Clinical Research Professionals Certification Exam Prep Session #4
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Regulations & Guidance: Declaration of Helsinki ICH-GCP E8 (R1) General Considerations in Clinical Studies

Jennifer Phillips, RN, CCRC; iTHRIV Workforce Development Program Manager

integrated Translational Health Research Institute of Virginia

Objectives

- The Ethical Principles for Medical Research Involving human subjects-Nuremberg Code, Belmont Report & DOH
- E8 (R1) deals with the clinical trial development lifecycle
- E9 Statistical Principles & E11 Studies involving Children
- Practice Questions

ICH
harmonisation for better health

INTERNATIONAL COUNCIL FOR HARMONISATION OF TECHNICAL REQUIREMENTS FOR PHARMACEUTICALS FOR HUMAN USE

ICH HARMONISED GUIDELINE

GENERAL CONSIDERATIONS FOR CLINICAL STUDIES

E8(R1)

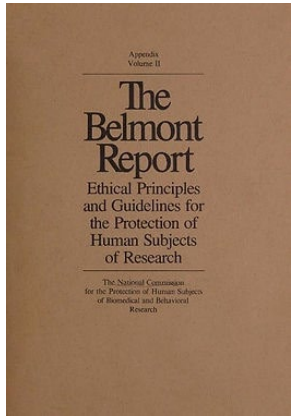
Final version

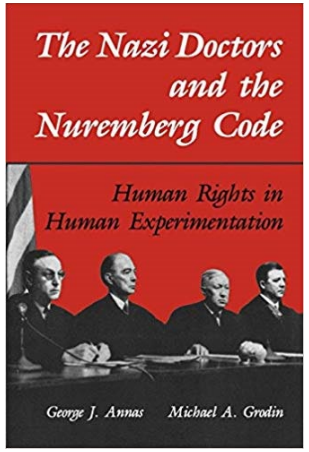
Adopted on 6 October 2021

This Guideline has been developed by the appropriate ICH Expert Working Group and has been subject to consultation by the regulatory parties, in accordance with the ICH Process. At Step 4 of the Process the final draft is recommended for adoption to the regulatory bodies of ICH regions.

WMA DECLARATION OF HELSINKI – ETHICAL PRINCIPLES FOR MEDICAL RESEARCH INVOLVING HUMAN SUBJECTS

Adopted by the 18th WMA General Assembly, Helsinki, Finland, June 1964
and amended by the:
29th WMA General Assembly, Tokyo, Japan, October 1975
35th WMA General Assembly, Venice, Italy, October 1983
41st WMA General Assembly, Hong Kong, September 1989
48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996
52nd WMA General Assembly, Edinburgh, Scotland, October 2000
53rd WMA General Assembly, Washington DC, USA, October 2002 (Note of Clarification added)
55th WMA General Assembly, Tokyo, Japan, October 2004 (Note of Clarification added)
59th WMA General Assembly, Seoul, Republic of Korea, October 2008
64th WMA General Assembly, Fortaleza, Brazil, October 2013





History of Human Subject Research

- **The Nuremberg Code**, written following the Nuremberg Nazi trials in 1946, established guidelines for the ethical treatment of research subjects.

- **The Declaration of Helsinki**, an international document written initially in 1964 and adopted by the World Medical Association, emphasizes the basic ethical principles for medical research involving humans.

- **The Belmont Report** was issued by the United States National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research in 1979 following exposure of the Tuskegee Syphilis study and provides a distinction between medical research and medical care.

History of Human Subject Research

The basic ethical principles of the Nuremberg Code:

- Voluntary Consent is essential
- Benefit society
- Designed and based on results from animal experimentation
- Avoid physical and mental suffering or injury
- Avoid if death or disabling injury will likely occur
- Risk should not outweigh the benefits
- Conducted by qualified persons
- Subjects can withdraw at anytime
- Researchers can terminate if risk of injury, disability or death are high

History of Human Subject Research

Belmont Report

I. the boundaries between biomedical and behavioral research and the accepted and routine practice of medicine,
II. the role of assessment of risk-benefit criteria in the determination of the appropriateness of research involving human subjects,
III. appropriate guidelines for the selection of human subjects for participation in such research
IV. the nature and definition of informed consent in various research settings.

Justice – no one 'class' will reap all the benefits; nor another 'class' assume all the risk of research.

Beneficence – the researcher has an obligation to maximize possible benefit while minimizing possible harms.

Respect – individuals are to be treated as autonomous agents, and those individuals with diminished autonomy are to be protected. (voluntary informed consent)

Practice Questions

1. The principle of respect for persons in the Belmont Report refers to

a) Protection from harms
b) Risk benefit ratio
c) Decision on the part of subjects to voluntarily participate or not in research
d) Compensation for medical injury

Answer: C

Practice Questions

2. The Belmont Report Addresses

a) Differences between practice and research
b) Disclosure of results
c) Conflict of interest
d) Compensation for medical injury

Answer: A

Declaration of Helsinki-DOH

- The Declaration of Helsinki, an international document written initially in 1964 and adopted by the World Medical Association, emphasizes the basic ethical principles for medical research involving human subjects.
- Been revised multiple times-most recent version 2013
- Refers to the following ethical principles (Declaration of Helsinki):
  - General Principles
  - Risks, Burdens, Benefits
  - Vulnerable Groups and Individuals
  - Scientific Requirements and Research Protocols
  - Research Ethics Committees
  - Privacy and Confidentiality
  - Informed Consent
  - Use of Placebo
  - Post-Trial Provisions
  - Research Registration and Publication and Dissemination of Results
  - Unproven Interventions in Clinical Practice

Declaration of Helsinki-DOH

- **GENERAL PRINCIPLES**:
  - Duty of the physician to promote and safeguard the health, well-being and rights of patients involved in medical research
  - Medical progress is based on research
  - Primary purpose to understand causes, development, and effects of diseases and improve preventative, diagnostic and therapeutic interventions
  - Must ensure respect for human subjects and protect their health and rights
  - Conducted in a manner that minimizes possible harm to the environment
  - Research must be conducted only by trained and qualified individuals
  - Groups that are underrepresented in medical research should be provided appropriate access to research
  - Physicians who combine medical research with medical care should involve their patients in research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects
  - Compensation & treatment for subjects who are harmed as a result of participation in research must be ensured

Declaration of Helsinki-DOH

- **RISKS, BURDENS AND BENEFITS**:
  - Medical practice & medical research involve risks and burdens:
    "Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects."
  - Benefits must outweigh risks:
    "Measures to minimize the risks must be implemented. The risks must be continuously monitored, assessed and documented by the researcher."
  - Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed.
    "When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study."

Declaration of Helsinki-DOH

- **VULNERABLE GROUPS AND INDIVIDUALS**:
  - Vulnerable groups/ individuals may have increased likelihood of being wronged or incurring additional harm:

    "All vulnerable groups and individuals should receive specifically considered protection."

  - Research only justified if the research is responsive to the health needs or priorities of these groups or individuals and cannot be carried out in non-vulnerable groups. AND the group should stand to benefit from the knowledge, practices or interventions that result from the research

Declaration of Helsinki-DOH

- **SCIENTIFIC REQUIREMENTS AND RESEARCH PROTOCOLS**
  - Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animals used for research must be respected.

  - The design and performance of each research study must be clearly described and justified in a research protocol.
    - The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed.
    - The protocol should include information regarding funding, sponsors, institutional affiliations, potential conflicts of interest, incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.
    - In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.

Declaration of Helsinki-DOH

- **RESEARCH ETHICS COMMITTEES**
  - The research protocol must be submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins.
  - This Research Ethics Committee MUST:
    - Be transparent in its functioning
    - Be independent of the researcher, the sponsor and any other undue influence
    - Duly qualified
    - Take into consideration the laws and regulations of the country or countries
    - Consider applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research subjects set forth in this Declaration.
    - Have the right to monitor ongoing studies
  - The Researcher MUST:
    - Provide monitoring information including serious adverse events to the committee
    - Submit amendments to the protocol for consideration and approval by the committee
    - Submit final report containing a summary of the study's findings and conclusions
- **PRIVACY AND CONFIDENTIALITY**
  - Every precaution must be taken to protect the privacy of research subjects and the confidentiality of their personal information.

Declaration of Helsinki-DOH

- **INFORMED CONSENT**
  - Participation by individuals in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees.
  - Potential subject must be adequately informed of the following:
    - aims
    - methods
    - sources of funding
    - any possible conflicts of interest
    - institutional affiliations of the researcher
    - the anticipated benefits and potential risks of the study
    - any discomfort it may entail
    - post-study provisions and any other relevant aspects of the study
    - right to refuse or withdraw without reprisal
    - option to being informed about the general outcome and results of the study

"*After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.*"

Declaration of Helsinki-DOH

- **INFORMED CONSENT**
  - Physicians should be cautious if a potential subject is in a dependent relationship with the physician. In such situations consent should be sought by a qualified individual who is completely independent of this relationship
  - For individuals incapable of providing informed consent, consent can be provided by the legally authorized representative under the following conditions:
    - must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject
    - the research cannot instead be performed with persons capable of providing informed consent
    - the research entails only minimal risk and minimal burden
  - When an individual is capable of giving assent, this should be obtained in addition to consent by the legally authorized representative. Dissent should be respected
  - Research involving subjects who are physically or mentally incapable of giving consent, (i.e. unconscious patients) may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group. Consent may be obtained from the legally authorized representative.
  - If no legally authorized representative is available and the research cannot be delayed, the study may provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorized representative.
  - For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse when possible.

Declaration of Helsinki-DOH

- **USE OF PLACEBO**
  - The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best proven intervention(s), except in the following circumstances:
    - no proven intervention exists
    - necessary to determine the efficacy or safety of an intervention
    - will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention
  - Extreme care must be taken to avoid abuse of this option

- **POST-TRIAL PROVISIONS**
  - Sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial
  - Must be disclosed in the consent

- **RESEARCH REGISTRATION AND PUBLICATION AND DISSEMINATION OF RESULTS**
  - Every study involving human subjects must be registered in a publicly accessible database before recruitment of first subject
  - Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports
  - Negative and inconclusive as well as positive results must be published or otherwise made publicly available.
  - Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication.

Declaration of Helsinki-DOH

- **UNPROVEN INTERVENTIONS IN CLINICAL PRACTICE**
  - In the treatment of an individual patient, where proven interventions do not exist or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgement it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available.

"Emergency Use"

Practice Questions

3. Who produced the Declaration of Helsinki?

a) Congress
b) World Medical Association
c) Council for International Research
d) International Research Ethics Committee

Answer: B

Practice Questions

4. In the Declaration of Helsinki the informed consent process does <u>not</u> include which of the following:

a) When a dependent relationship with a physician exists, the informed consent process should be performed by an independent party
b) It may be appropriate to consult family members or community leaders
c) Any Conflict of interest must be disclosed in the consent form
d) Non Written consent must be formally documented and witnessed
e) The potential subject's dissent should be respected when a subject is capable of assent

Answer: B

ICH E8 R1-General Considerations for Clinical Studies

E8 (Revision 1) Final Version Adopted 6 October 2021

- General Principles
- Designing Quality into Clinical Studies
- Drug Development Planning
- Design Elements and Data Sources for Clinical Studies
- Conduct, Safety Monitoring, and Reporting
- Considerations in Identifying Critical to Quality Factors

https://database.ich.org/sites/default/files/ICH_E8-R1_Guideline_Step4_2021_1006.pdf

ICH E8 R1-General Considerations for Clinical Studies

- **General Principles**
  - Ethical conduct of clinical studies and safety of participants
  - Clinical studies should be designed, planned, conducted, analyzed, and reported according to sound scientific principles to achieve their objectives. **The purpose of a clinical study is to generate reliable information to answer the research questions and support decision making while protecting study participants.**

ICH E8 R1-General Considerations for Clinical Studies

➢ Designing Quality into Clinical Studies

- Quality is a primary consideration in the design, planning, conduct, analysis, and reporting of clinical studies
- The goal is to answer a research question while preventing errors that may impact the results
- Good planning and implementation derive from attention to design elements:
  - Clear pre-defined study objectives that address the primary scientific question
  - Appropriate participant selections that the disease, condition or molecular/genetic profile being studied
  - Approaches to minimize bias (randomization, blinding, use of controls, etc.)
  - Endpoints that are well-defined, measurable, clinically meaningful and relevant to patients
- Operational considerations include:
  - Feasibility
  - Site Selection
  - Quality of analytical and testing facilities
  - Processes that ensure data integrity

ICH E8 R1-General Considerations for Clinical Studies

➢ Designing Quality into Clinical Studies

- Basic set of factors relevant to ensuring study quality-Critical to quality factors
- Those whose integrity is fundamental to the protection of study participants, the reliability and interpretability of the study results, and the decisions made based on the study results.
- Mitigate risks that threaten quality
- Approach to Identifying Critical to Quality Factors:

  1. Culture of open dialogue, open communication (including engagement with the patient stakeholders) and multidisciplinary approach.

  2. Focusing on activities essential to the study: Efforts should be focused on activities that are essential to the reliability and meaningfulness of study outcomes for patients and public health, and the safe, ethical conduct of the study for participants.

  3. Engaging Stakeholders

  4. Reassessing Critical to quality factors

  5. Critical to quality factors: The foundation of a successful study is a protocol that is both scientifically sound and operationally feasible

ICH E8 R1-General Considerations for Clinical Studies

➢ Drug Development Planning

- Efficient drug development includes appropriately planned interactions with regulatory authorities throughout development to ensure alignment with requirements for product quality and to support approval in the condition or disease, including possible post-approval studies to address remaining questions.
- Include stakeholders in the development process
- Ensure quality of the product

- Non-clinical assessments include (may be in vivo or in vitro, animal models)
  - Toxicology
  - Carcinogenicity
  - Immunogenicity
  - Pharmacology
  - Pharmacokinetics

ICH E8 R1-General Considerations for Clinical Studies

➢Drug Development Planning

- ICH terms for drug development phases
  - Human Pharmacology (Phase I) may be conducted in healthy volunteers or in a selected population of patients with a disease or condition (people with cancer)

    a. Estimation of initial safety and tolerability

    b. Pharmacokinetics-particularly important to assess the clearance of the drug and anticipate possible accumulation of part drug or metabolites (may also be conducted in later phases to answer specified questions)

    c. Pharmacodynamics & & Early measurement of drug activity
  - Exploratory & Confirmatory Safety & Efficacy Studies (Phase II/III)

    a. Exploratory studies are designed to investigate safety and efficacy in a selected population of patients for whom the drug is intended. (Phase II)

    b. Confirmatory: designed to confirm the preliminary evidence accumulated in earlier clinical studies that a drug is safe and effective for use for the intended indication and recipient population, may also evaluate the efficacy and safety of more than one dose or the use of the drug in different stages of disease or in combination with one or more other drugs (Phase III)
  - Post Approval Studies (Phase IV)- These are studies that were not considered necessary for approval but are often important for optimizing the drug's use. Might be to address a regulatory requirement.
  - Special Populations Considerations-additional investigation during drug development because they have unique risk/benefit considerations and are conducted during any phase of development

    a. Pregnant Women

    b. Lactating Women

    c. Children

ICH E8 R1-General Considerations for Clinical Studies

➢DESIGN ELEMENTS AND DATA SOURCES FOR CLINICAL STUDIES

- Types of Study Design
  - Adaptive Design Studies: prospectively planned modifications over the course of the study, based on accumulating data
    - Changes in population studied
    - Changes in doses of drug studied
  - Master Protocol Studies: allow for the investigation of multiple drugs or multiple conditions under a shared framework
  - Platform Studies: allow for multiple drugs to be investigated in a continuous manner, with different drugs entering the study at different times and leaving the study based on pre-specified decision rules.

- Study Population
  - Defined through inclusion & exclusion criteria
  - Narrowly defined to reduce risk & maximize detection of effect
  - Sample size: number of participants will be determined by the primary objective

- Treatment Description-can include controls an should align with the objectives

- Choice of Control Group-may be made with placebo, no treatment, standard of care, other treatments, or different doses of the drug under investigation

- Response Variables-an attribute of interest that may be affected by the drug. Study endpoints are the response variables that are chosen to assess drug effects.

ICH E8 R1-General Considerations for Clinical Studies

➢DESIGN ELEMENTS AND DATA SOURCES FOR CLINICAL STUDIES

- Methods to Reduce Bias
  - Randomization
  - Blinding
    - Single blind-only the participant is blinded
    - Double blind-both the investigator and participant are blinded.
- Statistical Analysis-Need to be described in the protocol and should include:
  - Primary & Secondary endpoints
  - Interim analyses and/or planned design adaptions
  - Analytical methods
- Study Data-should contain necessary information to conduct analysis, monitor patient safety, evaluate protocol adherence and assess data integrity

ICH E8 R1-General Considerations for Clinical Studies

➢CONDUCT, SAFETY MONITORING, AND REPORTING

- Study Conduct
  - Protocol adherence-a quality designed study will minimize the need for modification and make adherence easier
  - Training-training should be commensurate with role on the study
  - Data Management-Operational checks, centralized data monitoring, and statistical surveillance can identify important data quality issues for corrective action.
  - Access to Interim Data-inappropriate access to data during the conduct of a study may compromise the study integrity
- Participant Safety during the study conduct:
  - Safety monitoring-The approach should reflect the type and objectives of the study, the risks to the study participants and what is known about the drug and the study population.
  - Withdrawal Criteria-Clear criteria for stopping treatment or study procedures for a study participant while remaining in the study are necessary to ensure the protection of the participants but should also minimize loss of critical data
  - Data Monitoring Committee-This group monitors accumulating data while the study is being conducted to make recommendations on whether to continue, modify, or terminate a study.

ICH E8 R1-General Considerations for Clinical Studies

➢CONSIDERATIONS IN IDENTIFYING CRITICAL TO QUALITY FACTORS

- Engagement of all relevant stakeholders, including patients, is considered during study planning and design.
- The prerequisite non-clinical studies, and where applicable, clinical studies, are complete and adequate to support the study being designed.
- The study objectives address relevant scientific questions appropriate for a given study's role in the development program, taking into account the accumulated knowledge about the product.
- The clinical study design supports a meaningful comparison of the effects of the drug when compared to the chosen control group.
- Adequate measures are used to protect participants' rights, safety, and welfare (informed consent process, Institutional Review Board/Ethics Committee review, investigator and clinical study site training,).
- Information provided to the study participants should be clear and understandable
- Competencies and training required for the study by sponsor and investigator staff, relevant to their role, should be identified.
- The feasibility of the study should be assessed to ensure the study is operationally viable.
- The number of participants included, the duration of the study, and the frequency of study visits are sufficient to support the study objective
- The eligibility criteria should be reflective of the study objectives and be well documented in the clinical study protocol.
- The protocol specifies the collection of data needed to meet the study objectives, understand the benefit/risk of the drug, and monitor participant safety.
- The choice of response variables and the methods to assess them are well-defined and support evaluation of the effects of the drug
- Clinical study procedures include adequate measures to minimize bias (e.g., randomization, blinding).
- The statistical analysis plan is pre-specified and defines the analysis methods appropriate for the endpoints and the populations of interest
- Systems and processes are in place that support the study conduct to ensure the integrity of critical study data.
- The extent and nature of study monitoring are tailored to the specific study design and objectives and the need to ensure participants' safety
- The need for and appropriate role of a data monitoring committee is assessed.
- The reporting of the study results is planned, comprehensive, accurate, timely, and publicly accessible.

ICH E9-Statistical Principles for Clinical Trials

➢**OVERVIEW OF GUIDANCE AND DEFINITIONS** **(*highly recommend reviewing this guidance on your own)**

- Relevant mostly for Later Stage Clinical Trials (Confirmatory and some Exploratory)
- Deals with procedures to minimize bias and maximizing precision (Blinding & Randomization)
- Trial Design Considerations
  - Parallel Group Design -subjects are randomized to one of two or more arms, each arm being allocated a different treatment (investigational product at one or more doses and one or more control groups (i.e. placebo))
  - Crossover Design -each subject is randomized to a sequence of two or more treatments, and hence acts as his own control for treatment comparisons. (often a washout period between treatments, often used to demonstrate bioequivalence of two formulations of the same medication)
  - Factorial Design - two or more treatments are evaluated simultaneously through the use of varying combinations of the treatments (i.e. A alone, B alone, Both A & B, Neither A or B)
  - Multicenter Trials -a way of evaluating a new medication more efficiently to accrue sufficient number of subjects AND provides a better basis for the subsequent generalization of the trials' findings. (more diverse pool of subjects)
- Type of Comparison
  - Trials to Show Superiority –most convincingly way to demonstrate efficacy by demonstrating superiority to placebo, or the active control, or dose-response relationship.
  - Trials to Show Equivalence or Non-inferiority -designed to show that the efficacy of an investigational product is no worse than that of the active comparator

https://database.ich.org/sites/default/files/E9_Guideline.pdf

ICH E11-Clinical Investigation of Medicinal Products in the Pediatric Population

➢OVERVIEW OF GUIDANCE AND DEFINITIONS (*highly recommend reviewing this guidance on your own)

- Pediatric Drug Development & Timing Considerations
  - Prevalence and seriousness of the condition
  - Safety considerations
  - Efficacy and safety of alternative treatments
- Formulation Considerations
  - Flavors and colors may be more acceptable in one region than another
  - Consider different types of formulations: liquids, suspensions, and chewable tablets
  - Differing drug concentrations
  - Single use vials should be dose-appropriate single-dosing packaging
- Pharmacokinetics & Dosing
  - Need to be performed in different age groups
  - Based on Mg/Kg
  - Minimization of blood volume drawn (define max amount based on ml/kg or percentage of total blood volume)
- ICH Age Classifications
  - Preterm newborn infants
  - Term newborn infants (0-27 days)
  - Infants and toddlers (28 days to 23 months)
  - Children (2 to 11 years)
  - Adolescents (12 to 16-18 years (dependent on region))

https://database.ich.org/sites/default/files/E11_R1_Addendum.pdf

Other Resources

- **Other resources to consider reviewing prior to the certification exam**

- The Nuremberg Code: Directives for Human Experimentation
- The Belmont Report
- 21 U.S. Code of Federal Regulations: Parts 11, 50, 56, 312 & 812
  - Part 11-Electronic Records: Electronic Signatures
  - Part 50-Protections of Human Subjects
  - Part 56-Institutional Review Boards
  - Part 312-Investigational New Drug Application
  - Part 812-Investigational New Device Exemptions
- 45 U.S. Code of Federal Regulations: Part 46
  - Subpart A- known as Common Rule- robust set of protections of research subjects
  - Subpart B-additional protections for research with pregnant women and fetuses
  - Subpart C-Additional protections for research with prisoners
  - Subpart D-Additional protections for research with children

Practice Questions

5. A “Phase I” study is defined by ICH as:

a) Exploratory
b) Confirmatory
c) Human Pharmacology
d) Estimation

Answer: C

Practice Questions

6. A “Phase III” study is defined by ICH as:

a) Exploratory
b) Human Pharmacology
c) Estimation
d) Confirmatory

Answer: D

Practice Questions

7. According to ICH E8, the following special populations require additional consideration during the drug development phase EXCEPT:

a) Pediatric
b) Geriatric
c) Pregnant Women
d) Lactating Women

Answer: B

Practice Questions

8. Methods to minimize bias include

a) Review of Data
b) Informed consent
c) Blinding
d) None of the above

Answer: C

Practice Questions

9. The decision to proceed with the development of a pediatric drug program includes all of the following except:

a) Results of phase I trials in adults
b) Prevalence and seriousness of the condition
c) Safety profile of alternative treatments
d) Efficacy of alternative treatments

Answer: A

Practice Questions

10. ICH Defines “Children” as:

a) Between 1-4 years of age
b) Between 2-11 years of age
c) Between 3-10 years of age
d) Between 5-14 years of age

Answer: B

Questions?

https://www.ithriv.org/
https://portal.ithriv.org

Please help us continue our support for clinical and translational research by citing our grant number in relevant publications: National Center for Advancing Translational Science of the National Institutes of Health Award UL1TR003015/ KL2TR003016.