Ethical and Regulatory Aspects of Clinical Research
NIH CC Department of Bioethics
Wednesdays, Sept. 26, 2012 - November 7, 2012

Course Readings
Readings are listed under each topic below. The list includes both readings assigned for each session and some additional recommendations. Assigned readings are found either in the following course textbook (listed by chapter) or on the supplemental course CD provided.

Course Textbook:

September 26, 2012  Session 1: History, Guidance, and Framework for Ethical Clinical Research

8:30-8:40  Pre-test

8:40-9:20  Framework for the Ethics of Research with Human Subjects
Christine Grady RN PhD
NIH Clinical Center Dept of Bioethics

9:20-9:30  Discussion

Readings:

9:30- 10:15  History, Scandals and Tragedies: Beecher, Tuskegee, Willowbrook and the Rest
Susan E. Lederer PhD
University of Wisconsin

10:15- 10:25  Discussion

Readings:
Chapter 1. Faden et al. “US medical researchers, the Nuremberg Doctors Trial, and the Nuremberg Code.”
Chapter 4. Brandt, A. “Racism and Research: The case of the Tuskegee Syphilis Study.”

10:25-10:40  Break
10:40-11:20  Do the Codes Apply to My Research? Nuremberg, Helsinki, the Belmont Report, CIOMS, and the Common Rule
Ivor Pritchard PhD
Office of Human Research Protections/DHHS

11:20-11:30  Discussion

Readings
Chapter 5. The Nuremberg Code
Chapter 6. The Declaration of Helsinki
Chapter 7. The Belmont Report
Chapter 8. The Common Rule

CD
Emanuel E, Menikoff J. Reforming the Regulations Governing Research with Human Subjects
NEJM; 2011 Jul 25

October 3, 2012  Session 2: IRB review, Informed Consent and Investigator Panel

8:30-9:15  Purpose and Function of IRBs: Successes and Current Challenges
Barbara Karp MD
Chair of CNS and NIDA IRBs/NIH

9:15-9:25  Discussion

Readings:
Chapter 8. The Common Rule

CD

9:25-10:10  Informed Consent
Christine Grady RN PhD
NIH Clinical Center Dept of Bioethics

10:10-10:20  Discussion

Readings
Chapter 31 Inglefinger, F. Informed (but uneducated) consent
Chapter 32 Freedman, B. A moral theory of informed consent
Chapter 33. Truog R, et al. Is Informed Consent Always Necessary for Randomized, Controlled Trials?
CD

10:20-10:35 Break

10:35-11:30 Investigator Panel
Kathleen Morton RN MSN- NCI
Maryland Pao MD – NIMH
Kristina Rother MD MHSc- NIDDK
Antonio Fojo MD PhD- NCI

October 10, 2012 Session 3: Subject selection, Coercion and Undue inducement, and the ethics of research with children

8:30-9:15 Fair Subject Selection
Dave Wendler PhD
NIH Clinical Center Dept of Bioethics

9:15-9:25 Discussion

Readings:
Wendler D. When should ‘riskier' subjects be excluded from research? Kennedy Institute of Ethics Journal 1998; 8:307-327.

9:25-10:10 Coercion, Undue inducement, and Incentives in Research
Alan Wertheimer PhD
NIH Clinical Center Dept of Bioethics

10:10-10:20 Discussion

Readings:
Chapter 27, Dickert N, Grady C. “What’s the price of a research subject”?


Supplementary readings
Chapter 28, Lemmens T, Elliott C. “Justice for the professional guinea pig”
Chapter 29, McNeil P. “Paying people to participate: why not?”
10:20-10:35  Break

10:35-11:20  Ethical issues in research with children
Robert Nelson MD PhD
FDA

11:20-11:30  Discussion

Readings:
Chapter 42. Freedman B, Fuks A, Weijer C. “In loco parentis: Minimal risk as an ethical threshold for research upon children,”
Chapter 41. Tauer C. “The NIH trials of growth hormone for short stature,”
Chapter 43. Leikin S. “Minors assent, consent, or dissent to medical research.”
CD

October 17, 2012  Session 4: Risks and Benefits, Research with Adults who cannot consent, and Participant Panel

8:30-9:15  Risks and Benefits
Dave Wendler, PhD
NIH Clinical Center Department of Bioethics

9:15-9:25  Discussion

Readings
Chapter 42. Freedman B, Fuks A, Weijer C. “In loco parentis: Minimal risk as an ethical threshold for research upon children.
CD
King N, Defining and Describing Benefit Appropriately in Clinical Trials
Rid A; Emanuel E; Wendler D Evaluating the Risks of Clinical Research.
JAMA. 2010; 304(13):1472-1479


9:25-10:10  Research Involving Persons at Risk for Impaired Decision-Making
Donald Rosenstein, MD
University of North Carolina Medical Center

10:10-10:20  Discussion
Readings
Chapter 38. National Bioethics Advisory Commission, excerpts from “Research Involving Persons with Mental Disorders That May Affect Decision-making Capacity”
CD

Supplementary readings
Misra S, Ganzini L. Capacity to consent to research among patients with bipolar disorder. Journal of Affective Disorders. 2004; 80:115-123

10:20- 10:35 Break

10:35-11:30 Participant Panel (TBA)

October 24, 2012 Session 5: Ethics and International Research

8:30-9:15 Exploitation
Alan Wertheimer PhD
NIH Clinical Center Dept of Bioethics

9:15-9:25 Discussion

9:25-10:10 Ethical Issues in International research
Joe Millum PhD
NIH Clinical Center Department of Bioethics and Fogarty International Center

10:10-10:20 Discussion

Readings
Chapter 65. Lurie P & Wolfe S. “Unethical Trials of Interventions to Reduce Perinatal Transmission of the Human Immunodeficiency Virus in Developing Countries”
Chapter 68. Participants in the 2001 conference on Ethical Aspects of Research in Developing Countries. Fair benefits for Research in Developing countries.
CD

10:20-10:35 Break
10:35-11:30 mock IRB

Please read the protocol on the CD

October 31, 2012 Session 6: Ethics of randomized trials, the use of placebo in trials, and Conflicts of Interest

8:30-9:15 Ethics of Placebo Controlled Trials
Frank Miller, PhD
NIH Clinical Center Department of Bioethics

9:15-9:25 Discussion

Readings:
Chapter 17. Freedman B. “Placebo-Controlled trials and the logic of clinical purpose”
Chapter 19. Emanuel EJ, Miller FG. “The Ethics of Placebo-Controlled Trials – A Middle Ground.”
Chapter 16. Rothman K, Michels K. “The continuing unethical use of placebo controls.”

9:25-10:10 Ethics of Randomized Clinical Trials: Clinical Equipoise
Robert Truog MD
Harvard Medical School

10:05-10:20 Discussion

Readings
Chapter 11. Levine R. "Research and practice,"
Chapter 14. Freedman B. “Equipoise and the ethics of clinical research.”
Chapter 15. Truog R. “Randomized Controlled Trials: Lessons from ECMO

10:20-10:35 Break
10:35-11:20 Conflicts of Interest
11:20- 11:30  Discussion

Readings

Chapter 72. Thompson D. “Understanding Financial Conflicts of Interest”

Chapter 75. Martin, JB and Kasper, DL. "In whose best interest? Breaching the academic-industrial wall."

CD
Krumholz HM et al. What have we learnt from Vioxx? BMJ 2007; 334:120-123

November 7, 2012  Session 7: The Research Use of Stored Tissue and Data, and Incidental Findings in Research

8:30-9:15  Ethical Issues in the Use of Stored Tissue and Data
Sara Chandros Hull PhD
NHGRI and NIH Clinical Center Department of Bioethics

9:15-9:25  Discussion

Readings


doi:10.1371/journal.pbio.1001373

Emanuel E, Menikoff J. Reforming the Regulations Governing Research with Human Subjects

*NEJM* 2011 Jul 25 (See Session 1)

**9:25-10:10**  
**How to think about Incidental Genetic Findings**  
Ben Berkman JD  
NHGRI and NIH Clinical Center Department of Bioethics

**10:10-10:20**  
**Discussion**

**Readings:**

Ravitsky, Vardit and Wilfond, Benjamin S.(2006) 'Disclosing Individual Genetic Results to Research Participants', The American Journal of Bioethics. 2006. 6: 6, 8 — 17,


F A Miller,1 R Christensen,1 M Giacomini,2,3 J S Robert4,5 Duty to disclose what? Querying the putative obligation to return research results to participants *J Med Ethics* 2008. 34: 210-213

**10:20- 10:35**  
**Break**

**10:35- 11:20**  
**Case Discussion**

**11:20- 11:30**  
**Post tests and evaluations**