptional and must in all cases be approved by ethical review committee.

Guideline 5: obtaining informed consent

Essential information for prospective research subject before requesting an individual's consent to participate in research.

The investigator must provide the information, in language or another form of communication

that the individual can understand.

Guideline 6: Obtaining informed consent: Obligation of sponsors and investigators:

Sponsors and investigators have a duty to refrain (خودداری کردن) from unjustified deception, undue influence or intimidation.

Seek consent only after ascertaining that the prospective subject has adequate understanding of the relevant facts and of the consequences of the participation and has sufficient opportunity to consider whether to participate.

- Investigators should justify any exceptions to this general rules and obtain the approval of ethical review committee.

Renew the informed consent of each subject if there are significant changes in the conditions or procedures of research or if new information becomes available that could affect the willingness of subject to continue to participate.

Renew the new informed consent of each subject in long-term studies at pre-determined intervals, even if there are no changes in the design or objective of research.

Guideline 7: Inducement to participate

Subjects may be reimbursed for lost earning, travel costs and other expenses incurred in taking part in the study; they may also receive free medical services.

Subjects, particularly those who receive no direct benefit from research may also be paid or otherwise compensated for inconvenience and time spent.

The payment should not be so large, however or the medical services so extensive as to induce subjects to consent to participate in the research.

All payments, reimbursement and services provided to research subject must have been

approved by an ethical review committee.

Guideline 8: benefits and risks of study participation (2m)

For all biomedical research involving human subjects, the investigator must ensure that potential benefits and risks are reasonably balanced and risks are minimized.

Interventions or procedures of direct diagnostic, therapeutic or preventive benefit for individual subject must be justified by the expectation that they will be at least as advantageous to individual subject.

Guideline 9: Special limitation on risk when research involves individuals who are not capable of giving informed consent:

Research with individual who are incapable of giving informed consent, the risk from research interventions that do not hold up direct benefit for the individual subject should be

not greater than the risk attached to routine medical or psychological examination of such person.

Guideline 10: Research in populations and communities with limited resources:

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

Guideline 11: Choice of control in clinical trials

As a general rule, research subjects in this control group of a trial of diagnostic, therapeu-

tic or preventive intervention should receive an established effective intervention.

- In some circumstances it may be ethically acceptable to use an alternative comparator such a placebo or no treatment.

Placebo may be used when:

There is no established effective intervention or when withholding a established effective intervention would expose subjects to at most, temporary discomfort or delay in relief of symptoms.

Guideline 12: Equitable distribution of burdens and benefits in the selection of group of subjects in research:

Group or communities to be invited to be subjects of research should be selected in such a way that the burdens, and benefits of the research will be equitably distributed. The exclusion of groups or communities that

might benefit from study participation must be justified.

Guideline 13: research involving vulnerable persons.

Special justification is required for inviting vulnerable individuals to serve as research subjects and if they are selected, the means of protecting their rights and welfare must be strictly applied.

Guideline 14: research involving children

Before undertaking research involving children, the investigator must be ensuring that:

i- research might not equally well be carried out with adults.

ii- The purpose of research is to obtain knowledge relevant to health needs of children.

iii- Parent or legal representative of each child has given permission.

iv- The agreement of each child has been obtained to

the extent of the child capabilities.

v. A child's refusal to participate or continue in the research will be respected.

Guideline 15: research involving individuals who by reason of mental or behavioural disorders are not capable of giving adequate informed consent:

The investigator must ensure that:

i. Such a person will not be subjects of research that might equally well be carried out on persons who is giving adequately informed consent.

ii. The purpose of the research is to obtain knowledge relevant to health needs of persons with mental or behavioural disorders.

iii. The consent of each subject has been obtained to the extent of person's capabilities.

iv. Prospective subject's refusal of participate in research always respected, unless in exceptional circumstances, there is no reasonable medical alternatives.

. In cases where the subject is incapable of giving informed consent the latter must be given from the family member or legally authorized representative in accordance with applicable law.

Guideline 16: Women as research subjects

Investigators, sponsors or ethical review committees should not exclude women of reproductive age from biomedical research.

The potential for becoming pregnant during study should not be used as reason for limiting participation.

The sponsors or investigators should guarantee the prospective subject a pregnancy test and access to effective contraceptive methods before the research commences.

Where such an access is not possible for legal or religious reasons investigators should not recruit.

Guideline 17: Pregnant women as research participant

Pregnant women should be presumed to eligible for participation in biomedical research.

Investigators and ethical review committees should ensure that prospective subjects who are pregnant are adequately informed about the risk and benefits to themselves, their pregnancy, the foetus and their subsequent offspring, and to their fertility.

Research in this population should be performed only if it is relevant to particular health needs of a pregnant woman or her foetus. And if it is supported by reliable evidence from animal experiments, particularly as to risks of teratogenicity and mutagenicity.

Guideline 18: Safeguarding confidentiality

The investigators must establish secure safeguards of confidentiality of subject's research data. Subjects should be told the limits, legal or other to the investigator's ability to safeguard.

Guideline 19: right of injured subjects to treatment and compensation

Investigators should ensure that research subjects who suffer injury as a result of their participation are entitled to free medical treatment for such injury and to such financial or other assistance as would compensate them equitably for any resultant impairment, disability and handicap.

In case of death as a result of their participation their dependants are entitled to compensation. Subjects must not be asking to waive the right to compensation.

Guideline 20: Strengthening the capacity for

ethical and scientific review and biomedical research:

Many countries lack the capacity to asses or ensure the scientific quality or ethical acceptability of biomedical research carried out in their jurisdiction.

- In externally sponsored collaborative research, sponsors and investigators have an ethical obligation to ensure that biomedical research projects for which they are responsible in each 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 obligation of external sponsors to provide health-care services:

External sponsors are ethically obligated to ensure the availability of:

Health care services that are essential to ...

the safe conduct of the research; treatment for subjects who suffering injury as a consequence of research interventions; and beneficial intervention or product developed as a result of the research reasonably available to the population or community concerned.