UTHealth
The University of Texas
Health Science Center at Houston

Ethics of Clinical Trials

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Foundations of Cancer Therapeutics Course
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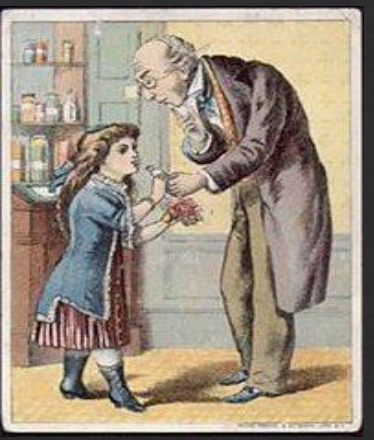
OBJECTIVES

- Learn about regulatory requirements that apply to human subjects research.
  - Define ethical values and principles and explain how they differ from laws, policies, and codes of conduct.
  - Describe the ethical oversight regulations and guidance.
  - Informed consent process and document.
- Apply basic regulatory knowledge to illustrate ethical considerations made by IRBs in reviewing human subjects.
  - Identify common ethical challenges that arise in research.

History of Clinical Trials



6th Century BC	1st century BC	1537	1747	1863	1943
Book of Daniels Meat vs Vegan	Cleopatra Gender experiment	Surgeon Pare Wound care – Boiling Oil vs Egg yolks, rose petals and turpentine	James Lind Scurvy Trial	Austin Flint Placebo Effect of Mint Water for Rheumatic Fever	MRC Double blind randomized trial Patulin for Common Cold

History of Clinical Trial Regulations

1945

Nuremberg Code

Voluntary consent of the human subject is absolutely essential.

1962

Kefauver Harris Amend.

Safety, effectiveness and reliability of drugs.

1964

Declaration of Helsinki

Ethical principles for medical research involving human subjects.

1979-81

Belmont Report and HSR Regulations

Common Rule for biomedical and behavioral research involving human subjects.

1996

ICH

International quality standard for clinical trials.

PHASES of a CLINICAL TRIAL

Preclinical
LABORATORY STUDIES
Duration: Several years

- ✓ Provide information on dosing and toxicity levels

Phase 1
SAFETY
Duration: Several months

- ✓ Evaluate safety
- ✓ Gather information about how a drug interacts with the human body

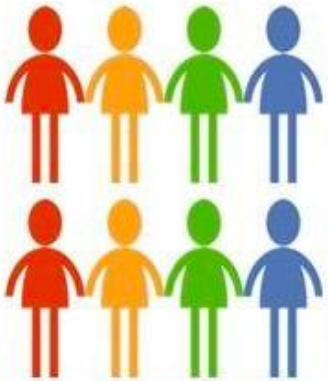
Phase 2
SAFETY AND DOSING
Duration: Several months

- ✓ Further evaluate safety
- ✓ Monitor side effects
- ✓ Check which dose works best
- ✓ Check effectiveness

Phase 3
SAFETY AND EFFICACY
Duration: Several years

- ✓ Confirm effectiveness
- ✓ Monitor safety

FDA APPROVAL

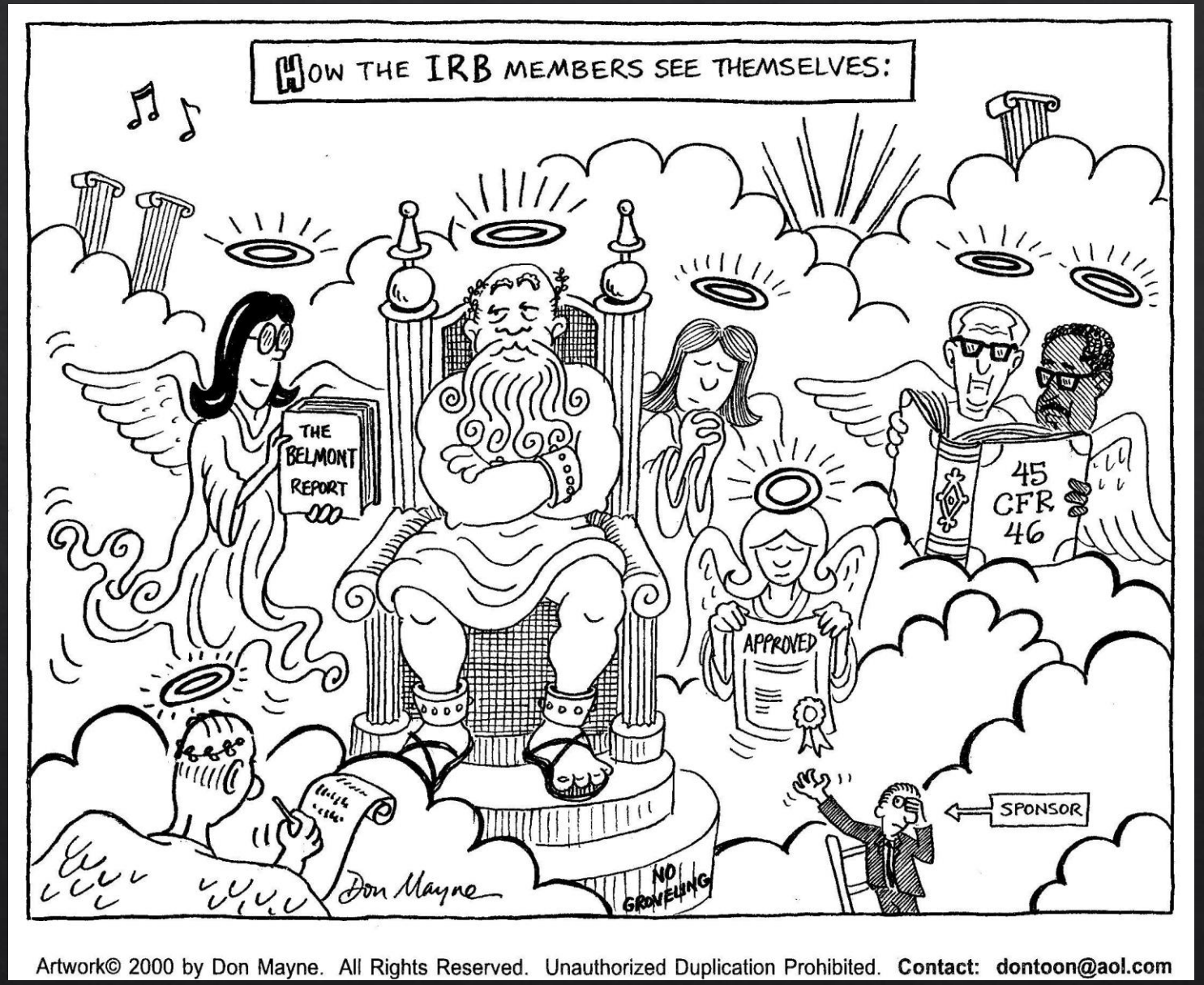


Phase 4
POST MARKETING SAFETY AND EFFICACY

- ✓ Gather information on the drug's effect in various populations and any side effects associated with long-term use

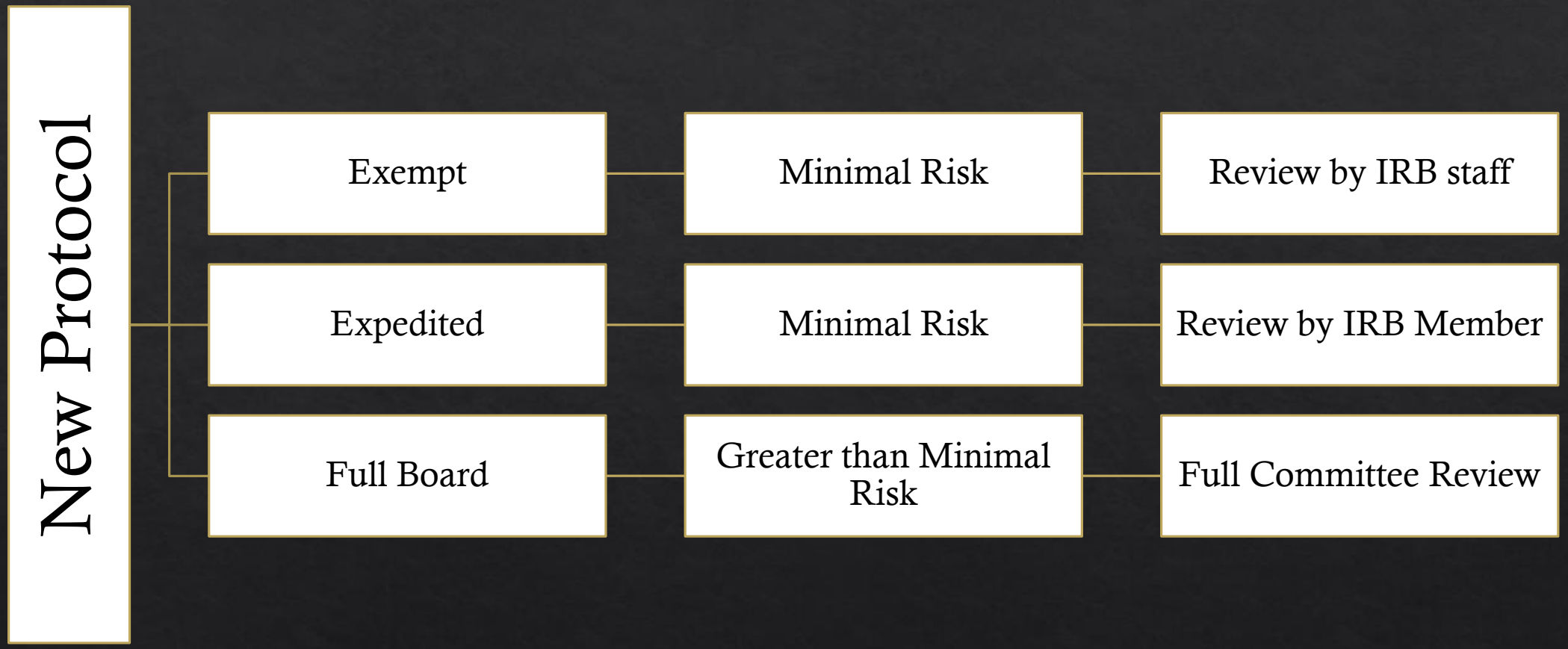
https://www.slhn.org/cancer/clinical-trials

INSTITUTIONAL REVIEW BOARDS



https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/index.html

IRB Review Process



Approved; Approved Pending Modifications; Deferred; Disapproved

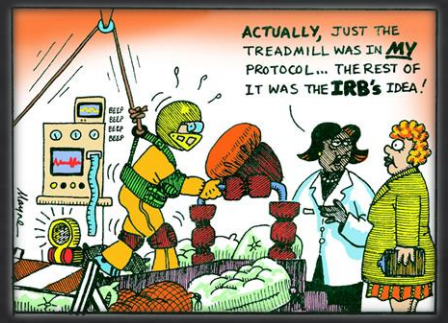
The Belmont Report

Respect for Persons	• individuals should be treated as autonomous agents • persons with diminished autonomy are entitled to protection
Beneficence	• do not harm • maximize possible benefits and minimize possible harms.
Justice	• to each person an equal share according to individual need, individual effort, societal contribution and merit.

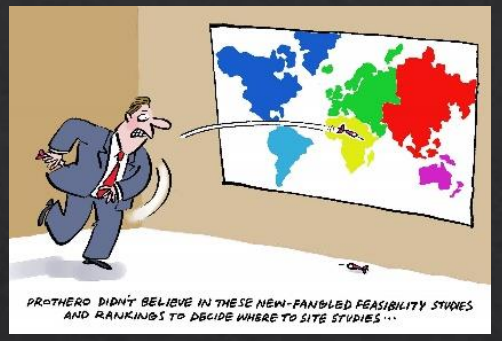
https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/index.html

Criteria for Approval

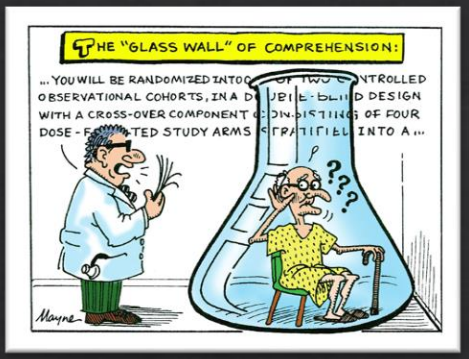
Risks are reasonable
Risks and benefits that may result from the research.
Do not consider possible long-range effects of applying knowledge gained in the research as among those research risks.



Risks are minimized
Evaluate if the research design is sound.
Evaluate if subjects will be exposed to unnecessary risks.

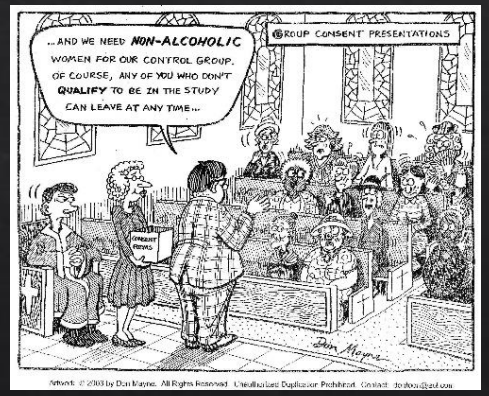


Subject selection is equitable
Review eligibility criteria.
Consider if research burdens and benefits are distributed fairly.



Informed Consent
Consider if information provided is adequate.
Consider who is giving consent and who is obtaining consent.
Consider documentation of consent.

Adequate provisions for confidentiality
Consider if only minimum necessary data is collected.
Evaluate plan for access control, security – electronic and physical.

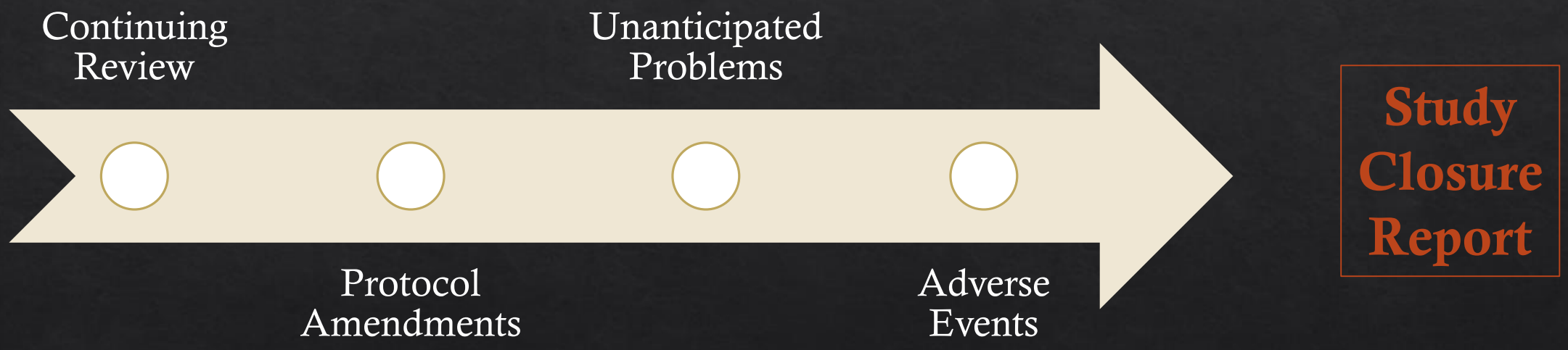


Adequate provisions for privacy
Privacy refers to persons and their interest in controlling access to themselves.
Consider recruitment strategy.

Data and Safety Monitoring
DSMP for all studies greater than minimal risk.
Consider if safety and efficacy data will be reviewed, frequency of review and who will review this.

Additional protections for vulnerable populations.
Children – parental permission – one or both parents, assent. Risk category – no greater than minimal risk (404), greater than minimal risk with prospect of direct benefit to participant (405), minor increase over minimal risk with no prospect of direct benefit (406).
Pregnant women – is there a prospect of biomedical benefits?
Prisoners- specific regulatory criteria – refer to policy.

IRB Oversight



THE BELMONT REPORT

HHS 45 CFR 46		FDA 21 CFR 50 FDA 21 CFR 56	
FDA IND REGULATIONS		FDA IDE REGULATIONS	
OHRP GUIDANCE	FDA GUIDANCE	ICH GCP	DECLARATION OF HELSINKI
Institution P & P	IRB P & P	Clinical Research SOPs	STUDY MOP

GOOD CLINICAL PRACTICE GUIDELINES

Glossary	GCP Principles	IRB/IEC	Investigator Responsibilities
Sponsor Responsibilities	Clinical Trial Protocol	Investigator's Brochure	Essential Documents

References

- OHRP Regulations - 45 CFR 46
- OHRP Guidance for Investigators
- FDA Regulations - 21CFR 50 ; 21 CFR 56
- FDA Information Sheets – IND
- FDA Information Sheets - IDE