Ethical and Regulatory Aspects of Clinical Research
NIH CC Department of Bioethics

REVISED SYLLABUS POST SHUT DOWN

Wednesday, Oct 23, 2013- November 13, 2013

I am very sorry that we missed 3 sessions of the 2013 course because of the closure of the government. We will have the next three scheduled sessions with some small changes (Oct. 23, Oct 30, and Nov. 6), and I am adding a session on *Wednesday Nov. 13* to capture some of the lectures and activities that were missed.

Unfortunately, there is not enough time to make up all of the sessions and I have had to make some choices. Below are the topics, speakers, and readings, for the dates scheduled. Below that I have listed links to NIH Webcast lectures from last year's course on topics that I cannot fit in so that you can view the content if interested.

For those in the intramural program who are trying to complete requirements for the *Clinical Research Curriculum Certificate* OR for HRPP training required by *OHSRP,* the requirement for successful completion of the class this year will be participation in 4 out of the 5 sessions. (instead of 6 out of 7)

Thank you for your understanding and patience.

October 23, 2013 **Session 2: Risks and Benefits, Research with Children, and Conflicts of Interest.**

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

9:15-9:25 **Discussion**

Readings: (book)
Chapter 42. Freedman B, Fuks A, Weijer C. "*In loco parentis*: Minimal risk as an ethical threshold for research upon children.
Readings: (CD)
King N, Defining and Describing Benefit Appropriately in Clinical Trials
J Law Med Ethics 2000; 28:332-43
Rid A; Emanuel E; Wendler D Evaluating the Risks of Clinical Research.
JAMA. 2010; 304(13):1472-1479
Weijer C & Miller PB When Are Research Risks Reasonable in Relation to Anticipated Benefits? *Nature Medicine* 2004; 10(6):570-3

Supplemental: Rid A, Wendler D. A Framework for Risk-Benefit Evaluations in Biomedical Research, *Kennedy Institute of Ethics Journal 2011;* Vol. 21, No. 2, 141–179

9:25- 10:10 **Ethical issues in research with children**
Robert Nelson MD PhD
Pediatric Ethicist, Office of Pediatric Therapeutics
Food and Drug Administration

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

Readings: (book)
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."
Readings: (CD)
Roth-Cline MD, Gerson J, Bright P, Lee CS, Nelson RM. Ethical considerations in conducting pediatric research. In H Seyberth, A Rane, M Schwab, (Eds.) *Pediatric Clinical Pharmacology.* 1st Edition. Springer. 2011

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

10:35- 11:20 **Conflicts of Interest**
Steve Joffe MD MPH
Associate Professor of Medical Ethics and Health Policy
University of Pennsylvania

11:20-11:30 **Discussion**

Readings: (book)
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."
Readings: (CD)
Zinner D, Bjankovic D, Clarridge B, Blumenthal D, Campbell E. Participation Of Academic Scientists In Relationships With Industry. *Health Aff* (Millwood) 2009;28(6):1814–25
Krumholz HM et al. What have we learnt from Vioxx? *BMJ* 2007; 334:120-123
Lexchin J, Bero L, Djulbegovic B, Clark O. Pharmaceutical industry sponsorship and research outcome and quality: systematic review. *BMJ* 2003; 326: 1167-11701**.**
Licurse A, Barber E, Joffe S, Gross C. The impact of disclosing financial ties in research and clinical care: a systematic review. *Arch Intern Med*. 2010 Apr 26; 170(8):675-82.
Stossel TP. Regulating academic-industrial research relationships--solving problems or stifling progress? *N Engl J Med*. 2005 Sep 8; 353(10):1060-5.

October 30, 2013 **Session 3: Informed Consent, Randomized Clinical Trials, and Participant Panel**

8:30-9:15 **Informed Consent**
Christine Grady RN PhD
NIH Clinical Center Dept of Bioethics

9:15-9:25 **Discussion**

Readings: (book)
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?
Readings: (CD)
Flory J, Emanuel E. Interventions to improve research participants' understanding in informed consent for research: a systematic review, *JAMA*. 2004 Oct 6; 292(13):1593-601.
Mandava A, Pace C, Campbell B, Emanuel E, Grady C. The quality of informed consent: mapping the landscape. A review of empirical data from developing and developed countries, *J Med Ethics* 2012; 38:356-365

9:25- 10:10 **Ethics of Randomized Clinical Trials: Clinical Equipoise**
Robert Truog MD
Professor of Medical Ethics & Anaesthesia (Pediatrics)
Harvard Medical School

10:05-10:20 **Discussion**

Readings: (book)
Chapter 11. Levine R. "Research and practice,"
Chapter 13. Hellman S, & Hellman DS. "Of mice but not men: Problems of the randomized clinical trial."
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**

10:35-11:30 **Participant/Investigator panel**

November 6, 2013 **Session 4: Stored Tissues, and Incidental Findings**

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: (CD)
Caulfield T, McGuire AL, Cho M, Buchanan JA, Burgess MM, et al. (2008) Research ethics recommendations for whole-genome research: Consensus statement. *PLoS Biol* 6(3): 430-435
Giesbertz NAA, Bredenoord AL, van Delden JJM (2012) Inclusion of Residual Tissue in Biobanks: Opt-In or Opt-Out? *PLoS Biol* 10(8): e1001373. doi:10.1371/journal.pbio.1001373
Wendler D (2006) "One-time general consent for research on biological samples," BMJ, 332: 544.

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

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

Readings: (CD)
Ravitsky, Vardit and Wilfond, Benjamin S.(2006) 'Disclosing Individual Genetic Results to Research Participants', *The American Journal of Bioethics*. 2006. 6: 6, 8 — 17,
Feero WG, Guttmacher A, Collins F. Genomic Medicine — An Updated Primer *NEJM* 2010. 362:2001-11
Wolf S et al. Managing Incidental Findings in Human Subjects Research: Analysis and Recommendations 2008. *J Law, Med & Ethics*
F A Miller, R Christensen, M Giacomini, J S Robert. Duty to disclose what? Querying the putative obligation to return research results to participants *J Med Ethics* 2008. 34: 210-213
American College of Medical Genetics and Genomics, ACMG Recommendations for Reporting of Incidental Findings in Clinical Exome and Genome Sequencing, available at: https://www.acmg.net/docs/ACMG_Releases_Highly-Anticipated_Recommendations_on_Incidental_Findings_in_Clinical_Exome_and_Genome_Sequencing.pdf
Catherine Gliwa & Benjamin E. Berkman, Do Researchers Have an Obligation to Actively Look for Genetic Incidental Findings? *The American Journal of Bioethics*, 13:2, 32-42 (2013)

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

10:35- 11:30 **MOCK IRB**

PLEASE READ the Protocol and consent forms, found on the CD (under session 4)

Nov. 13, 2013 Session 5:

8:30- 9:10 **Fair Subject Selection**
Dave Wendler PhD
NIH Clinical Center Department of Bioethics

9:10-9:20 **Discussion**

Readings: (CD)
Wendler D. When should 'riskier' subjects be excluded from research? *Kennedy Institute of Ethics Journal* 1998; 8:307-327.
Lyerly AD, Little M, Faden R. Reframing the Framework: Toward Responsible Inclusion of Pregnant Women as Participants in Research. *American Journal of Bioethics* 2011, 11(5):50-1.

9:20- 10:00 **Research Involving Persons at Risk for Impaired Decision-Making**
Scott Kim MD PhD
NIH Clinical Center Department of Bioethics

10:00- 10:10 **Discussion**

Readings: (book)
Chapter 38. National Bioethics Advisory Commission, excerpts from "Research Involving Persons with Mental Disorders That May Affect Decision-making Capacity"
Readings: (CD)
Kim S, Appelbaum P, Jeste D, Olin J. Proxy and Surrogate Consent in Geriatric Neuropsychiatric Research: Update and Recommendations. *Am J Psychiatry 2004; 161:797–806*

Supplementary readings
Kim SY The ethics of informed consent in Alzheimer disease research. *Nat. Rev. Neurol.* advance online publication 24 May 2011
Kim SY. Capacity to Consent to Research. Chapter 8 of *Evaluation of Capacity to Consent.* Oxford University Press, 2010

10:10-10:25 **Break**

10:25-11:10 **Ethics of International Research**
Seema Shah JD
NIH Clinical Center Department of Bioethics and DAIDS

11:10-11:20 **Discussion**

Readings:

Declaration of Helsinki, http://www.wma.net/en/30publications/10policies/b3/
NIH guidance on ART http://grants.nih.gov/grants/policy/antiretroviral/guidance.doc

Readings: (CD)

Excerpts from CIOMS

Emanuel E, Wendler D, Killen J, Grady C. What Makes Clinical Research in Developing Countries Ethical? The Benchmarks of Ethical Research J Inf Dis 2004; 189:930

Wertheimer A. Exploitation. Chapter 20 in E. Emanuel et al (eds). The Oxford Textbook of Clinical Research Ethics. New York: Oxford University Press, 2008, pages 201-210

Supplementary

Chapter 65. Lurie P & Wolfe S. "Unethical Trials of Interventions to Reduce Perinatal Transmission of the Human Immunodeficiency Virus in Developing Countries"

Chapter 66. Annas G & Grodin M. "Human Rights and Maternal-Fetal HIV Transmission Prevention Trials in Africa"

Chapter 68. Participants in the 2001 conference on Ethical Aspects of Research in Developing Countries. Fair benefits for Research in Developing countries.

11:20- 11:30 Post Test and Evaluations.

THANK YOU

FYI- to view the following missed topics (from last year's NIH Videocast):

Purpose and Function of IRBs: Successes and Current Challenges

Barbara Karp MD, first third of video found at
http://videocast.nih.gov/summary.asp?Live=11632

Coercion and Undue Inducement

Alan Wertheimer PhD, middle third of video found at
http://videocast.nih.gov/summary.asp?Live=11634

Exploitation

Alan Wertheimer PhD, first third of video found at
http://videocast.nih.gov/summary.asp?Live=11638

Ethics of Placebo Controlled Trials

Frank Miller, PhD, first third of video found at
http://videocast.nih.gov/summary.asp?Live=10686