Ethics in medical research: part 1 introduction

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Research

- Research is the *systematic collection, analysis* and *interpretation of data* to answer a certain question or solve a problem

How to Minimize Risks to Research Participants:

- Studies that require IRB approval:

a. Data from living individuals

b. Biological material from living individuals

c. Interaction or intervention with a living individual

d. Use of a non-approved, drug, device or biological

Clinical Trials Phases (0-IV)

- Each of these types of study requires the appropriate design to reach scientifically sound conclusions while protecting the participants and their identifiable human information.

Ethical Design In Clinical Research

Although this may be morally obvious, it's also important practically because of the huge investments in money, effort, and personal risk and discomfort that the sponsor, investigators and the participants make.

Ethical Design In Clinical Research

- Poorly designed and executed studies are frequently reported and can even influence practice and policy development.

- Among elements that make for poor and therefore unethical science are:

1. Excessive risks compared to benefits
2. Inadequate power
3. Inappropriate allocation of dosages in comparison trials
4. Poor selection and misallocation of participants
5. Midstream changes of protocol
6. Failure to either monitor or record significant adverse events.

Data Analysis

- An important part of research integrity is the analysis of data.
- It's critical to recognize the importance of appropriate statistical analysis.
- Statistical approaches should be developed as part of the study design.
- If possible, hypotheses should be well defined in advance.

- Current statistical packages permit the mining of entire databases to identify statistically significant results that were not anticipated.
- No statistically significant different is an important result and must be published

Efficacy Versus Safety

- Efficacy: maximum response achievable from an applied or dosed agent
- In therapeutic studies, both efficacy of the interventions and their safety are generally studied simultaneously but the design may focus on one or the other.

Appropriate Risk to Benefit Ratio

- Risk is defined as the probability of physical, psychological, social, or economic harm occurring as a result of participation in a research study.
- Both the probability and magnitude of possible harm in human research may vary from minimal to considerable.

Minimal Harm

- Minimal harm is defined as:

  "that the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests".

Moderate and Maximal Risk

- Risk above this standard is more than minimal (moderate, maximal) and that imposes limitations on the conduct of the research and increases the requirements for monitoring.
- It also requires more stringent approval processes when studying children or otherwise vulnerable populations.
- Increased risk should be accompanied by the probability of appropriately increased benefits.

Benefits

- Benefit applies to the potential of the research treatment to ameliorate a condition or treat a disease.
- This can apply to an individual participant or to a population.
- In research as in clinical medicine, results cannot be guaranteed but, as a consequence of prior work, a benefit may appear to be a reasonable expectation.
- Since this is research, an advantage for the treatment groups cannot be presupposed.
- Since the risks have not been fully evaluated, a statement of individual benefit should be made most cautiously if at all.
- The investigator should always distinguish between research and treatment and never lure the patient into participating in hopes of remission or cure.

Risk Versus Benefit Ratio

- A main role of IRBs is to determine the risk versus benefit ratio for clinical studies.
- They must make sure that the physical risk is not disproportionate to the benefits.
- When the physical risk is minimal they must determine that psychological and social risks such as stigma are not important.
- It is not ethical to conduct a study in which an individual or a group is labeled so as to be stigmatized or to be made less employable or insurable.

Controls

- Controls are research participants who receive an inactive treatment or stay on standard treatment
- In most trials they are selected by computer lottery from the group of eligible candidates with the condition under study.

Normal Controls

- Normal Controls are research participants who do not have the condition under study.
- Those taking current treatment according to updated clinical guidelines

Historical Controls

- Historical controls are subjects from prior studies or observational investigations whose data are compared with those of the current participants.
- Historical controls were used for years in clinical research and are still sometimes employed because they do not require additional data collection and risk.
- They often produce biases because the research population rarely duplicates the historical population.

Blinding

- Blinding refers to a process whereby the participant does not know whether he/she is receiving an active agent or a similar appearing inactive substance or mock procedure.
- Blinding is also used in research to refer to investigators who analyze components of a study without knowing the identity and treatment of the participant.

Double Blinding

- Double blinding is a process whereby neither the investigator nor the participant knows which agent the participant is receiving.
- Usually the research pharmacy holds the master list in case there are complications.
- Triple blinding: blind the statistician

When Blinding is Impossible

- Sometimes the effects of the agent in question are so obvious that true blinding is impossible.
- For example: open versus laparoscopic cholecystectomy

Use of Placebos

- A placebo is an inactive version of a treatment identical in appearance to the real thing.

Standard of Care:

- This term applies to the expected care in the medical community as a whole.
- Often, standard of care can be defined on the basis of practice guidelines, which are being developed by all medical specialties, element by element.
- The issue of standard of care becomes problematic when a study is to be performed in a developing country where it is impossible to provide medical care at anywhere near the level available in the developed world.
- The current expectation is that controls will be treated at the level of the Western standard of care, not the indigenous standard.

B. Selection of Subject Populations

- Selection of the appropriate participant population plays a critical role in the experimental design.
- They must be selected and dealt with on the basis of the three principles of Human Research, Autonomy, Beneficence and Justice.

Protection of Research Participants Who and What?

Who should be involved?

- Individuals involved in the design and/or conduct of human subjects research.

What is the purpose?

- Preparation of investigators involved in the design and/or conduct of research involving human subjects to understand their obligations to protect the rights and welfare of subjects in research.

Autonomy

- Autonomy is understood to mean that becoming a research subject is a totally voluntary act.
- Individuals must be solicited without coercion or even implied coercion.
- Individuals must be fully informed and understand what they are signing up for.
- IRBs require that the prospective participants understand a long list of things before they can sign a consent document.

Autonomy

- If the study requires a vulnerable population to be studied, (children, cognitively impaired) then a surrogate who, presumably, has their best interests at heart (parent for child, relative for the patient with Alzheimer's disease) must sign for the participant.

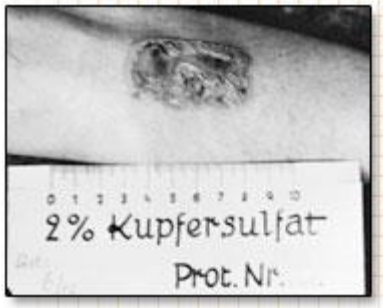
- Individuals under the age of 18 are given special protections; so many studies pertain to adults only.
- The rule of autonomy requires that individuals are able to provide informed consent.

Goals and Principles of Human Subjects Protection

- Human subjects are essential to the conduct of research intended to improve human health. As such, the relationship between investigators and human subjects is critical and should be based on **honesty**, **trust**, and **respect.**

Historical Events
Nazi Medical War Crimes (1939–1945)

- The experiments conducted by Nazi physicians during World War II were unprecedented in their scope and the degree of harm and suffering.
- “Medical experiments” were performed on thousands of camp prisoners and included deadly studies and tortures such as injecting people with gasoline and live viruses, and forcing people to ingest poisons.
- In December 1946, the War Crimes Tribunal at Nuremberg indicted 20 physicians and 3 administrators because they had:corrupted the ethics of the medical and scientific professions and repeatedly and deliberately violated the rights of the subjects



Historical Events
The Nuremburg Code

- In the August 1947 the judges included a section called **Permissible Medical Experiments**.
- This section became known as the Nuremberg Code and was the first international code of research ethics.
- This set of directives established the basic principles that must be observed in order to satisfy moral, ethical, and legal concepts in the conduct of human subject research.

The Nuremburg Code
TEN Directives for Human Experimentation:

1. Voluntary consent of the human subject is absolutely essential

2. The experiment must yield generalizable knowledge that could not be obtained in any other way and is not random and unnecessary in nature

3. Animal experimentation should precede human experimentation

4. All unnecessary physical and mental suffering and injury should be avoided

5. No experiment should be conducted if there is reason to believe that death or disabling injury will occur

The Nuremburg Code (Cont.)
TEN Directives for Human Experimentation:

6. The degree of risk to subjects should never exceed the humanitarian importance of the problem

7. Risks to the subjects should be minimized through proper preparations

8. Experiments should only be conducted by scientifically qualified investigators

9. Subjects should always be at liberty to withdraw from experiments

10. Investigators must be ready to end the experiment at any stage if there is cause to believe that continuing the experiment is likely to result in injury, disability or death to the subject

1. Respect for Persons

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- The principle of respect for persons can be broken down into two basic ideas:

1. Individuals should be treated as autonomous agents

- An autonomous person is able to:
  - Consider the potential harms and benefits of a situation.
  - Analyze how those risks and potential benefits relate to his or her personal goals and values.
  - Take action based on that analysis.

1. Respect for Persons (Cont.)

2. Persons with diminished autonomy are entitled to additional protections

- "Special provisions may need to be made when an individual's comprehension is severely limited or when a class of research participants is considered incapable of informed decision making (e.g. children, people with severe developmental disorders, or individuals suffering from dementias).
- In some cases, respect for persons may require seeking the permission of other parties, such as a parent or legal guardian."

Coercion

"Influencing an individual decision about whether or not to do something by using explicit or implied threats (loss of good standing in job, poor grades, etc.)"

Undue Influence

"An offer of an excessive, unwarranted, inappropriate, or improper reward or other overture in order to obtain compliance" "excessive compensation"

- Undue inducements are troublesome because:
  - offers that are too attractive may blind prospective subjects to the risks or impair their ability to exercise proper judgment; and
  - they may prompt subjects to lie or conceal information that, if known, would disqualify them from enrolling — or continuing — as participants in a research project ".

Undue Influence versus Compensation

- Some types of research involve a significant commitment from research participants in terms of time or effort, and investigators may wish to provide compensation .
- Institutions should consider establishing standards for fair and appropriate compensation .
- Compensation is meant to reimburse research participants for their time, research-related inconveniences and/or research-related discomforts
- Compensation **is not** a benefit of the research.

Informed Consent

- Definition: A legally-effective, voluntary agreement that is given by a prospective research participant following comprehension and consideration of all relevant information pertinent to the decision to participate in a study.

- The HHS regulations require that investigators obtain legally effective informed consent from prospective participants in a way that allows them to consider whether or not to participate and that minimizes the possibility for coercion or Undue influence.

Voluntariness

- Individuals' decisions about participation in research should not be influenced by anyone involved in conducting the research: "...consent must be freely given or truly voluntary."

Comprehension

- Individuals must have the mental or decisional capacity to understand the information presented to them in order to make an informed decision about participation in research.

Disclosure

- Researchers must disclose:

1. **The purpose of the study**
2. **Any reasonably foreseeable risks to the individual**
3. **Potential benefits to the individual or others**
4. **Alternatives to the research protocol**
5. **The extent of confidentiality protections for the individual**
6. **Compensation in case of injury due to the protocol**
7. **Contact information for questions regarding the study, participants' rights, and in case of injury**
8. **The conditions of participation, including right to refuse or withdraw without penalty**

- This disclosure must be made in such a way that it provides a *reasonable person* the information she or he would need in order to make an informed decision.

Participation of Pregnant Women in Research

- It is essential to prohibit:
  - Inducements of any kind to terminate a pregnancy.
  - Investigators from taking part in decisions about terminating a pregnancy.
  - Investigators from determining the viability of a neonate.

Children's Participation in Research

- Children may not have full capacity to make decisions in their own best interests; and therefore :
  - Children are considered a vulnerable population, and
  - Children are unable to provide "legally effective informed consent "

- Because children cannot provide informed consent, children provide assent* to participate in research, to the extent that they are able, and parents/guardians give permission for a child to participate in research .

* Assent: affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent."

Excluding Children From Research

- The NIH Policy and Guidelines on the Inclusion of Children in Research states that children must be included in all NIH-supported human subjects research unless "… there are scientific and ethical reasons not to include them ".

Obtaining Informed Consent From Prisoners

- Requirements specific to informed consent for prisoners are:
- Not to be under constraints as a result of their incarceration that could affect their ability to make a truly voluntary decision about whether or not to participate in research.
- Adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole

2. Beneficence

2. Beneficence

Two general rules have been articulated as complementary expressions of beneficent actions:

- Do no harm.
- Maximize possible benefits and minimize possible harms.

The challenge inherent in applying the **Belmont principle of beneficence** is how to determine when potential benefits outweigh considerations of risks and vice versa.

Privacy and Confidentiality

Investigators are responsible for

- Protecting privacy of individuals.
- Confidentiality of data .
  - *Privacy* means being “free from unsanctioned intrusion”.
  - *Confidentiality* means holding secret all information relating to an individual, unless the individual gives consent permitting disclosure.

Coded Private Information and Human Subjects Research

- Research with coded private information or specimens does not involve human subjects if:
  - The private information or specimens were not collected specifically for the currently proposed research project through an interaction or intervention with living individuals; and
  - The investigator(s) cannot readily ascertain the identity of the individual(s) to whom the coded private information or specimens

Case Study: Research With Anonymized Data

- You are an investigator proposing to use data from a colleague's database to conduct secondary analyses. Your colleague will provide coded data for your proposed studies, and you and he enter into an agreement by which he will keep the key to the code and will have no other involvement in the research.

- Does this study involve human subjects?
- Yes, this study involves human subjects .
- No, this study does not involve human subje

Anticipated Benefits Greater than Potential Harms

- Research requires that:
  - Risks are minimized
  - Unavoidable risks are justified as necessary for sound scientific design
  - Research studies are anticipated to make progress toward important, generalizable knowledge

Institutional Review Boards(IRB)

- IRBs determine:
  - “the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice ”

3. Justice

3. Justice

- Justice requires that individuals and groups be treated fairly and equitably in terms of bearing the burdens and receiving the benefits of research.

- The principle of justice may arise in decisions about inclusion and exclusion criteria for participation in research and requires investigators to question whether groups are considered for inclusion simply because of their availability, their compromised position, or their vulnerability — rather than for reasons directly related to the problem being studied .

Justice

- Justice relates to access to research of all relevant populations specifically including age, ethnicity, gender and preexisting conditions.

- Several countries have made it clear that studies should try to include ethnic groups and women in proportion to the population in the community unless there is a good scientific reason not to (for example studying hypertension in African Americans).
- Issues that must be considered in justice determinations include:
  - Socioeconomic Status
  - Gender,
  - Race,
  - Age,
  - Existing medical conditions
  - Vulnerable populations (as noted above)
  - Determining ability to consent
  - Ensuring understanding of protocol
  - Appropriate surrogate for consent
  - Coercive nature of relationship (prisoners)
- The need to use such populations must be justified

Equity vs. Equality in Human Subjects Research

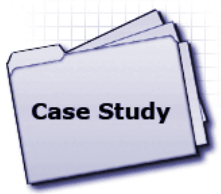
- The meanings of “equity” and “equality” are similar, but not the same.
  - To treat“ **equitably** ”means to treat fairly;
  - To treat“ **equally** ”means to treat in exactly the same way.

Case Study: Migraine Intervention Trial

- A researcher seeks to improve treatment for severe migraines that are partially responsive to oral medication. He proposes to test whether acupuncture, in addition to a sufferer's oral medication, is more effective treatment than oral medication alone. Because women are three times more likely to experience migraines than men ,he proposes to enroll three times as many women as men. They will be recruited from racially and ethnically diverse communities .

- **Does this study design fulfill the principle of justice?**

- **Yes, this study design does fulfill the principle of justice**
- **No, this study design does not fulfill the principle of justice**



Yes, this Study Design Does Fulfill the Principle of Justice

Correct!

Stratification in sampling

- The research includes women and men in proportion to the rates of severe migraines experienced by each sex, and is designed to have racial and ethnic diversity.
- The study provides both sexes and racial/ethnic communities with the opportunity for benefits from the clinical trials ,and does not unfairly burden any single group with the risks of research. Its design is fair .

Justice and the Use of Placebos

- A researcher's duty is not to exploit or deceive* research participants and to treat them fairly.

- The informed consent process must disclose sufficient information to ensure that potential research participants:
  - Understand what placebos are
  - Understand the likelihood that they will receive a placebo
  - Are able to provide their fully informed consent that they are willing to receive a placebo

*Misleading research participants about the research purpose or procedures

Review

Investigators should allow Individuals to make their own decisions

Investigators should design research studies as to maximize benefit and minimize risk to individuals

Individuals who are less able to take decisions for themselves require additional protection

The burdens and benefits of research should be fairly distributed among individuals and society

Justice

Respect

Beneficence

Research Ethics and Good Clinical practice: Part 2

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After WW2, in October 1946, the *Nuremberg Medical Trial* began, lasting until August of 1947. Twenty-three German physicians and scientists were accused of performing cruel and lethal medical experiments on concentration camp inmates and other living humans between 1933 and 1945.

Fifteen defendants were found guilty, and eight were acquitted. Of the 15, seven were executed and eight were imprisoned.

1947 The Nuremberg Code

The voluntary consent of the human subject is absolutely essential. This means that the person involved should have legal capacity to give consent; should be so situated as to be able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, over-reaching, or other ulterior form of constraint or coercion; and should have sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision.

1947 The Nuremberg Code

- The duty and responsibility for ascertaining the quality of the consent rests upon each individual who initiates, directs or engages in the experiment. It is a personal duty and responsibility which may not be delegated to another with impunity.

- The experiment should be such as to yield fruitful results for the good of society, unprocurable by other methods or means of study, and not random and unnecessary in nature.

1964 Declaration of Helsinki (Finland)

"*In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject*."

Why is Research Ethics Important?

- It is a reflection of respect for those who ‘take part’ in research
- It ensures no unreasonable, unsafe or thoughtless demands are made by researchers
- It ensures sufficient knowledge is shared by all concerned
- It imposes a common standard in all the above respects

Why is Research Ethics Important

- It has become the norm as an expectation for research activity
- …. a professional requirement for practitioners in some disciplines e.g. psychology
- … a requirement for access to participants in others e.g. health
- … and a requirement to comply with external REF's to obtain funding e.g. ESRC

The six key principles:

1. Research should be designed, reviewed and undertaken to ensure integrity, quality and transparency.

2. Research staff and participants must normally be informed fully about the purpose, methods and intended possible uses of the research, what their participation in the research entails and what risks, if any, are involved. Some variation is allowed in very specific research contexts.

3. The confidentiality of information supplied by research participants and the anonymity of respondents must be respected.

The six key principles:

4. Research participants must take part voluntarily, free from any coercion.

5. Harm to research participants must be avoided in all instances.

6. The independence of research must be clear, and any conflicts of interest or partiality must be explicit.

BPS Code of Human Research Ethics
By the British Psychological Society

- Respect for the Autonomy and Dignity of Persons
- Scientific Value
- Social Responsibility
- Maximising Benefit and Minimising Harm

BPS Code of Human Research Ethics

- Respect for the Autonomy and Dignity of Persons

Adherence to the concept of moral rights is an essential component of respect for the dignity of persons. Rights to privacy, self-determination, personal liberty and natural justice are of particular importance to psychologists, and they have a responsibility to protect and promote these rights in their research activities. As such, psychologists have a responsibility to develop and follow procedures for valid consent, confidentiality, anonymity, fair treatment and due process that are consistent with those rights.

BPS Code of Human Research Ethics

- Scientific Value

Research should be designed, reviewed and conducted in a way that ensures its quality, integrity and contribution to the development of knowledge and understanding. Research that is judged within a research community to be poorly designed or conducted wastes resources and devalues the contribution of the participants. At worst it can lead to misleading information being promulgated and can have the potential to cause harm.

BPS Code of Human Research Ethics

- Social Responsibility

The discipline of psychology, both as a science and a profession, exists within the context of human society. Accordingly, a shared collective duty for the welfare of human and non-human beings, both within the societies in which psychology researchers live and work, and beyond them, must be acknowledged by those conducting the research.

BPS Code of Human Research Ethics

- Maximising Benefit and Minimising Harm

… psychologists should consider all research from the standpoint of the research participants, with the aim of avoiding potential risks to psychological well-being, mental health, personal values, or dignity.

Research risks and harm, benefits and goods, and constituencies

Risks and harm

- physical trauma/injury?
- distress?
- offence?
- breach of confidentiality?
- inconvenience?
- coercion?
- waste of time?
- waste of resources / funds?
- disrepute or litigation?
- failure to publish

Benefits and goods

- research as intrinsic good?
- contribution to knowledge?
- development of theories?
- improvements to lives?
- training researchers?
- career advancement?
- enhancing reputation/image?
- increasing commercial success?
- entertainment and enjoyment?

Constituencies

- participants
- researchers
- institutions
- sponsors / funding bodies
- society

Institutional Review Board (IRB)

- Also known as an *Independent Ethics Committee (IEC)* or *Ethical Review Board (ERB)* is a committee that has been formally designated to approve, monitor, and review biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the research subjects .

Structure of Ethics Committees

1. Chair: Preferably from outside the Institution
2. Member secretary: from the same organization or institute
3. 1-2 Clinicians from various specialties
4. 1-2 Basic medical Scientists
5. One legal expert or retired judge
6. One social scientist or representative of voluntary agency
7. One philosopher/ethicist
8. One lay person
9. According to the application, subject experts could be invited to offer views

- The IRB must have at least five members.
- The members must have enough experience, expertise, and diversity
- If the IRB works with studies that include vulnerable populations, the IRB should have members who are familiar with these groups.

- The IRB should include both men and women.
- The members of the IRB must not be all of the same profession.
- The IRB must include at least one scientist and at least one non-scientist. These terms are not defined in the regulations.

- The IRB must include at least one person who is not affiliated with the institution or in the immediate family of a person affiliated with the institution. These are commonly called "Community Members".
- IRB members may not vote on their own projects.
- The IRB may include consultants in their discussions to meet requirements for expertise or diversity, but only actual IRB members may vote.

Responsibilities of IRB

- Risks to study participants are minimized
- Risks are reasonable in relation to anticipated benefits
- Selection of study participants is equitable
- Informed consent is obtained and appropriately documented for each participant
- Adequate provisions for monitoring data collection to ensure safety of the study participants
- Participant privacy and confidentiality is protected

The IRB/IEC should obtain the following documents

- Trial protocol(s)/amendment(s),
- Written informed consent form(s)
- Consent form updates that the investigator proposes for use in the trial
- subject recruitment procedures (e.g., advertisements), written information to be provided to subjects, Investigator's Brochure (IB),

- Available safety information,
- Information about payments and compensation available to subjects, the investigator's current curriculum vitae and/or other documentation evidencing qualifications,
- Any other documents that the IRB/IEC may need to fulfill its responsibilities.

What Projects Need Ethical Approval?

- Human participants
- Use of the ‘products’ of human participants
- Animal participants
- Work that potentially impacts on human participants

- *Where ethical approval is deemed unnecessary a disclaimer may be signed by researcher (and supervisor)*

Key Ethical Issues

- Informed Consent – special consideration for minors
- Deception
- Need for debriefing
- Right to withdraw
- Confidentiality
- Safety and risk

What Else Does the Panel Need to Know?

- Summary of background to and rationale for proposal
- Nature of data to be collected
- Procedures and measuring tools/equipment
- Who are the participants?
- Where will data collection occur?
- How will data be stored and for how long?

Full Procedure

- Complete Full Approval form
- Attach consent form, information sheet and additional material e.g. questionnaires
- Students must get form checked & signed by supervisor
- Submit to appropriate Ethics Panel – where Sub-Panels exist, staff and PG researchers must still submit to Faculty Panel
- DATA COLLECTION MUST NOT START UNTIL PANEL INFORMS

Outcomes of First Application

- Approved – must begin within the timescale indicated
- Approved subject to amendments – supervisor confirms with Chair of FEP
- Deferred
- Not Approved – major revisions and resubmit

Additional Issues

- Changes to original proposal must be notified
- Completion of project must be notified
- Adverse events must be notified
- Some applications will require evidence of risk assessment
- Some applications will require evidence of Police Clearance

What Is GCP?

Good Clinical Practice (GCP) is defined as 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 and accurate, and that the rights, integrity and confidentiality of trial subjects are rotected’

Good Clinical Practice Guidelines

- Are mainly focused on the protection of human rights in clinical trial.
- Provide assurance of the safety of the newly developed compounds.
- Provide standards on how clinical trials should be conducted.
- Define the roles and responsibilities of clinical sponsors, clinical research investigators, Clinical Research Associates, and monitors.

Good Clinical Practice Guidelines

- GCPs are generally accepted, international best practices for conducting clinical trials and device studies
  - They are defined as an international ethical and scientific standard for designing, conducting, recording and reporting trials that involve the participation of human subjects
  - Compliance with GCPs provide public assurance that the rights and safety of participants in human subject research are protected and that the data that arises from the study is credible

Under GCP, the FDA Requires That People be Informed:

- The study involves research of an unproven drug, the purpose of the research
- How long the participant will be expected to participate in the study
- What will happen in the study
- Possible risks/benefits to the participant
- Participation is voluntary and that participants can quit the study at any time without penalty or loss of benefits to which they are otherwise entitled.

The Core of the Consolidated GCP Guidance

1. Clinical trials should be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with GCP and the applicable regulatory requirements

2. Before a trial is initiated, foreseeable risks and inconveniences should be weighed against the anticipated benefit for the individual trial subject and society. A trial should be initiated and continued only if the anticipated benefits justify the risks

The Core of the Consolidated GCP Guidance

3. The rights, safety, and well-being of the trial subjects are the most important considerations and should prevail over interests of science and society

4. The available non clinical and clinical information on an investigational product should be adequate to support the proposed clinical trial

5. Clinical trials should be scientifically sound, and described in a clear, detailed protocol

The Core of the Consolidated GCP Guidance

6. A trial should be conducted in compliance with the protocol that has received prior institutional review board (IRB)/independent ethics committee (IEC) approval/favorable opinion

7. The medical care given to, and medical decisions made on behalf of, subjects should always be the responsibility of a qualified physician or, when appropriate, of a qualified dentist

Thirteen principles of GCP Guidance

8. Each individual involved in conducting a trial should be qualified by education, training, and experience to perform his or her respective tasks

9. Freely given informed consent should be obtained from every subject prior to clinical trial participation

Thirteen principles of GCP Guidance

10. All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation, and verification

11. The confidentiality of records that could identify subjects should be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirements

Thirteen principles of GCP Guidance

12. Investigational products should be manufactured, handled, and stored in accordance with applicable good manufacturing practice (GMP). They should be used in accordance with the approved protocol

13. Systems with procedures that assure the quality of every aspect of the trial should be implemented