RESEARCH ETHICS AND INTEGRITY: US and International Issues
HPM 306.665
Tuesday/Thursday 1:30-2:50 PM
Becton-Dickenson Hall (W1020)

Nancy Kass, ScD, Instructor
Andrea Ruff, MD, Instructor
Ginny Barton, Teaching Assistant
Amy Medley, Teaching Assistant

COURSE OBJECTIVES:

The purpose of this course is to acquaint students with an introduction to ethical theory and principles of bioethics, for students to become familiar with ethics requirements when conducting research with human subjects and with animals in the U.S. and/or developing countries, and for students to become more sensitive to the moral considerations inherent to public health research. Through lectures and small group case discussion, the following topics will be covered: ethical theory and principles, informed consent in research; Institutional Review Boards; privacy and confidentiality; the just selection and recruitment of research participants; cultural relativism; ethics and human rights; ethical issues in health services and epidemiological research; appropriate use of placebos; obligations to research participants and communities during studies and after research is completed; the use of animals in research; and scientific and academic integrity. Student evaluation is based on classroom participation and small group case discussion, a consent assignment, a written case analysis, and a final examination or paper. This course satisfies the NIH's and the School's requirement for training in the responsible conduct of research.

REQUIRED READINGS:

The majority of course readings can be found in the following text:

Emanuel EJ, Crouch RA, Arras John D, Moreno JD, and Grady, C eds. (2003). *Ethical and Regulatory Aspects of Clinical Research*. The Johns Hopkins University Press, Baltimore.

The reader is available for purchase through the Johns Hopkins Matthews Bookstore. There will also be one copy of the reader on reserve in the Lilienfeld library in Hampton House.

Additional readings are posted on the CoursePlus website (http://courseplus.jhsph.edu). You must create an eLearning account to access the *CoursePlus* website for this course. If you experience problems doing this, please contact one of the TAs. The "online library" of the course website will be updated every class to include readings, handouts and assignments, as relevant. Please go to the website to get these materials if you miss class.

COURSE REQUIREMENTS and ASSIGNMENTS:

1. **Participation:** You are required to attend class, keep up with the reading, and participate in class. If you miss class, it is your responsibility to go to the course website (described below) to get any handouts that were distributed that day.

2. **In-class exercises:** There are several in-class exercises during the term in which cases are analyzed in a small group setting. Working with other students on these exercises is important, as the cases are designed to facilitate discussion about difficult and interesting ethical issues in conducting research. In-class exercises will not be officially graded, though they are required parts of the course. *If you need to miss one of these sessions*, you will be required to write a short (1/2 to 1 page) analysis of that case to hand in. This must be handed in within one week of returning to class.

3. **Completion of CITI training module on research ethics**: Before the end of the term, you must go to the CITI website and complete the training module on human subjects research. This will allow you to submit or be study staff for projects that go through the JHSPH IRB. It also satisfies research ethics training requirements for several federal funders. The website is **http://www.citiprogram.org**. Once on the website:

   a. Click on 'Register for the Course'. Select the Johns Hopkins University Bloomberg School of Public Health from the 'Participating Institutions' drop-down menu.
   b. Create your username and password.
   c. Enter your contact and member information.
   d. Select 'Biomedical Research Investigators' as your Learner Group.
   e. Click on the 'Grade Book' link next to the Human Research Curriculum.
   f. There are five modules in this curriculum:
   1)Belmont Report; 2) History and Ethical Principles; 3) Basic Institutional Review Board Regulations and Review Process; 4) Informed Consent; 5) Research with Protected Populations. You must **complete all** of the required modules. You will **not** be able to access your completion report if you do not complete all of the required modules. You do not, however, have to complete all modules on the same day. You can complete a module and then come back at a different time to complete the other modules by entering your username and password into the login page.
   g. After you have completed all five modules, go to the main menu. Select the option, "View course completion history for *Johns Hopkins Bloomberg School of Public Health* and print completion certificates" Then print a copy of the completion report **and provide a copy to one of the TAs.**

   Note: *You must print out a copy of your "certificate" stating that you have completed the module and provide a copy to the TAs before the end of the term in order to receive a grade for the course. Failure to provide the certificate will result in an "Incomplete" for the course.*

4. **Completion of Academic Ethics Board module on academic ethics**: If you have not already done so during your time at JHSPH, you must go to the academic ethics website and complete the training module on academic ethics. **The module can be accessed at http://apps1.jhsph.edu/academicethics** and is available directly from the School's

homepage from the Resource area for students, faculty, and staff. In the module you will find the School's academic ethics code, case studies, and a short quiz, plus a list of resources. *This also is a pass/fail requirement of the course. You must forward the email certification stating that you have completed the module to the course email address at rei@jhsph.edu You can alternatively provide a hard copy to one of the TAs. This must be completed in order to receive a grade for the course*.

5. **Consent assignment:** You will be provided with a choice of two research projects (one from the U.S.; one international). You must write a consent *form* for one of these studies. More extensive instructions will be distributed with the assignment. This assignment will be graded, and it must be done *on your own*; you should not work with other students on this assignment. We will post a sample consent form on our class website to help those of you who have not drafted consent forms previously. TAs will also provide guidance on writing consent forms, according to the JHSPH template, during office hours.

   The consent form assignment will be distributed in class on Thursday, January 31st, and is due on **Thursday, February 7th.** *One point will be deducted for every day the assignment is late, if no prior arrangements were made*.

6. **Mid-term case assignment**: You will be provided with three cases and must choose one. This assignment will be distributed on Tuesday, February 12th and is due in class on **Thursday, February 21st**. You must write an analysis of one of the three cases in 3-4 pages, double-spaced and in 12-point font. You should use at least 3 references from the course readings in your analysis and are welcome to use additional, outside resources if you wish. More description of this assignment will be provided when the cases are distributed in class.

7. **In-class final exam:** A final exam will be given in class on **Thursday, March 13th**. The exam will contain multiple choice, true-false, short answer, and essay questions regarding the material presented in the course. There will be about 30 questions on the exam.

   *In lieu of taking the final exam, s*tudents may write an original paper on any topic related to research ethics of interest. However, this *must be approved by Dr. Kass in advance*, ideally 2 weeks before the end of the term and in no circumstances less than 1 week before the end of the term. NOTE: This is a great option for people with a strong interest in exploring a particular topic, but students who have chosen this option in the past have found it more challenging than taking the final exam.

GRADING POLICY:

Your final grade for this class is based on the total number of points you accumulate out of a possible total of 100 points.

1. The consent assignment is worth 20 points;
2 The mid term case is worth 30 points;
3. The final exam is worth 50 points.

Late assignments: One point will be deducted for every day an assignment is late, if no prior arrangements were made.

Missed small-group sessions: 2 points will be deducted for each small group session that is missed without turning in a summary of the session that was missed.

COMMUNICATION WITH COURSE INSTRUCTORS:

Please address e-mail inquiries concerning the class to rei@jhsph.edu.

Dr. Kass can be reached by email at nkass@jhsph.edu or by phone at 410-955-0310**.** Dr. Kass is in HH 344.

Ginny Barton can be reached by email at vbarton@jhsph.edu. Ginny will hold office hours Tuesdays and Thursdays before class, 12-1 PM in the Daily Grind.

Amy Medley can be reached by email at amedley@jhsph.edu. Amy will hold office hours by appointment.

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SYLLABUS

<u>TUESDAY, JANUARY 22:</u> Introduction to course; Introduction to Ethical Theory and Principles of Bioethics: Dr. Nancy Kass

<u>THURSDAY, JANUARY 24:</u> Small group case discussion: Willowbrook. Follow-up discussion (Dr. Ruth Karron, Director, Center for Immunization Research)

A. Beauchamp TL and Walters L. *Contemporary Issues in Bioethics, 6th edition*. Belmont, California: Wadsworth Publishing Company, 2003, Chapter 1, "Ethical Theory and Bioethics", pp. 12-33.
B. Gorovitz, Samuel, et al. *Moral Problems in Medicine*. Englewood Cliffs, New Jersey: Prentice-Hall, Inc., 1976, "Informed Consent and Coercion." pp. 123-129.
C. Ward, Robert, et al. (1958). Infectious Hepatitis: Studies of its Natural History and Prevention. *NEJM*. 258(9): 407-416. (*original report of Willowbrook studies. Relevant parts marked on scanned reading*).
D. Case materials "Willowbrook" distributed in class

RECOMMENDED ONLY: Krugman, Saul (1986). The Willowbrook Hepatitis Studies Revisited: Ethical Aspects. *Reviews of Infectious Diseases*. 8(1): 157-162.

<u>TUESDAY, JANUARY 29:</u> Introduction to Institutional Review Boards (IRBs) (Dr. Nancy Kass); Interactive lecture/discussion panel on IRBs (Reverend Charles Goods, School of Medicine IRB Member; Prof. Jonathan Links, JHSPH IRB Chair)

A. **Reader # 85 (pp. 436-440)** Edgar H and Rothman D. (1995) The Institutional Review Board and Beyond: Future Challenges to the Ethics of Human Experimentation. *The Milbank Quarterly*, 73(4): 489-506.
B. Strauss R, Sengupta S, Quinn S, Goesppinger J, Spaulding C, Kegeles S, Millet G. (2001) The role of community advisory boards: Involving communities in the informed consent process. *Am J Public Health*. 91(12):1938-43.
C. Tindana P, Kass N, Akweongo P. (2006). The informed consent process in a rural African setting: A case study of the Kassena-Nankana District of Northern Ghana. *IRB,* 28(3):1-6.
D. Emanuel EJ, Wendler D, Grady C. (2000). What makes clinical research ethical? *JAMA* 283(20): 2701-11.
E. JHU IRB Checklist for Reviewers

Review Reference Material: Code of Federal Regulations Title 45, Part 46 "Protection of Human Subjects"

<u>THURSDAY, JANUARY 31:</u> Informed Consent: Dr. Nancy Kass.

→ CONSENT ASSIGNMENT DISTRIBUTED IN CLASS

A. **Reader #30 (pp. 197-201)-** Levine, RJ. (1995). Consent Issues in Human Research. in *Encyclopedia of Bioethics,* ed. Reich WT, 2nd ed. New York: Macmillan Reference, 1241-50.
B. **Reader #36 (pp. 216-223)-** Appelbaum PS, Roth LH, Lidz CW, Benson P, and Winslade W. (1987). False Hopes and Best Data: Consent to Research and the Therapeutic Misconception. *Hastings Center Report*. 17(2): 20-24.
C. Marshall P. (2006). Informed consent in international health research. *J of Emp Research on Human Research Ethics,* 25-42.

Review Reference Material: The Nuremberg Code; Declaration of Helsinki; and the Belmont Report

<u>TUESDAY, FEBRUARY 5:</u> Documentary on Tuskegee Syphilis Trials, "The Deadly Deception"

A. **Reader Introduction (pp. 1-5)** "Scandals and Tragedies of Research with Human Participants"
B. **Reader #4 (pp. 20-23) –** Brandt A. (1978). Racism and Research: The Case of the Tuskegee Syphilis Study. *Hastings Center Report,* 8(6):21-29.
C. Braunstein J, Sherber N, Schulman S, Ding E, Powe N. (2008). Race, medical researcher distrust, perceived harm, and willingness to participate in cardiovascular prevention trials. *Medicine,* 87(1):1-9.

<u>THURSDAY, FEBRUARY 7:</u> Small Group Discussion: Ethical issues in epidemiologic and health services research and case studies in research vs. quality assurance. Follow-up discussion, Dr. Nancy Kass

→ INFORMED CONSENT ASSIGNMENT DUE IN CLASS

A. Brett, A and Grodin M. (1991). Ethical aspects of human experimentation in health services research. *JAMA* 265(14): 1854-1857.
B. Cassell, J and Young A. (2002). Why we should not seek individual informed consent for participation in health services research. *J Med Ethics* 28: 313-317
C. Gawande A. A Lifesaving Checklist. *New York Times,* Op-Ed Contribution, published Dec. 30, 2007.

<u>TUESDAY, FEBRUARY 12:</u> Ethics of Study Design- Dr. Steven Goodman, MD, PhD (Associate Professor, Division of Oncology, Biostatistics, Epidemiology, SOM and BSPH)

→ MIDTERM CASE ANALYSIS DISTRIBUTED IN CLASS

A. Levine RJ. *Ethics and Regulation of Clinical Research*, New Haven: Yale University Press, 1988, Chapter 3, "Balance of Harms and Benefits", pp. 37-65.
B. **Reader #13 (pp. 113-116) -** Hellman S and Hellman D. (1991). Of mice but not men: problems of the randomized clinical trial. *NEJM* 324: 1585-9.
C. **Reader #14 (pp. 117-121) -** Freedman B. (1987). Equipoise and the Ethics of Clinical Research. *NEJM*. 317: 141-45.

Review Reference Material: Declaration of Helsinki

THURSDAY, FEBRUARY 14: Clinical research issues: Phase 1 research with healthy volunteers- Dr. Charles Flexner, MD (Associate Professor, Department of Clinical Pharmacology, Medicine, International Health, SOM and BSPH. Assistant Program Director of the General Clinical Research Center, SOM).

A. Macklin, R (1981). On paying money to research subjects: 'due' and 'undue' inducements. *IRB*. 3: 1-6.
B. Beauchamp TL, Jennings B, Kinney ED, and Levine RJ (2002). Pharmaceutical research involving the homeless. *Journal of Medicine and Philosophy*. 27: 547-564.
C. Kass, N.E., Myers, R.A., Fuchs, E.J., Carson, K.A., Flexner, C.W. "Balancing Justice and Autonomy in Clinical Research with Healthy Volunteers." Clinical Pharmacology and Therapeutics, 2007;82(2):219-27.
D. Elliott, C. Guinea-Pigging. The New Yorker. January 7, 2008, pgs. 36-41.

RECOMMENDED ONLY: **Reader #27 (pp. 179-183)-** Dickert N and Grady C. (1999). What's the Price of a Research Subject? Approaches to Payment for Research Participation. *NEJM*. 341: 198-203.

TUESDAY, FEBRUARY 19: Pediatric Research Ethics- Dr. Andy Ruff

A. Anna Mastroianni and Daniel Federmen (eds.) *Women and Health Research, Vol I*, Washington, D.C: National Academy Press, 1994, Chapter 3, "Justice in Clinical Studies: Guiding Principles," pp. 75-83.
B. **Reader #42 (pg. 247-252)**-B. Freedman B, Fuks A, Weijer C. (1992) *In Loco Parentis*: Minimal risk as an ethical threshold for research upon children. *Hastings Center Report* 23(2):13-19.
C. **Reader #43 (pg. 252-258)**-Leikin S. (1993) Minors' assent, consent, or dissent to medical research. *IRB: A Review of Human Subjects Research* 15(2):1-7.

THURSDAY, FEBRUARY 21: Ethics in Environmental Health Research: Dr. Nancy Kass, Dr. Jonathan Links PhD (Professor, Department of Environmental Health Sciences, JHSPH),

→ MIDTERM CASE ANALYSIS DUE IN CLASS

A. Lavery JV; Upshur RE; Sharp RR; Hofman KJ. (2003) Ethical issues in international environmental health research. *International Journal of Hygiene and Environmental Health.* Aug; 206(4-5):453-63.

B. Pollack J. (2002). The lead-based paint abatement repair and maintenance study in Baltimore: Historical framework and study design. *J of Health Care Law and Policy,* 6(1):89-108.

TUESDAY, FEBRUARY 26: Research with Animals- Dr. Nancy Kass; Dr. Alan Goldberg, PhD (Professor, Environmental Health Sciences and Director, Center for Alternatives to Animal Testing); Dr. Anna Durbin, PhD (Assistant Professor, International Health)

A. Orlans FB. (1993). *In the Name of Science: Issues in Responsible Animal Experimentation*. New York: Oxford University Press, Chapter 3: "Main Issues," pp. 35-43.

THURSDAY, FEBRUARY 28: Small Group Case Discussion: UNAIDS vaccine case

A. **Reader #68 (Pg. 354-356)**- Participants in the 2001 Conference on Ethical Aspects of Research in Developing Countries (2002) Fair benefits for research in developing countries. *Science* 298:2133-34.

B. Belsky L. and Richardson H. (2004). Medical researchers' ancillary clinical care responsibilities. *BMJ*. 328:1494-1496.

C. Wertheimer A. (2005). Exploitation. Stanford Encyclopedia of Philosophy entry. Available at: http://plato.stanford.edu/entries/exploitation/. Updated May 16, 2005.

Review Reference Material: Universal Declaration of Human Rights and CIOMS Guidelines

TUESDAY, MARCH 4: Human Rights- Dr. Chris Beyrer, MD, MPH (Department of Epidemiology, International Health, JHSPH) and Dr. Courtland Robinson, PhD (Department of International Health, JHSPH).

A. Beyrer C and Kass N. (2002). Human rights, politics, and reviews of research ethics. *Lancet* 360: 246-51.

B. **Reader #65 (pp. 343-346)-** Lurie P and Wolfe S. (1997). Unethical trials of interventions to reduce perinatal transmission of the human immunodeficiency virus in developing countries. *NEJM* 337, (12): 853-856.*

C. Varmus H and Satcher D. (1997). Ethical complexities of conducting research in developing countries. *NEJM,* 337(14): 1003-1005.

D. Levine, RJ. *Ethics and Regulation of Clinical Research,* 2nd edition. New Haven: Yale University Press, 1988, "Privacy and Confidentiality" pg. 163-181.

Review Reference Material: Universal Declaration of Human Rights

<u>THURSDAY, MARCH 6:</u> Ethical Issues in Qualitative Research: Dr. Katherine Fritz, PhD (Associate Professor, International Health)

A. Moore L; Savage J. (2002) Participant Observation, informed consent, and ethical approval. *Nurse Researcher* 9(4):58-69.

B. Wong L. (1998) The Ethics of Rapport: Institutional Safeguards, Resistance, and Betrayal. *Qualitative Inquiry,* 4(2): 178-199

C. Richards HM; Schwartz LJ. (2002) Ethics of qualitative research: Are there special issues for health services research? *Family Practice*. 19: 135-139.

<u>TUESDAY, MARCH 11:</u> Responsible Conduct of Research: Conflict of Interest, Authorship, and Good Clinical Practice- Dr. Andrea Ruff

A. Martinson, MC; Anderson MS; deVries R. (2005) Scientists Behaving Badly. *Nature.* 435: (9 June), 737-738

B. **Reader #72 (pp. 375-377)-** Thompson DF. (1993). Understanding Financial Conflicts of Interest. *NEJM*. 329: 573-76.

C. **Reader #74 (pp. 378-381)-** Brody BA. (1996). Conflicts of Interests and the Validity of Clinical Trials. in *Conflicts of Interest in Clinical Practice and Research*. eds, Speece RG, Shimm DS, and Buchanan AE. New York: Oxford University Press, 407-17.

D. International Committee of Medical Journal Editors. (2006) Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication. Updated February 2006.

RECOMMENDED ONLY: Press E and Washburn J. (2000). The Kept University. *Atlantic Monthly* (March): 39-54.

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<u>THURSDAY, MARCH 13</u>: IN-CLASS FINAL EXAM

- **GOOD LUCK!**
- **REMINDER: Certificate from IRB training module and Academic Ethics module required to receive course grade**

ETHICAL GUIDELINES FOR HUMAN SUBJECTS RESEARCH
REFERENCE READING LIST

A. **Reader #5 (p. 29)-** "The Nuremberg Code" (1947) from *U.S. v .Karl Brandt*, et al., 1947.
B. **Reader #6 (pp. 30-32)-** World Medical Association (2000). Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects. Edinburgh.
C. **Reader #7 (pp. 33-38)-** The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (1979). The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. Washington, DC.
D. **Reader #8 (pp. 39-55)-** Department of Health and Human Services, National Institutes of Health, Office for Protection from Research Risks, Code of Federal Regulations, Title 45, Part 46 "Protection of Human Subjects."
E. **Reader #9 (pp. 56-80)-** Council for International Organizations of Medical Sciences (CIOMS), in collaboration with the World Health Organization (WHO) (2002). International Ethical Guidelines for Biomedical Research Involving Human Subjects, Geneva: CIOMS.
F. United Nations General Assembly Resolution 217 (1*). Universal Declaration of Human Rights.* December 10, 1948. http://www.un.org/Overview/rights.html

These Ethical Guidelines are not associated with any one lecture. Instead, they should be read as background material for the entire course. Some lectures require a review of certain guidelines. Below is a schedule for which Guidelines to review for selected lectures.

Date of Lecture	**Title**	**Guideline(s) to Review**
Tuesday, Jan. 29	Introduction to IRBs	• Code of Federal Regulations, Title 45, Part 46
Thursday, Jan. 31	Informed Consent	• The Nuremberg Code • Declaration of Helsinki • The Belmont Report
Tuesday, Feb. 12	Ethics of study design	• Declaration of Helsinki
Thursday, Feb. 28	UNAIDS Case Discussion	• CIOMS Guidelines • Universal Declaration of Human Rights
Tuesday, March 4	Human Rights	• Universal Declaration of Human Rights