Responsible Conduct of Patient Oriented Clinical Research (MEDI 5070)
2 hours - Semester 1 – Fall 2008 – Monday – 3-5 p.m.

Course Directors: Angie Khan and Michael J. Lichtenstein, M.D.

LEARNING OBJECTIVES

At the end of the course, degree candidates will be able to:

1. Delineate a history of hallmark abuses of humans enrolled in clinical research.
2. Describe the evolution of national and international codes and regulations guiding inclusion of human subjects in clinical investigations.
3. List the elements of consent and describe procedures and precautions for enrolling special populations (e.g., children or persons with dementia) into clinical investigation.
4. Write a consent form in understandable language.
5. Recognize and identify different forms of scientific misconduct.
6. Develop strategies for self-assessment and validation of scientific objectivity in one's own research.

Wk	Date	Module	Topic
1	08.26.2008	HISTORY	Eugenics and Medical Science
2	09.02.2008		Nazi Medical Experiments and the Nuremberg Code
3	09.09.2008		The Tuskegee Experience
4	09.16.2008		The Declaration of Helsinki/Belmont Report/Common Rule
5	09.23.2008		Structure and Function of the IRB, OHRP, and ORI
6	09.30.2008	INFORMED CONSENT	Elements of Consent: Volunteering, Risks, and Benefits
7	10.07.2008		Conducting Research Where Individuals May not be Able to Provide Consent
8	10.14.2008		Drafting and Editing Consent Forms
9	10.21.2008		Recruiting Fairly: Inclusion of Special Populations in Research
10	10.28.2008	SCIENTIFIC INTEGRITY	Ethics and Responsibility in Authorship and Publication
11	11.04.2008		Investigator and Company Responsibility in Drug Development
12	11.11.2008		VETERANS DAY HOLIDAY
13	11.18.2008		Stem Cell Research and the Ethics of Cloning
14	11.25.2008		THANKSGIVING WEEK – No Class
15	12.02.2008		Conflicts of Interest
16	12.09.2008		Ethical Use of Animals in Biomedical Research
17	12.16.2008		Protecting the Subject's Confidentiality – HIPAA and Research

Responsible Conduct of Patient Oriented Clinical Research
Week 1
Date: August 26, 2008
Room: 2.042
Topic: HISTORY: Eugenics and Medical Science
Instructor: Michael Lichtenstein
Learning Objectives – participants will be able to: 1. Describe the history of the eugenics movement in the United States during the 19th and 20th Century 2. Delineate the differences between 'positive' and 'negative' eugenics 3. Provide examples of how eugenics affected U.S. public policy in the first half of the 20th Century 4. Contrast 21st century issues related to gene therapy with 20th century eugenics practices
Class Assignment: Read the following papers and come prepared to discuss: 1. Kevles, DJ. Eugenics and human rights. BMJ 1999; 319:435-438. 2. Caplan, AI, McGee, G, Magnus, D. What is immoral about eugenics? BMJ 1999; 319: 1284-1285. 3. Miclos, D, Carlson, E. Engineering American society: the lesson of eugenics. Nature Reviews: Genetics 2000; 1:153-158.

Responsible Conduct of Patient Oriented Clinical Research
Week 2
Date: September 2, 2008
Room: 2.042
Topic: HISTORY: Nazi Medical Experiments and the Nuremberg Code
Instructor: Michael Lichtenstein
Learning Objectives – participants will be able to: 1. Describe the difference between medical treatment vs. medical research 2. Compare and contrast the role of the physician in treating patients with that of an investigator 3. Describe how Nazi medical care arose out of the eugenics and race medicine theories of the time. 4. Describe one example, in detail, of Nazi medical experiments conducted in concentration camps. 5. Describe the formulation of the Nuremberg Code 6. Discuss the responsibility of individual investigators conducting research with human subjects 7. Delineate the influence the Nuremberg Code was to have on subsequent human subject regulations.
Class Assignment: Read the attached chapters and come prepared to discuss: 1. Mozes-Kor, E. Historical Origins of the Nuremberg Code. Chapter 7 pages 121-144, in The Nazi Doctors and the Nuremberg Code: Human Rights and Human Experimentation. Annas, GJ, Grodin, MA, Editors, Oxford University Press, New York, 1992 2. Grodin, MA. The Mengele Twins and Human Experimentation: A Personal Account. Chapter 4 pages 53-59, in The Nazi Doctors and the Nuremberg Code: Human Rights and Human Experimentation. Annas, GJ, Grodin, MA, Editors, Oxford University Press, New York, 1992

Responsible Conduct of Patient Oriented Clinical Research
Week: 3
Date: September 9, 2008
Room: 2.042
Instructor: Michael Lichtenstein
Topic: HISTORY: The Tuskegee Experience
Learning Objectives – Participants will be able to: 1. Describe the timeline and central events during the conduct of the Tuskegee study 2. Present the rationale for the initiation of the study in the context of the 1930s 3. Present the arguments for and against the treatment of participants with penicillin in the 1950s 4. Describe potential effects of social and economic factors in the recruitment and retention of subjects 5. Determine whether the methodology of the study is sufficiently rigorous to provide valid information 6. Describe the United States Government's response and ongoing responsibility to the survivors of the cohort
Class Assignment: The readings will be circulated a week before the class. Please read the materials in preparation for the class discussion.
Readings and Bibliography: 1. Internet Resources: Centers for Disease Control (CDC) National Center for HIV, STD, and TB Prevention (www.cdc.gov/nchstp/od/tuskegee) A. Timeline – The Tuskegee Syphilis Study: A Hard Lesson Learned B. Aftershocks: How Tuskegee Changed Research Practice C. Mission Statement; Tuskegee Health Benefit Program D. President Clinton's Statement: Remarks by the President in Apology for Study Done in Tuskegee 2. Jones JH, "A Moral Astigmatism," Chapter 1, pp 1-15, in *Bad Blood: The Tuskegee Syphilis Experiment*. 1st Edition, The Free Press, New York, 1981 3. Kampmeier RH. The Tuskegee Study of Untreated Syphilis. Southern Medical Journal 1972; 65: 1247-51. 4. Benedek T. The "Tuskegee Study" of Syphilis: Analysis of Moral versus Methodologic Aspects. Journal of Chronic Diseases 1978; 31: 35-50.

Responsible Conduct of Patient Oriented Clinical Research
Week: 4
Date: September 16, 2008
Room: 2.042
Instructors: **Michael Lichtenstein**
Topic: HISTORY: The Declaration of Helsinki/Belmont Report/Common Rule
Learning Objectives – Participants will be able to: 1. Describe the development and purposes of the Declaration of Helsinki 2. Compare and Contrast the Nuremberg Code with the Declaration of Helsinki 3. Delineate reasons for the revisions in the Declaration of Helsinki 4. Debate the issues related to placebo controlled trials and the influence on United States Policy 5. Discuss the underlying principles in the Belmont report: Respect for Persons, Beneficence, Justice 6. Relate the prinicples outlined in the Belmont report to the context of the Nuremberg Code, the Tuskegee Experience, and the Declaration of Helsinki. 7. Describe the history of adoption of a common federal code for the conduct of research with human subjects in the United States 8. Identify the elements of informed consent as laid out in the Common Rule 9. Outline the structure of Institutional Review Boards as specified in Federal Law 10. Define and debate the levels of risk in forms of patient oriented clinical research as specified in Federal Law.
Class Assignment: The readings will be circulated a week before the class. Please read the materials in preparation for the class discussion.
Readings and Bibliography: 1. The Declaration of Helsinki – 52nd World Medical Association General Assembly – Edinburgh, Scotland, October 2000. 2. Perley, S, Fluss, SS, Bankowski, Z, Simon, F. "The Nuremberg Code: An International Overview," chapter 8, pp 149-173, in *The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation.* Annas, GJ, Grodin, MA, editors. Oxford University Press, New York, 1992. 3. Levine RJ. The Need to Revise the Declaration of Helsinki. N Engl J Med 1999; 341:531-534 (Correspondence – Should the Declaration of Helsinki be Revised? N Engl J Med 1999, 341:1851-1853). 4. The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research. OPRR Reports April 18, 1979. 5. The Common Rule. Federal Policy for the Protection of Human Subjects; Notices and Rules – Part II, Federal Register, June 18, 1991 – Reprinted April 2, 1996.

Responsible Conduct of Patient Oriented Clinical Research

Week: 5

Date: September 23, 2008

Room: 2.042

Topic: HISTORY: Structure and Function of the IRB, OHRP, and ORI: Evolution of the Research Oversight Process

Instructors: Angie Khan, Michael Lichtenstein, Linda McManus

Learning Objectives – Participants will be able to:

1. Describe the organization and structure of the Institutional Review Board (IRB)
2. Describe the purpose and organization of research oversight entities, e.g., OHRP
3. Describe the interrelationships between investigators, universities, and research oversight entities

Class Assignment:

1. Using the Internet, each student will look up and research the functions of one of the following entities:

   OHRP -- Office of Human Research Protections
   FDA -- Food and Drug Administration
   DHHS--Dept of Health and Human Services
   ORI --Office of Research Integrity
   NCQA -- National Center for Quality Assurance
   PCBE – President's Council on Bioethics
   ICH – International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals

2. Prepare a 1-2 page handout to share with your classmates (20 copies) describing:
   A. The purpose of the agency or entity
   B. It's regulatory responsibility, if any
   C. It's relationship to (a) the other entities (how do they work together, if at all), and to (b) investigators (individuals, universities, companies)

3. Give a 10 minute presentation to the class on the background and information you discovered.

Readings and Bibliography: No specific readings

Responsible Conduct of Patient Oriented Clinical Research
Week 6
Date: September 30, 2008
Room: 2.042
Topic: INFORMED CONSENT: Elements of Consent: Volunteering, Risks, and Benefits
Instructor: Angie Khan
Learning Objectives – Participants will be able to: 1. Relate the elements of consent to their origins in the Nuremberg Code, Declarataion of Helsinki, the Belmont Report, and the Common Rule. 2. Describe the elements of consent that must be included in a consent form. 3. Analyze and critique consent forms. 4. Debate the circumstances under which surrogate consent would be acceptable 5. Describe the current Federal and State guidelines for acceptance of surrogate consent.
Class Assignment: 1. Read the Common Rule and IRB Handbook on writing a consent form 2. Compare and contrast the elements of consent with the elements in the source documents 3. Bring a consent form to class to share and analyze with the group.
Readings and Bibliography: 1. Consent forms from course participants' work. 2. UTHSCSA IRB Policies and Procedures – available online at http://research.uthscsa.edu/irb/handbook.shtml

Responsible Conduct of Patient Oriented Clinical Research
Week: 7
Date: October 7, 2008
Room: 2.042
Topic: INFORMED CONSENT: Conducting Research Where Individuals May not be Able to Provide Consent
Instructor: Dan Dent, Janet McCarthy
Learning Objectives – participants will be able to: 1. Identify barriers to research conduct in settings where consent may not be obtainable – e.g., trauma, sudden death 2. Discuss the strengths and weaknesses of processes for ethically conducting research with human subjects in these circumstances.
Class Assignment: To be identified.
Readings and Bibliography: To be identified

Responsible Conduct of Patient Oriented Clinical Research
Week: 8
Date: October 14, 2008
Room: 2.042
Topic: INFORMED CONSENT: Drafting and Editing Consent Forms
Instructor: Angie Khan
Learning Objectives – Participants will be able to: 1. Edit a consent form for their research project 2. Offer and accept criticism in the preparation of a consent form.
Class Assignment: 1. Participants will bring draft copies of consent forms to the class. Working in pairs, they will read and edit each other's consent forms. 2. The consent forms will then be presented to the class for discussion and input.
Readings and Bibliography: Consent forms from the course participants' work.

Responsible Conduct of Patient Oriented Clinical Research
Week: 9
Date: October 21, 2008
Room: 2.042
Topic: INFORMED CONSENT: Recruiting Fairly: Inclusion of Special Populations in Research
Instructor: Helen Hazuda
Learning Objectives – Participants will be able to apply the principle of justice to: 1. Debate the merits of inclusion or exclusion of special populations (children, women of reproductive potential, prisoners, persons with diminished mental capacity) in research studies. 2. Describe methods for appropriately advertising for subjects 3. Recognize when incentives may become coercive 4. Identify potential conflicts when indigent persons may be enrolled in research studies 5. Identify safeguards for enrolling students or subordinates in University based studies 6. Recognize the potential conflict of interest when physician investigators recruit subjects from their patient populations.
Class Assignment: To be identified
Readings and Bibliography: To be identified

Responsible Conduct of Patient Oriented Clinical Research
Week: 10
Date: October 28, 2008
Room: 2.042
Topic: SCIENTIFIC INTEGRITY: Ethics and Responsibility in Authorship and Publication
Instructor: Linda McManus and Michael Lichtenstein
Learning Objectives – Participants will be able to: 1. Describe the contributions to research that merit inclusion as an author on a paper. 2. Delineate reasons for disclosing potential conflicts of interest in publication. 3. Identify processes for determining who should be an author among investigators. 4. Determine whether the order of authorship really means anything.
Class Assignment: Read the assigned book chapter and references. Be prepared to discuss various scenarios regarding authorship during the class.
Readings and Bibliography: **1.** Macrina, FL "Authorship and Peer Review" Chapter 4, pp 49-72 in Scientific Integrity: An Introductory Text with Cases. Second Edition. ASM Press, Washington DC 2000. **2.** Coats AJS, Henein M, Flather M, Sigwart U, Seggewiss H, Wang D, Yousufuddin M, Shamin W. Retraction: Shamin et.al. Nonsurgical Reduction of the Interventricular Septum in Patients with Hypertrophic Cardiomyopathy. N Engl J Med 2002; 347:1326-1333. N Engl J Med 2003; 348:951. **3.** Curfman GD, Morrissey S, Drazen JM. Notice of Retraction. N Engl J Med 2003; 348:945.

Responsible Conduct of Patient Oriented Clinical Research
Week: 11
Date: November 4, 2008
Room: 2.042
Topic: SCIENTIFIC INTEGRITY: Investigator and Company Responsibility in Drug Development
Instructor: Alexander Shepherd
Learning Objectives – Participants will be able to: 1. Become familiar with FDA requirements for data monitoring and record keeping during studies. 2. Develop a process for the accurate collection, storage, and management of clinical research data. 3. Delineate the consequences of data fabrication.
Class Assignment: To be identified
Readings and Bibliography: To be identified

Responsible Conduct of Patient Oriented Clinical Research
Week: 12
Date: November 11, 2008
Topic: Veterans' Day – No Class

Responsible Conduct of Patient Oriented Clinical Research
Week: 13
Date: November 18, 2008
Room: 2.042
Topic: SCIENTIFIC INTEGRITY: Stem Cell Research and the Ethics of Cloning
Instructors: Peter Hornsby and Bettie Sue Masters
Learning Objectives- Participants will be able to: 1. Know what is currently achievable with respect to somatic nuclear transfer technology ("cloning") in humans and animals. 2. Know what classes of stem cells exist and what their potential therapeutic potential is. 3. Understand the ethical questions concerning the derivation and use of embryonic stem cells, including so-called "therapeutic cloning." 4. Understand the ethical questions concerning other (e.g. adult) stem cells. 5. Understand the ethical, medical and scientific questions concerning reproductive cloning (cloning of human beings).
Class Assignment: To be identified
Readings and Bibliography: To be identified

Responsible Conduct of Patient Oriented Clinical Research
Week: 14
Date: November 25, 2008
Topic: Thanksgiving Week – No Class

Responsible Conduct of Patient Oriented Clinical Research
Week: 15
Date: December 2, 2008
Room: 2.042
Topic: SCIENTIFIC INTEGRITY: Conflicts of Interest
Instructor: Gary Sertich
Learning Objectives – Participants will be able to: 1. Describe how conflicts of interest interfere with scientific integrity 2. Delineate methods for identifying different forms of conflicts of interest 3. Know the local UTHSCSA policies and procedures for identifying and disclosing conflicts of interest
Class Assignment: To be identified
Readings and Bibliography: To be identified

Responsible Conduct of Patient Oriented Clinical Research
Week: 16
Date: December 9, 2008
Room: 2.042
Topic: Ethical Use of Animals in Biomedical Research
Instructors: Steven Austad, Ph.D. and Veronika Kiklevich, D.V.M.
Learning Objectives – Participants will be able to: 1. Delineate the rationale for using animals and animal models in biomedical research. 2. Cite examples of hallmark cases where animals have not been used appropriately 3. Describe the social and political climate regarding the use of animals in research 4. Identify and access local resources for appropriate use and protection of animals in research
Class Assignment: To be identified
Readings and Bibliography: Handouts at the time of the class.

Responsible Conduct of Patient Oriented Clinical Research
Week: 17
Date: December 16, 2008
Room: 2.042
Topic: SCIENTIFIC INTEGRITY: Protecting the Subject's Confidentiality/HIPAA and Research
Instructor: Angie Khan
Students will be able to: 1. Understand the development and intent of the Health Insurance Protability and Accountability Act of 1996 (HIPAA) 2. Recognize the significance of the "Privacy Rule" as it affects research 3. Comprehend protected health information use and disclosure as it relates to research 4. Differentiate between the "Privacy Rule" , the Common Rule, and FDA human subjects regulations as related to confidentiality and privacy
Class Assignment: To be identified
Readings and Bibliography: To be identified