Introduction to Clinical Research

GCP Lecture I

Dr. Laila Tutunji

Nov 2024

Good Clinical Practice (GCP)

What is GCP

Acquiring a GCP Certification

GCP Certification

This is an introduction to our medial students on the **WHO** designed global principles and regulations governing research on human subjects

GCP Certification is part of the Graduation Research Project Requirements

GCP Certification

It builds upon previous courses including Quantitative and Qualitative Research.

Each student should obtain official GCP certification by the Beginning of Feb 2024

GCP Certification

Session 1:

Introduction/ Ethics/

Session 2:

Global Regulatory Framework

Session 3:

GCP Training/ IRBs.

Session 4:

GCP Training/ Research Protocol Basics.

GCP Course

The chosen course certificate by our Medical School is issued by the US NIH because it is recognized globally.

The NIH GCP Certificate will be recognized in the USA and worldwide and valid for three years

Link to the Course

- Link to the course:
- https://gcp.nidatraining.org/
- Create an account to sign in:
- https://gcp.nidatraining.org/register
- Under organization kindly write:
  The University of Jordan

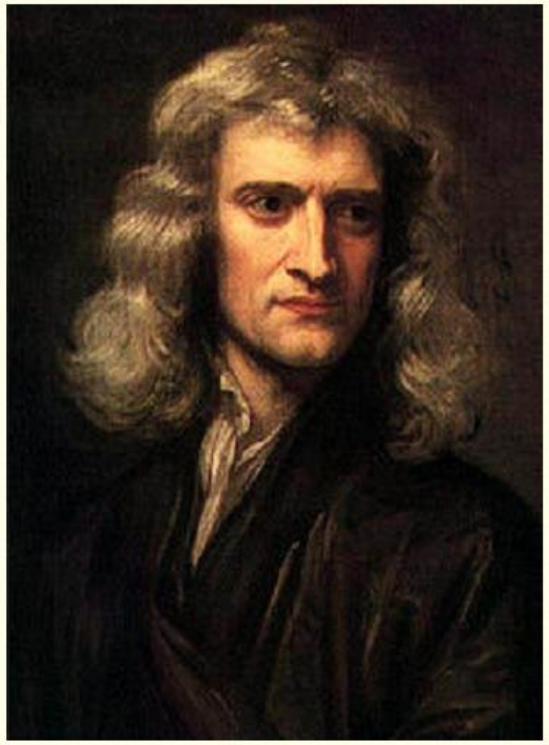
GCP Course Information

Enter your Name

Enter your Institution as the University of Jordan

Our IRB requires 80% of answers correct

Why Clinical Research ?



Sir Isaac Newton

(1642-1727)

Born in Lincolnshire, England

"If I have seen a little further, it is by standing on the shoulders of giants"

- Sir Isaac Newton, 1676

- *“If I have seen a little further, it is by standing on the shoulders of giants”*

Isaac Newton

Definition of Clinical Research

- **Patient-Oriented Research**

  Research conducted with human subjects (or on material of human origin such as tissues, specimens and cognitive phenomena) for which an investigator (or colleague) directly interacts with human subjects…includes:

  - Development of new technologies
  - Mechanisms of human disease
  - Therapeutic interventions
  - Clinical Trials

- **Epidemiologic and Behavioral Studies**
- **Outcomes Research and Health Services Research**

*From NIH Director's Panel on Clinical Research, 1996


History of Clinical Research
- A Merging of Diverse Cultures -

History of Clinical Research

- A Merging of Diverse Cultures -

John I. Gallin, M.D.

Director, NIH Clinical Center

October 13, 2015

National Institutes of Health
Clinical Center

Ethics
The Soul of Medicine

Hippocrates, Principles of Medical Ethics

1. Non-Maleficence
2. Beneficence
3. Justice
4. Respect for Autonomy
5. Confidentiality

The First Principle

Non-Maleficence

“Primum, Non Nocere”

First, DO NO HARM

The Second Principle

Beneficence

The Third Principle

Justice

The Forth Principle

Respect for Autonomy

The Fifth Principle

Confidentiality

To see and See Again

- Shoulder of giants
- The spirit of inquiry, our responsibility ?
- Al Rhazi
- Ibn Sena
- Ibn Al Haitham
- Where do We Stand?

Introduction to Clinical Research

GCP Lecture II

Dr. Laila Tutunji

Nov 2024

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What Went Wrong in Medical Research ?

Germany The Nuremberg Trials

- Starting in the mid-1920s, German physicians, usually proponents of racial hygiene, were accused by the public and the medical society of unethical medical practices.
- In response to the criticism of unethical human experimentation, the Reich government issued "Guidelines for New Therapy and Human Experimentation" in Weimar, Germany.
- The guidelines were based on beneficence and non-maleficence, but also stressed the legal doctrine of informed consent

Germany The Nuremberg Trials

- The guidelines from Weimar were negated by Adolf Hitler.
- By 1942, the Nazi party included more than 38,000 German physicians, who helped carry out medical programs such as the Sterilization Law, as well as trials conducted in concentration camps.
- German physicians responsible for conducting unethical medical procedures on humans during the war were tried.

Germany The Nuremberg Trials

- After World War II, a series of trials were held to hold members of the Nazi party responsible for a multitude of war crimes. The trials were approved by President Harry Truman in January 1946 and were led exclusively by the United States.

- They began on December 9, 1946 in Nuremberg, Germany, in what became known as the Nuremberg trials.

- The 10 points constituted the "Nuremberg Code", which includes such principles as informed consent and absence of coercion; properly formulated scientific experimentation; and beneficence towards experiment participants. It is thought to have been mainly based on the Hippocratic Oath and the basic ethics governing Medicine.

Milestones in Clinical Trial Regulations
1947
The Nuremberg Code

1947 **Nuremberg Code**

Thalidomide Tragedy

- Thalidomide was one of the greatest cases in history of a drug disaster tragedy
- Thalidomide had been tested on animals extensively prior to its marketing
- The first drug recognized to cause birth defect in humans.
- Around 20,000 children were born with physical disability

Thalidomide Tragedy *(cont…)*

- Thalidomide was first marketed in 1957 in West Germany under the trade name **Contergan**.
- The German drug company Chemie Grünenthal developed and sold the drug. Primarily prescribed as a sedative or hypnotic, thalidomide also claimed to cure "anxiety, insomnia, gastritis, and tension". Afterwards, it was used against nausea and to alleviate morning sickness in pregnant women.
- Thalidomide became an over-the-counter drug in West Germany on October 1, 1957.
- Shortly after the drug was sold in West Germany, between 5,000 and 7,000 infants were born with phocomelia (malformation of the limbs). Only 40% of these children survived

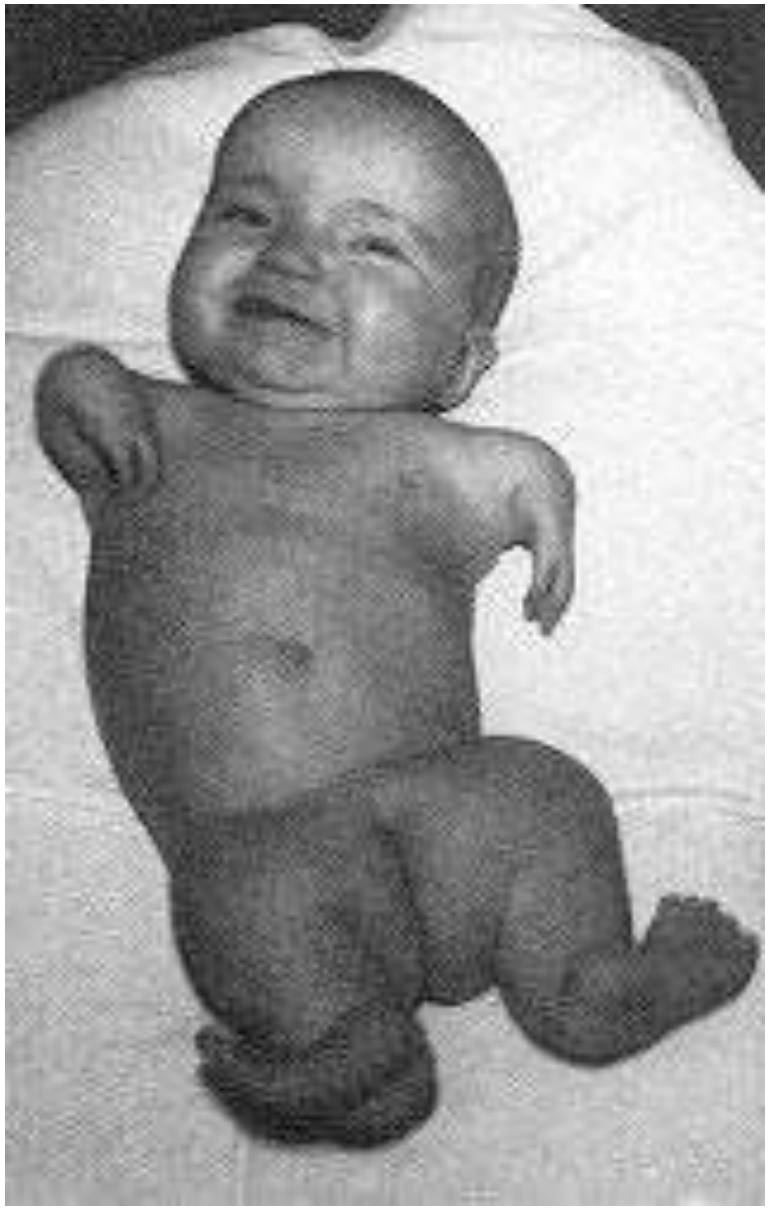
Thalidomide Tragedy *(cont…)*

- Throughout the world, about 10,000 cases were reported of infants with phocomelia due to thalidomide; only 50% of the 10,000 survived.

- Those subjected to thalidomide while in the womb experienced limb deficiencies in a way that the long limbs either were not developed or presented themselves as stumps.
- Other effects included deformed eyes and hearts, deformed alimentary and urinary tracts, blindness and deafness

Thalidomide Tragedy *(cont…)*

- The Medical Research Council maintained that the vast bulk of evidence from laboratory and animal tests is against thalidomide having any genetic effects



- **Researchers tried to reproduce the same effect in dozens of species of lab animals without success.**

Thalidomide Tragedy *(cont…)*

- **The negative effects of thalidomide led to the development of more structured drug regulations and control over drug use and development.**

Milestones in Clinical Trial Regulations
1964 – Declaration of Helsinki

1947 Nuremberg Code

1964 **Declaration of Helsinki**

The Declaration of Helsinki

- **Is a set of ethical principles regarding human experimentation developed for the medical community by the World Medical Association (WMA).[1]**

- **It is widely regarded as the cornerstone document on human research ethics.**

- **The Declaration was originally adopted in June 1964 in Helsinki, Finland, and has since undergone seven revisions (the most recent *by the 75th WMA General Assembly, Helsinki, Finland, October 2024***

The Tuskegee Experiment

- An unethical clinical study conducted between 1932 and 1972 by the U.S. Public Health Service.
- Investigators enrolled in the study a total of 600 impoverished, African-American sharecroppers from Macon County, Alabama.
- Of these men, 399 had previously contracted syphilis before the study began, and 201 did not have the disease and were purposely infected.

The Tuskegee Experiment

- The participants were primarily sharecroppers, and many had never before visited a doctor.

- Doctors from the U.S. Public Health Service (PHS), which was running the study, informed the participants—399 men with latent syphilis and a control group of 201 others who were free of the disease—they were being treated for bad blood, a term commonly used in the area at the time to refer to a variety of ailments

The Tuskegee Experiment

- The men were monitored by health workers but only given placebos such as aspirin and mineral supplements, despite the fact that penicillin became the recommended treatment for syphilis in 1947, some 15 years into the study.
- PHS researchers convinced local physicians in Macon County not to treat the participants, and instead, research was done at the Tuskegee Institute. (Now called Tuskegee University, the school was founded in 1881 with Booker T. Washington as its first teacher.)
- In order to track the disease's full progression, researchers provided no effective care as the men died, went blind or insane or experienced other severe health problems due to their untreated syphilis.

The Tuskegee Experiment

- In the mid-1960s, a PHS venereal disease investigator in San Francisco named Peter Buxton found out about the Tuskegee study and expressed his concerns to his superiors that it was unethical.
- In response, PHS officials formed a committee to review the study but ultimately opted to continue it—with the goal of tracking the participants until all had died, autopsies were performed, and the project data could be analyzed.

The Tuskegee Experiment- The Whistleblower

- **Buxton then leaked the story to a reporter friend, who passed it on to a fellow reporter, Jean Heller of the Associated Press.**
- **Heller broke the story in July 1972, prompting public outrage and forcing the study to finally shut down.**

- **By that time, 28 participants had perished from syphilis, 100 more had passed away from related complications, at least 40 spouses had been diagnosed with it and the disease had been passed to 19 children at birth.**

- **In 1973, Congress held hearings on the Tuskegee experiments, and the following year the study's surviving participants, along with the heirs of those who died, received a $10 million out-of-court settlement. Additionally, new guidelines were issued to protect human subjects in U.S. government-funded research projects.**

The Tuskegee Experiment

- The Tuskegee Syphilis Study, cited as "arguably the most infamous biomedical research study in U.S. history",[8] led to the **1979 Belmont Report** and to the establishment of the **Office for Human Research Protection (OHRP).**[9]
- It also led to federal laws and regulations requiring **Institutional Review Boards for the protection of human subjects in studies involving them.**

The Belmont Report 1978/1979

The *Belmont Report* summarizes ethical principles and guidelines for research involving human subjects.

Three core principles are identified: respect for persons, beneficence, and justice.

Three primary areas of application are also stated: informed consent, assessment of risks and benefits, and selection of subjects.

The Tuskegee Experiment

On May 16, 1997, President Bill Clinton formally apologized on behalf of the United States to victims of the experiment.

During his apology, Clinton announced plans for the establishment of Tuskegee University's National Center for Bioethics in Research and Health Care.

The final study participant passed away in 2004.

Hippocrates, Principles of Medical Ethics

1. Non-Maleficence
2. Beneficence
3. Justice
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Milestones in Clinical Trial Regulations
1989 – US French and Japanese GCP Laws

1947 Nuremberg Code

1964 Declaration of Helsinki

1989 **US French and Japanese GCP Laws**

Milestones in Clinical Trial Regulations
1991 – European Union – GCP Guidelines

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Milestones in Clinical Trial Regulations
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Milestones in Clinical Trial Regulations
1997 – ICH – GCP Guidelines

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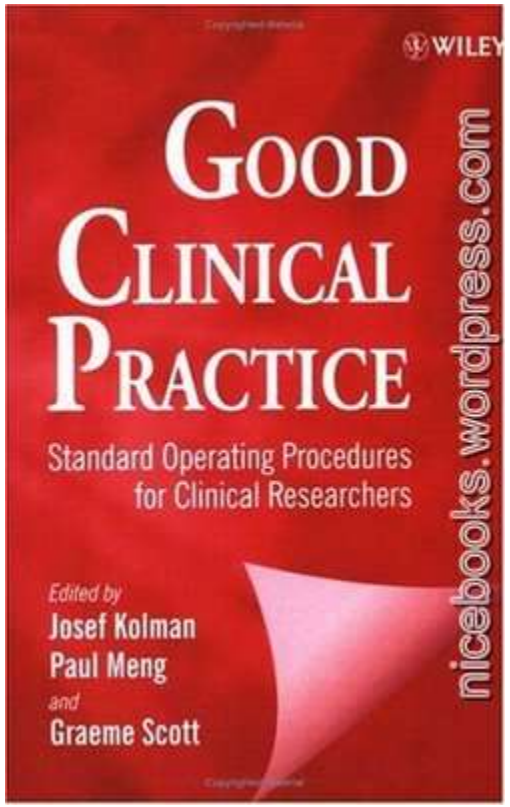
1989 US French and Japanese GCP Laws

1991 European Union – GCP Guidelines

1994 WHO - GCP Guidelines

1997 **International Conference on Harmonisation ICH – GCP Guidelines**

What is GCP



- Good Clinical Practice (GCP):

"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 protected"

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The Soul of Medicine

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To See and See Again

You Can Make A Difference

To See and See Again

You Can Make A Difference

GCP

IRBs

Institutional Review Board (IRB)

Contents

Clinical Quest

Part 1: What is an Institutional Review Board?

Part 1: What is an Institutional Review Board?

An Institutional Review Board (IRB) is an independent body established to protect the rights and welfare of human research participants.

Individual institutions or sponsors may require that all research, no matter how it is funded, be reviewed and approved by an IRB.

An IRB has specific authority over the conduct of research under its jurisdiction. No clinical study may begin enrolling participants until it has received IRB approval.

Clinical Quest

Part 1: What is an Institutional Review Board?

The IRB has the authority to:

- Approve, disapprove, or terminate all research activities that fall within its jurisdiction under federal regulations and institutional policy.

- Require modifications in protocols, including protocols of previously approved research.

Part 1: What is an Institutional Review Board?

- Require that participants be given any additional information that will assist them in making an informed decision to take part in research.

- Require documentation of informed consent or allow a waiver of documentation.

Part 1: What is an Institutional Review Board?

- Every institution that participates in research studies must identify an IRB to review and approve those studies.

- Some research sites are under the jurisdiction of two or more IRBs. In these cases, the IRBs may perform joint review, separate review or agree to abide by the review of one of the involved IRBs.

Part 2: Purpose of an IRB?

Part 2: Purpose of an IRB?

The purpose of an IRB is to safeguard the rights, safety, and well–being of all human research

Participants primarily

And

Ensuring that there is a scientific validity to the research and weighing risks vs benefits.

Part 2: Purpose of an IRB?

The IRB fulfills this purpose by:

- Reviewing the full study plan (IRB responsibilities for the documents which comprise a full protocol) for a research study.

- Confirming that the research plans do not expose participants to unreasonable risks.

- Reviewing and approving proposed payments or other compensation to study participants.

Part 2: Purpose of an IRB?

- Ensuring that human participant protections remain in force throughout the research by conducting continuing review of approved research. This continuing review is conducted at intervals appropriate to the degree of risk posed by each study, but not less frequently than once a year.

- Considering adverse events, interim findings, and any recent literature that may be relevant to the research.

- Assessing suspected or alleged protocol violations, complaints expressed by research participants, or violations of institutional policies.

- Reviewing proposed changes to previously approved studies.

Clinical Quest

Part 2: Purpose of an IRB?

The IRB may suspend or terminate ongoing research that:

- Is not being conducted in accordance with IRB requirements, or
- Is associated with unexpected or serious harm to participants.

The IRB may also suspend or terminate research when additional information results in a change to the study's likely risks or benefits.

Part 3: Membership of an IRB

Part 3: Membership of an IRB

- An IRB must have a diverse membership that includes both scientists and non-scientists.
- Scientist members may include researchers, physicians, psychologists, nurses, and other mental health professionals.
- Nonscientist members of an IRB may have special knowledge of a certain population (pregnant women, children, or prisoners).
- Collectively, IRB members must have the qualifications and experience to review and evaluate the scientific, medical, behavioral, social, legal, and ethical aspects of a proposed study.

Clinical Quest

Part 3: Membership of an IRB

- An IRB must have at least five members. However, it may have as many members as necessary to perform a complete and adequate review of research activities.

Diversity of Membership

- IRB membership must be diverse in terms of race, gender, and cultural heritage.
- Members must be sensitive to issues such as community attitudes.

Clinical Quest

Part 3: Membership of an IRB

- Every effort must be made to ensure that no IRB consists entirely of men or entirely of women. However, no one can be appointed to an IRB solely on the basis of gender.
- No IRB may consist entirely of members of one profession.
- Each IRB should include at least one member whose primary concerns are in scientific areas and one member whose primary concerns are in non-scientific areas.
- Each IRB should include at least one member who is not affiliated with the institution or study site

Clinical Quest

Part 3: Membership of an IRB

ICH	FDA
Minimum 5 members	Minimum 5 members
Minimum 1 member with scientific background	At least 1 scientific & 1 non-scientific
1 member not affiliated with any institution	1 member not affiliated with any institution
Independent of sponsor to provide opinion	Diverse (race, gender, culture, vulnerable population representative)
	No conflict of interest

Clinical Quest

Part 3: Membership of an IRB

Knowledge of Vulnerable Populations

- If the IRB reviews research that involves vulnerable populations — such as children, prisoners, pregnant women, or disabled or cognitively impaired persons — its membership should include one or more persons who are knowledgeable about and/or experienced in working with these populations.

- The individuals specializing in vulnerable populations may be fulltime voting members or alternates to fulltime voting members.

Clinical Quest

Part 3: Membership of an IRB

Conflicts of Interest

- No IRB member may participate in the review of any project in which he or she has a conflicting interest, except to provide information requested by the IRB.
- An investigator may be a member of an IRB. However, the investigator (or any other IRB member) cannot participate in the review or approval of any research in which he or she has a current or potential conflict of interest.
- The investigator should be absent from the meeting room while the IRB discusses and votes on the research in which he or she has an interest.

Clinical Quest

Part 3: Membership of an IRB

Non-Voting Members

- The IRB may invite individuals with competence in special areas to assist in the review of issues that require expertise beyond or in addition to that of the IRB members.
- These consultants are not voting members of the IRB. However, when research involves vulnerable populations, individuals specializing in these areas must be voting members of an IRB and maintained on the IRB roster accordingly.

Clinical Quest

Interactive: Assemble Your IRB

A multisite clinical study package (including the protocol, informed consent forms, recruitment materials, and other related documentation) is being submitted for IRB approval. This US-based study is to assess the efficacy of BioMedXYZ's drug for Attention Deficit Hyperactivity Disorder in children ages 7 to 15.

Clinical Quest

Interactive: Assemble Your IRB

From a list of eight, choose the most appropriate candidates as members of the IRB and ensure that the composition of the IRB meets the minimum criteria outlined for clinical research in the U.S.

- Each candidate has a bio or biography to review. After reviewing the candidates' bios determine if they are right for this clinical study.
- Choose a total of five voting members and one non-voting expert for consultation
- ‘must have’ criteria : (1) diversity, (2) a non-scientific member, and (3) a non-affiliated member.
- Be careful to avoid any conflict of interest with the chosen candidates.

Clinical Quest

Interactive: Assemble Your IRB

Listed below are the candidates for the IRB, including names, credentials, current title, and a brief bio on the candidate's background and expertise.

Candidate 1: Juan Telmo, PhD - Statistical Scientist
Juan has an MS degree in Data Analytics, with a concentration in Statistics, and PhD degree in Statistical Science. He has been a statistical scientist working for the past 5 years at BioMedXYZ firm that develops medical devices. He has expertise in statistical theory, methods, analyses, device development, and clinical research.

Clinical Quest

Interactive: Assemble Your IRB

Candidate 2: Tomer Teivel, RN - Social Worker
Tomer had a rough start in life, his mother was an alcoholic when he was a child. He found his passion helping people dealing with addiction. He earned his MS degree in social work and obtained his social worker license (LCSW). He has worked for the past 12 years in schools, hospitals, and other agencies and also in community drug treatment programs. Previously, Tome had participated in numerous research studies involving participant drug use. He has expertise in mental health treatment, research, families, and community.

Clinical Quest

Interactive: Assemble Your IRB

Candidate 3: Lilith O'Conner, BS - Teacher
For the past 3 years, Lilith has worked as a Teacher at the local Elementary School. She serves as the
Youth Committee Secretary for the local Community Center and is a teacher representative for the local
Board of Education. Lilith has expertise in children, education, and community. She earned her BS degree
in Psychology and Early Childhood Education.

Candidate 4: Carla Fox, JD, MHA - Ethicist
Carla earned her JD and MHA degrees in Health Care Law. She serves as Chairperson on the local chapter for the Board of Bioethics in Hospital Administration. She also works as a lawyer for healthcare organizations. Carla has expertise in health policy, bioethics law, and community engagement.

Clinical Quest

Interactive: Assemble Your IRB

Candidate 5: Brian Bradford, MD - Pediatrician
Brian attended medical school, completed residency in a children's hospital, and obtained his medical licensure. He is a partner pediatrician in general practice for 20 years. He has expertise in pediatrics and clinical care.

Candidate 6: Dorian Picard, MD - Therapist
Dr. Picard earned a PhD in behavioral therapy and has been working in both the hospital and private sector for the last 15 years, specializing in children and adolescent behaviors with a special interest in ADHD. Due to his schedule he has limited availability.

Clinical Quest

Interactive: Assemble Your IRB

Candidate 7: Dung Nguyen, MPH - Policy Analyst
Ms. Nguyen obtained a Master's degree of Public Health and Policy and now works as a management policy analyst at a firm that advises hospital and legislative administrators on health care policies. She has expertise in public health policies, epidemiology research, and biostatistics.

Candidate 8: Manfred Howard - Minister
Manfred was formerly incarcerated in the state criminal justice system. He is now a minister at the local church. He's worked for 6 years as an advocate for adults leaving the prison system and transitioning-to work programs. He has expertise in prisoners and community.

Clinical Quest

Interactive: Assemble Your IRB

Let's consider the feedback for the Non-Voting Member.

- One candidate has a conflict of interest – he works for BioMedXYZ. He would not be an appropriate choice for the IRB. That candidate is Juan Telmo, PhD.
- Additionally, while Manfred Howard may be an expert in his field, he is not a good choice in this case because his area of expertise is adults and prisoners.

Clinical Quest

Interactive: Assemble Your IRB

Several candidates would serve the IRB best as a voting member instead of a non-voting member for consultation.

For example, Tomer Teivel, RN, works in environments that cater to the age group targeted for the study. He would serve the IRB better as a voting member as well as Lilith O'Conner, BS, because she has experience in early childhood education and expertise working with the target study population.

Carla Brown, PhD, has legal experience and serves on a board of bioethics and Dr. Brian Bradford has a pediatric medical practice. Dung Nguyen, MPH, has expertise in epidemiology research and biostats. These candidates will be a good fit for the IRB as voting members.

That leaves one candidate who is a good choice to be added to the IRB as an advisor and a non-voting member, Dorian Picard, MD. His expertise is in children and adolescents with ADHD. However, his busy schedule only allows for limited availability. So, he has agreed to be available for expert advice only.

Clinical Quest

Interactive: Assemble Your IRB

آخر سلايد :

Now, consider the feedback for the ideal candidates to serve as voting members of the IRB for this clinical trial.

Several candidates have experience working directly with the age group targeted for the study – Tomer Teivel has additional experience in drug treatment and research, Lilith O'Conner has experience in early childhood education, and Dr. Brian Bradford has a pediatric medical practice.
Another candidate has legal experience and serves on a board of bioethics, Carla Brown.
Having regulations and ethics covered, the final ideal voting member has expertise on epidemiology research and biostatistics, Dung Nguyen.
Each of these candidates would serve the IRB well as voting members.

Clinical Quest

Interactive: Assemble Your IRB

Conversely, there a few candidates that are not ideal to serve on the IRB as voting members.

- Dr. Telmo has a conflict of interest. He works for BioMedXYZ, the pharmaceutical company supplying the drug for the study.
- While Manfred Howard may be an expert in his field, he is not a good choice in this case because his area of expertise is adults and prisoners.
- Dr. Picard would be a great addition to the IRB; however, his schedule does not allow him to commit to being a voting member of the team.

Clinical Quest

Part 4: Responsibilities of an IRB

Part 4: Responsibilities of an IRB

The principal responsibilities of an IRB include the following:

1. **Provision of an Infrastructure to Support the Ethical Review of Proposed and Ongoing Research**

This infrastructure includes the following IRB processes:

- Perform its functions according to written operating procedures.
- Maintain written records of its activities and minutes of its meetings.
- Comply with all applicable federal and state regulatory requirement(s).
- Should review a proposed clinical trial within a reasonable timeframe.

Clinical Quest

Part 4: Responsibilities of an IRB

- Make its decisions at announced meetings at which a quorum is present.

- Retain all relevant records (e.g., written procedures, membership lists, lists of occupations/affiliations of members, submitted documents, minutes of meetings, and correspondence) for a period of at least 3 years after completion of a study and make them available upon request from any regulatory authority.

- Notify investigators promptly in writing of its decisions, stating the reasons for those decisions and noting the procedures for appeal

Clinical Quest

Part 4: Responsibilities of an IRB

2. Reviewing and Understanding the Full Plan of Study

To provide a full review, the IRB should obtain the following documents (examples of information included in a full plan of study):

- Study protocol(s) and protocol amendment(s).
- Written Informed Consent Form(s) and consent form updates that the investigator proposes to use.
- Documents and other media relating to participant recruitment procedures (e.g., advertisements).
- Written information to be provided to participants including questionnaires and explanatory materials.

Clinical Quest

Part 4: Responsibilities of an IRB

- Information about payments and compensation available to participants.
- Investigator's Brochure.
- Available safety information, including references to relevant literature.
- Investigator's current curriculum vitae and/or other documentation that provides evidence of the investigator's qualifications.
- Any other documents needed to fulfill the IRB's responsibilities

Clinical Quest

Part 4: Responsibilities of an IRB

3. Keeping a Written Record of IRB Decisions

The following written records should be kept pertaining to an IRB's review of a proposed study:

- Identification of the study.
- List of documents reviewed.
- Decision reached:
  - Approval.
  - Disapproval.
  - Rationale for disapproval.
- Termination or suspension of prior approval.
- Date decision was reached.
- Correspondence with the investigator.

Clinical Quest

Part 4: Responsibilities of an IRB

4. Considering the Investigator's Qualifications

The IRB should consider the qualifications of the investigator for the proposed study, as documented by a current curriculum vitae or other relevant documentation.

5. Conducting Continuing Review of Ongoing Studies

The IRB conducts continuing review of each ongoing study at intervals appropriate to the degree of risk to human participants. By regulation, this interval must be at least once per year.

6. Requesting More Information When Necessary

The IRB may request more information to assist in their review. One of the reasons for such a request would be when the IRB judges that the additional information would add meaningfully to the protection of the rights, safety, or well-being of participants.

Clinical Quest

Part 4: Responsibilities of an IRB

7. Reviewing Incentives for Participation

Payment to participants for their participation in a research study must never be coercive in either amount or method of distribution.

The IRB should review both the amount and method of payment to participants to assure that neither exerts undue influence on study participants.

Payments to participants should be prorated (divided in a proportional manner) and not entirely contingent on a participant's completion of the study (no large, consolidated payment at the end).

Clinical Quest

Part 4: Responsibilities of an IRB

The IRB should confirm that information regarding payment to participants, including the methods, amounts, and schedule of payments to study participants, is justified by the protocol and set forth in the written Informed Consent Form and any other written information provided to participants. The way payment will be prorated should be specified.

Some IRBs have written requirements concerning what is adequate compensation for study participants. Investigators should be familiar with these requirements before submitting a protocol to the IRB for approval.

Clinical Quest

Part 5: Criteria for IRB Approval of Research

Part 5: Criteria for IRB Approval of Research

The **Belmont Report**, the report of the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research established three key principles that underlie the current system of human research protections:
Respect for persons,
Beneficence (do no harm/maximize possible benefits and minimize possible harms), and
Justice.
These principles are the basis for the criteria for Institutional Review Board (IRB) approval of research (Reference: The Belmont Report).

Select from the three principles as they relate to the given criteria and descriptions:

A. Respect
B. Beneficence
C. Justice

Clinical Quest

Part 5: Criteria for IRB Approval of Research

Criteria 1: Risks to Participants are Minimized
The IRB should ensure that procedures used in the proposed research are consistent with sound research design, that they do not expose participants to risk unnecessarily, and, when appropriate, involve diagnostic or treatment procedures that pose no further risk.

Feedback: Which of the three principles relates to this criterion: Respect, Beneficence, or Justice?

This criterion relates to the principle of beneficence in the Belmont Report.

Clinical Quest

Part 5: Criteria for IRB Approval of Research

Criteria 2: Risks to Participants are Reasonable in Relation to Anticipated Benefits

The IRB should consider only risks and benefits that may result from the research, as distinct from risks and benefits of therapies participants would receive even if they were not participating in the research.

The IRB should not consider the possible long-range effects of applying the knowledge gained in the research.

Feedback: Which of the three principles relates to this criterion: Respect, Beneficence, or Justice?

This criterion relates to the principle of beneficence in the Belmont Report.

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Part 5: Criteria for IRB Approval of Research

Criteria 3: Selection of Participants is Equitable

No single gender or racial, ethnic, or socioeconomic group should disproportionately carry the burden or reap the benefits of the research. The IRB should ensure that the gender and racial, ethnic, and socioeconomic status of the participants of a research study match as closely as possible to that of the persons expected to benefit from the research.

The IRB should also be mindful of the special challenges of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

Feedback: Which of the three principles relates to this criterion: Respect, Beneficence, or Justice?

This criterion relates to the principle of justice in the Belmont Report.

Clinical Quest

Part 5: Criteria for IRB Approval of Research

Criteria 4: Informed Consent is Properly Obtained and Documented

The IRB must review the informed consent form and ensure that Informed Consent is sought from each prospective participant or from the participant's legally authorized representative.

The IRB must also ensure that the process of obtaining Informed Consent is properly documented.

Adequate provision is made for monitoring the data collected to ensure the safety of participants.

The IRB must review the plans for data collection, storage and analysis and for ensuring participant safety. This includes the plan for capturing and reporting information about adverse events.

Clinical Quest

Part 5: Criteria for IRB Approval of Research

Criteria 4 (cont)

Complex or high-risk studies may be required to have a data and safety monitoring plan.

Some sponsors may require all studies to have a data safety monitoring plan. For example, in the Clinical Trials Network, all studies must have a data and safety monitoring plan and be monitored by a Data and Safety Monitoring Board.

Feedback: Which of the three principles relates to this criterion: Respect, Beneficence, or Justice?

This criterion relates to the principle of respect for persons in the Belmont Report.

Clinical Quest

Part 5: Criteria for IRB Approval of Research

Criteria 5: Adequate Provision is Made to Protect Participants' Privacy and Maintain the Confidentiality of Data
Protection of participants' privacy.

The IRB must consider whether the research involves an invasion of privacy.

Factors to be considered include:

- The private or sensitive nature of the information sought.
- The likelihood that participants will regard the study as an invasion of privacy.
- The importance of the research.
- The availability of alternative ways to conduct the study.

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Part 5: Criteria for IRB Approval of Research

Confidentiality of data.

IRBs must evaluate whether adequate provisions exist to safeguard the confidentiality of information that is collected.

Feedback: Which of the three principles relates to this criterion: Respect, Beneficence, or Justice?

This criterion relates to the principle of respect for persons in the Belmont Report.

Part 5: Criteria for IRB Approval of Research

Criteria 6: Additional Safeguards are Included for Vulnerable Populations

Some individuals' willingness to volunteer in a clinical trial may be unduly influenced by the expectation, whether justified or not, of benefits associated with participation, or by actual or perceived coercion by persons in positions of authority. Examples of such vulnerable populations include:

- Children.
- Prisoners.
- Pregnant women.
- Mentally disabled persons.
- Economically or educationally disadvantaged persons.
- Patients with incurable diseases.
- Patients in emergency situations.

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Part 5: Criteria for IRB Approval of Research

- Medical, nursing, dental, and pharmacy students.
- Subordinate hospital personnel.
- Members of the armed forces.

When some or all of a study's participants are likely to be drawn from a vulnerable population, the IRB must ensure that appropriate additional safeguards are included in the study to protect the rights and welfare of these participants

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Part 5: Criteria for IRB Approval of Research

. Such additional safeguards may include:

- Heightened monitoring of the informed consent process. In some cases, the IRB may wish to approve the enrollment of each participant in the study.
- Changes to the composition of the IRB. For example, when research involving prisoners is being reviewed, at least one voting member (or Alternate) of the IRB must be a prisoner or a prisoners' representative with appropriate background and experience to serve in that capacity.
- If a particular research project is under the jurisdiction of more than one IRB, each IRB of record needs to satisfy this requirement.

Feedback: Which of the three principles relates to this criterion: Respect, Beneficence, or Justice?

This criterion relates to the principle of Beneficence and Respect for persons in the Belmont Report.

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Part 6: Expedited Review

Part 6: Expedited Review

An IRB may use an expedited review procedure for research that:

- Involves no more than minimal risk and
- Falls into a category that appears on an approved list of categories of research eligible for expedited review.

An IRB may also use expedited review to approve minor changes in previously approved research that are made during the period (1 year or less) for which the approval is authorized.

The IRB must have written procedures that specify how an expedited review will be conducted.

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Part 6: Expedited Review

An expedited review (which may involve less waiting time for IRB approval) may be carried out by the IRB chairperson or by one or more experienced IRB members designated by the chairperson.

The reviewers may exercise all of the authorities of the IRB except that of disapproving the research.

A proposal submitted for expedited review may be disapproved only by the full IRB.

Part 6: Expedited Review

Research Eligible for Expedited Review

- Collection of hair or baby teeth.
- Collection of external secretions, including sweat and saliva.
- Recording of data from adults using noninvasive procedures that are routinely employed in clinical practice (not including exposure to electromagnetic radiation outside the visible range, for example, x-rays or microwaves.)
- Collection of blood samples by venipuncture.
- Voice recordings made for research purposes, such as investigations of speech defects.
- Moderate exercise by healthy volunteers.
- **Study of existing data, documents, records, pathological specimens, or diagnostic specimens.**

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Part 7: Investigators' Responsibilities to the IRB

Part 7: Investigators' Responsibilities to the IRB

The investigator must:

- Ensure that the IRB receives all the documents it requires to review the proposed research.
- Admit no participant to a study before the IRB has issued its written approval of the study.
- Make no changes to or deviations from the study protocol without prior written approval from the IRB, except when necessary to eliminate immediate hazards to participants.
- Report promptly to the IRB:
  - Changes to or deviations from the protocol, including changes made to eliminate immediate hazards to study participants.
  - Changes that increase the risk to participants or significantly affect the conduct of the study.
  - All adverse drug reactions that are both serious and unexpected.
  - New information that may adversely affect the safety of participants or the conduct of the study.

Clinical Quest

Part 7: Investigators' Responsibilities to the IRB

Reporting requirements may vary, and it is the investigator's responsibility to know the individual reporting requirements of each IRB involved with the research study.

For example, an IRB may require that every serious adverse drug reaction be promptly reported, whether it was unexpected or not.

Responsibilities (cont.)

- Respond in a timely fashion to all requests from the IRB for additional information about a research study.
- Submit progress reports to the IRB annually, or more frequently, if requested by the IRB, and submit a final report to the IRB when the study is completed or terminated.

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Part 8: IRBs and Multi-Site Research

Part 8: IRBs and Multi-Site Research

Multi-site trials are characterized by the involvement of multiple institutions and study sites engaged in a single research study.

When a research study involves more than one institution, each institution is responsible for safeguarding the rights and well-being of research participants at that institution.

With the implementation of the NIH policy on Use of a Single Institutional Review Board for Multi-Site Research (effective May 25, 2017), multi-institutional research in the U.S. involving non-exempt human participants will use a single IRB. Based on 45 CFR 46.114, the use of a single IRB allows for a more streamlined IRB review and increases efficiencies while maintaining the protection of human study participants (NIH Office of Extramural Research, 2016).

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Part 9: Summary of Key Points

- The purpose of an Institutional Review Board (IRB) is to safeguard the rights, safety, and wellbeing of all human research participants.
- Any research involving human participants must be reviewed and approved by an IRB.
- Any clinical investigation involving a product regulated by the FDA must be reviewed and approved by an IRB.
- An IRB has the authority to approve or disapprove all research activities that fall within its jurisdiction. It may disapprove a research project with a request for modification. It also has the authority to suspend a research study that it previously approved.
- All previously approved ongoing research must be reviewed by an IRB at least once a year to determine whether approval should be continued.
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Part 9: Summary of Key Points

- Every institution, that participates in a clinical study must identify all IRBs that have jurisdiction to review and approve the protocol.
- To approve a research protocol, the IRB must ensure that:
  - Risks to participants are minimized.
  - Risks to participants are reasonable in relation to anticipated benefits.
  - Selection of participants is equitable.
  - Informed consent is properly obtained and documented.
  - Adequate provision is made for monitoring the data collected to ensure the safety of participants.
  - Adequate provision is made to protect participants and maintain confidentiality of data.
  - Additional safeguards are included for vulnerable populations

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