Good Clinical Practice (GCP) in Clinical Trial – Roles & Responsibilities

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Learning objectives

- What are the Roles & Responsibilities of –
  - Sponsor
  - Investigator
  - Institutional Ethics Committee in Clinical Trial

Clinical Trial (CT)

- **Clinical Trials (CT)** are **research investigations** in **diseased person/volunteer/subject** to test new treatments, interventions or tests as a means to prevent, detect, treat or manage various diseases or medical conditions.

- The **World Health Organization (WHO)** defines a clinical trial as-**'any research study that prospectively assigns human participants or groups of humans to one or more health-related interventions to evaluate the effects on health outcomes'.**

- **Clinical Trial (CT)** helps to determine if a new drug / treatment / intervention works - whether it is safe, and whether it is better than the drug / treatment / interventions that are already available.

Core Concepts of Clinical Trial

- Involve Human subjects
- Move forward with time
- Include – Randomization, Blinding concepts
- Use of Standard/Controlled group
- Test a certain hypothesis
- Must have method to measure Intervention & Outcome

Core Concepts of Clinical Trial

- Focus on **unknown effects of medication**, **effect of devices**, **effects of adverse reaction**, etc. before medication became part of standard of care

Current scenario….

- CT increased in numbers and importance, more studies, more sites, greater number of participants at each site, expansion of clinical investigator pool, new players in new roles (CROs, SMOs) & new technologies (electronic CRF, e-diary, e-medical notes)

- **Large studies conducted globally with *differences in***
- Cultures and practices/Emerging regulations/Research standards

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Familiarity of investigators and site staff with regularity (e.g. DCGI/FDA) structure and practice

Times of India

25th August 2012

- **Drugs getting approval without clinical trials**

- Drugs continue to be approved in India without having undergone proper clinical trials on the local population.

- **Union health minister Ghulam Nabi Azad said……** Central Drugs Standard Control Organization (CDSCO) — approved **33 new drugs** between **January, 2008 and October, 2010** without testing them through trials on Indian patients

- Between January and July 2012, the CDSCO has approved 14 new drug molecules of which only nine have undergone clinical trials.
- In 2011, 41 new drugs were approved by the CDSCO of which only 38 had undergone clinical trials.
- In 2010, 65 such molecules were approved of which 52 had undergone trials.
- In 2009, 72 new molecules were approved of which as many as 12 had not undergone clinical trials.

- The **standing committee on health** reported that - **On an average, Drug Controller General of India (DCGI) was approving one drug every month without trials.**

- **As many as 2,282 trials have been approved by the DCGI between 2005 and 2010.**

- As per the Union health ministry's status note, a total of **1,514 subjects have died** in the years 2008 to 2010 during clinical trials.

PATH study

- In 2009, **PATH** (**Programme for Appropriate Technology in Health**), a **US-based health charity(NGO)**, launched a project funded by the Bill and Melinda Gates Foundation to study the cost and feasibility of incorporating HPV vaccines, produced by Merck and GlaxoSmithKline, into India's public sector immunization programme.
- This Study - recruited hundreds of tribal girls without parental consent for an immunization
- Warden of government hostel provided permission
- Several girls subsequently died
- Later, the study was halted by the authorities

- **In the complex global scenario of clinical trial environment, it is important to ensure quality.**
- So, it is a must that CT should comply with standard.
- Therefore, compliance of ICH-GCP is important.

- **Who will ensure GCP Compliance?**
- **How is quality ensured?**
- **How is quality ensured on a *constant and* continuous basis?**

Good Clinical Practice (GCP)

- International **ethical and scientific standard**, **a Guideline,** related with conduction of **biomedical and behavioral research**, in research involving **human participants,** mainly Clinical Trial.

- Ensures the protection of **rights, safety, well-being, and confidentiality of the participants**

- GCP ensures the **accuracy** and **credibility** of data collected in clinical trials, as well as the reported results.

- **GCP is not specific to a protocol, but rather is general guideline and applicable to all protocols.**

Objectives of GCP

- **Protecting Research Subjects**, i.e.,
  - **Subject safety**
  - **Rights of subjects (research ethics)**
- **Ensuring the quality and integrity of research data**
- **Assuring the existence and operation of "quality systems"**

GCP stakeholders

- **Sponsor**
- **Investigator**
- **Clinical trial subjects or legal guardians**
- **Institutional Ethics committee**
- Site staffs
- **Regulatory authority**
- Data Safety Monitoring Board (DSMB)
- Contract Research Organization (CRO)
- Site Management Organization (SMO)

Role & Responsibilities of Sponsor

Who is a Sponsor

- An **individual, a company, an institution** or **an organization** which takes responsibility for the **initiation, management and/or financing** of a clinical trial is known as the sponsor.

- Sponsor may transfer any or all clinical trial-related activities to a scientific body (commercial, academic, or other), or to a contract research organization (CRO).

- **If the investigator initiates and takes full responsibility for a trial, the investigator then assumes the role of the sponsor.**

Role & Responsibilities of Sponsor

- "The sponsor is **responsible for implementing** and **maintaining quality assurance** and **quality control systems** with **written SOPs** to ensure that trials are conducted and data generated, documented and reported **in compliance with the protocol, GCP and the applicable regulatory requirements."**

Role of Sponsor

- **Submission of application** for authorization of a CT in accordance with the regulations and guidelines
- **Information and material** contained in, or referenced by, the application for a CT are **complete and accurate** and are not false or misleading
- Trial will not commence until the permission/authorization is received
- **Protocol** finalization
- **Protocol amendments are authorized by the Regulator & Ethics Committee prior to implementation**

- Before initiating the trial, the sponsors should evaluate whether-
- The **investigator is Educated / Experienced / Trained / Knowledgeable to conduct the trial**

- Other important factors like –
- **Time of the Investigator**
- **Space / Equipment / Laboratory facilities / Study team / Other facility available in a specific site**

- Sponsor should assess the **recruiting potential of the investigator** & **site** by checking the previous patient records

Sponsor should evaluate-

- Existence of a **Registered Ethics Committee (by DCGI/or Others)**
- To prepare **Investigator's brochure (IB),** which contains both clinical and non-clinical data pertaining to the new drug
- **Should provide- The Protocol/Case Record Form/Informed Consent Form/Other Study related materials**

Sponsor should monitor

- **Site activities**
- **Audit** as appropriate, to ensure conduct of the trial continues to meet GCP, the protocol, and regulations

Role of Sponsor

- **To manage Trial related injury to the subject/volunteer/patient**

- Any **Serious Adverse Events (SAE)** that can be defined associated with **death, admission to hospital, prolongation of hospital stay, persistent or significant disability or incapacity, or is otherwise life-threatening** in connection with a clinical trial needs to be reported within set timelines.

Sponsor-

- The **sponsor has to pay the compensation in case of clinical trial related injury** or **death** within thirty days of the receipt of order from Licensing Authority.

- **In case the sponsor fails to provide medical management and / or financial compensation**, the Licensing Authority may take necessary action as per rule, including **suspension or cancellation of the clinical trial and/or restrict sponsor including his representative(s) to conduct any further clinical trials in India.**

- Sponsor can discontinue the Clinical Research prematurely

- Role & Responsibilities of Investigator

Investigator's responsibilities

- Investigators are **In-charge of actually conducting the study** and are **accountable for conduct of the study** at a site by **personally supervising the investigations**.
- All trial investigators should possess **appropriate qualifications, training and experience**
- **Investigator should conduct the research work following the approved Protocol**

Investigator's responsibilities

- Prior to the trial, the **investigator(s) and the sponsor should establish an agreement on the protocol, SOP, the monitoring, and auditing** of the trial, and **the allocation of trial-related responsibilities.**

- **Investigator needs to obtain approval from Institutional ethics committee, facilitate review, inspections and reporting**.

Investigator's responsibilities

- An **informed consent** from **each participant is a mandatory prerequisite** for a clinical trial.
- **Any violation of the informed consent process will be dealt with as a serious lapse on the part of the Investigators,** for which the Investigator can be debarred from clinical trials.
- **Any SAE needs to be reported according to fixed timelines by the investigator.**

- Any **amendment to the original research protocol** or **unanticipated problems** involving risks to subjects has to be done only after **approval from the ethics committee.**

- The **investigator need to follow the protocol meticulously**, ensure that **all persons** assisting in the **study are informed of obligations and train** them, impart information to the patients, ensure **maintenance of accurate records.**

Role & Responsibilities of Institutional Ethics Committee (IEC)

What is ethics?

A branch of philosophy which is the systematic study of reflective choice (decision problems), of the standards of right and wrong (moral principles) by which it is to be guided, and of the good or bad (consequences) toward which it may ultimately be directed

An ethical problem occurs when a person mak
a choice among alternative actions
& the right choice is not absolutely clear

Often that choice affects the well-being of oth
persons

- Ethics may be defined as a method, procedure, or perspective for deciding how to act and for analyzing complex problems and issues
- While a medical practitioner will evaluate ethics on the basis of health, disease, survival, etc, an economist will examine the cost and benefits, a social worker will evaluate ethics in respect to impact on the society and principles at stake

Bioethics is a way of understanding and examining **what is "right" and what is "wrong" in biomedical research and practice**

Institutional Ethics Committee (IEC)

- **Institutional Ethics Committee (IEC) is a committee comprising of experts to lay person, formed by law**
- It is **mandatory by "Law"**,(**ICMR Ethical Guidelines for Biomedical Research On Human Participants**) that **all proposals** on **biomedical research** involving **human participants** should be cleared by an appropriate **"Institutional Ethics Committee (IEC)"**

Institutional Ethics Committee (IEC)

- The mandate of the IECs will be to review all research projects involving human subjects to be conducted at the Institute, irrespective of the funding agency
- Safeguard the welfare and the rights of the participants is the main objective of IEC
- The role of IEC can be modified according to the requirement of each Institute

Institutional Ethics Committee (IEC)

- Members should be a mix of **medical / non-medical**, **scientific and non-scientific** persons including **legal person, lay public** to reflect the differed viewpoints

- The IEC is entrusted not only with the initial **review of the proposed research protocols prior to initiation of the projects** but also have a continuing **responsibility of regular monitoring of the approved programmes** to foresee the compliance of the ethics during the period of the project.

Institutional Ethics Committee (IEC)

- **IECs should be multidisciplinary and multisectorial in composition**
- **It is a committee comprising of experts, non experts**
- **Independence** and **competence** are the two hallmarks of an IEC

Objectives of IEC

- The objective of Institutional Ethics Committee (IEC) is to **ensure quality and consistent ethical review mechanism for health and biomedical research**

- **Following standard guidelines**

Role of IEC

- IEC will **review and approve** all types of research proposals **involving human participants** with a view to safeguard the **dignity, rights, safety and well being** of all **actual and potential research participants**.

Role of IEC

- The goals of research, however important, should never be permitted to override the health and well being of the research subjects.

- The IEC will ensure principles of research ethics -
- Autonomy
- Beneficence
- Non maleficence
- Justice

IEC will ensure-

- Risk benefit ratio
- Planning, conduct and reporting of the proposed / ongoing research
- Informed consent process
- Provisions for appropriate compensations

Composition of IEC

The composition may be as follows-

- 1.**Chairperson**
- 2.**2 Basic medical scientists**
- 3.**2 Clinicians from various Institutes**
- 4.**One legal expert or retired judge**
- 5.**One social scientist / representative of nongovernmental voluntary agency**
- 6.**One philosopher / ethicist / theologian**
- 7.**One lay person from the community**
- 8.**Member Secretary**

IEC

- **IEC may call upon subject experts as independent consultants who may provide special review of selected research protocols, if needed**
- These experts may be specialists in ethical or legal aspects, specific diseases or methodologies, or represent specific communities, patient groups or special interest groups e.g. Cancer patients, HIV/AIDS positive persons or ethnic minorities
- They are required to give their **specialized views** but do not take part in the decision making process which will be made by the members of the IEC

IEC

- The meeting of the IEC should be held on scheduled intervals as prescribed and additional meetings may be held as and when the proposals are received for review

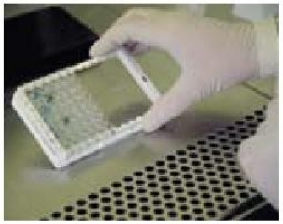
- **Decisions will be taken by consensus after discussions, and whenever needed voting will be done**

IEC

- The decisions will be minuted and **Chairperson's approval taken in writing**
- **All relevant new guidelines should be brought to the attention of the members**
- Members **should be encouraged to attend national and international training programs** in research ethics for maintaining quality in ethical review and be aware of the latest developments in this area

Ethical considerations
in biomedical HIV prevention trials

UNAIDS/WHO guidance document



UNAIDS
JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS
UNHCR UNICEF WFP UNDP UNFPA UNODC ILO UNESCO WHO WORLD BANK

World Health Organization

Science, Rationality & Ethics

- A clinical trial should be planned and conducted by a **trained investigator** following the **latest rules and regulations** with **meticulous record keeping and reporting**.

- It is crucial to maintain highest standards, as any compromise may jeopardize public confidence and participation in the clinical trials and may ultimately affect the availability of safe and effective products.

- Till recent times, the basic responsibility of **Good Clinical Practice compliance** used to lie mainly with the **sponsor**, however, with the current advancements in Schedule Y, GCP compliance is turning out to be a shared responsibility of all stakeholders such as the sponsor, investigator, regulatory authority and ethics committees.

Thank you

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- Wish you a Happy learning !!!