INTERNATIONAL LAW AND ETHICS OF HUMAN SUBJECTS RESEARCH

Interdisciplinary seminar on international law and ethics in protection of human subjects of transnational medical and behavioral research.

Michigan State University College of Human Medicine:
Special Problems in Human Medicine:
HM 591, Section 605.
Michigan State University College of Law:
International Law & Ethics of Human Subjects Research:
LAW 548W, Section 301, Section ID 774977.

7:45-9:45 p.m. Tuesdays, Room 340, Law College Building

SYLLABUS

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Course objectives:

To foster needed interdisciplinary understanding of the substance and interrelationships of law, particularly international law, and ethics in the protection of human subjects of transnational biomedical and behavioral research.

Around the world, researchers in the biomedical and behavioral and social sciences study people—in order to understand and counter the world's disease burden, especially in resource-poor countries, and to better understand people's troubles, beliefs, behavior, and hopes. Research on human beings incurs special ethical and legal responsibilities. But exposure to these responsibilities is limited in most courses to bioethical theory, voluntary codes, and minimum national compliance requirements. Similarly, international law as applicable in international health research operations is little understood.

This seminar brings together scholars and researchers from many fields to encourage interdisciplinary understanding of the substance and interrelationships of law, particularly international law, and ethics in the protection of human subjects of transnational biomedical and behavioral research.

Individuals who complete this seminar should be better qualified to address these issues as scholars, researchers, administrators, ethics review committee members, teachers, practitioners, and mentors.

Required reading:

From: Mann, Jonathan M., Sofia Gruskin, Michael A. Grodin, and George J. Annas, eds. Health and Human Rights: A Reader, 1999. As assigned.

From: Legal, medical, scientific, and other scholarly journal selections; policy, and briefing materials; and other readings (available on World Wide Web, on ANGEL, or to be supplied). As assigned.

Instructor will draw also upon these materials (in addition to required readings):

Articles, essays, monographs:

Appiah, Kwame Anthony. . The Ethics of Identity, Princeton University Press, 2005.

Fidler, David P. International Law and Infectious Diseases, 1999.

Fidler, David P. International Law and Public Health, 2000.

Garrett, Laurie. The Coming Plague: Newly Emerging Diseases in a World out of Balance, 1994.

Garrett, Laurie. "Betrayal of Trust: The Collapse of Global Public Health." (2000).

Anthologies:

Annas, George J., and Michael A. Grodin, eds. The Nazi Doctors and the Nuremberg Code: Human Rights in Human Experimentation, 1992.

Goldberg, Richard, and Julian Lonbaby, eds. Pharmaceutical Medicine, Bioetechnology, and European Law, 2000.

Gostin, Lawrence O., ed. Public Health and Ethics: A Reader, 2002.

Documents

Alfredsson, Gudmundur, and Katarina Tomaševski, eds. Thematic Guide to Documents on Health and Human Rights, 1998.

International Law Students Association. The Case Concerning the Vaccine Trials: The 2000 Philip C. Jessup International Law Moot Court Competition. 1999.

U.S. Advisory Committee on Human Radiation Experiments Final Report. 1995.

Selected journals

Material of interest in this seminar appears from time to time in several journals, none of which covers these areas consistently or always authoritatively.

Selected legal databases.

Selected World Wide Web resources. See below.

World Wide Web Resources and Search Strategy

Interrelationships of international law and the ethics of research on human subjects are little studied and present considerable although surmountable obstacles to study. No single authoritative source or comprehensive set of authoritative sources encompasses these topics. Many seemingly authoritative sources are unreliable. International law consists not only of texts, many of which are hard to find, but also of the behavior of national governments. There is little or no relevant case law. Much of the applicable international law (human rights law and humanitarian law, for examples) is not labeled clearly as concerning research on human subjects. Seemingly comprehensive legal documents may be entirely aspirational. Some of the documents that seem to be international in character are not necessarily law. Moreover, law and interpretations change. Some of the ethics statements are not in themselves law but have been incorporated by reference in regional international law, in local law. Proving what the law is and how it applies in can be a contentious issue. Some individuals who are well known in one or two topical areas but unfamiliar with the nuances in others have written seemingly authoritative but unreliable commentary, even in prominent journals. Some government agency guides and guidance reflect inadequate understanding of the breadth and limitations of applicable law, and government agencies as a matter of policy typically include in their guides only or little more than the law they are directly charged to enforce, and international law is ignored; compliance training and related materials often are similarly narrow. Agencies and their counsel are not necessarily aware of their country's international legal obligations, which may apply to domestic as well as transnational projects. Transnational research projects might be arranged without involving foreign ministries much if at all.

So examination of the interrelationships of international law and the ethics of human subjects research is not a straightforward task. It requires not a narrow, rule-seeking mindset but an understanding of what is definable as international law (the closest to a generally recognized definition is the sources-of-law provision of the Statute of the International Court of Justice; see the ICJ website). It requires an ethical realization that human subjects research is the touching of or intervention in the life of another person. A search for law and policy begins with this understanding, and with a sense of the sources of international law, rather than with a search for rules labeled "research" or the like. That there may not be a rule specifically labeled "research" or "human subjects" does not mean that there is no law to deal with these circumstances. It is important also to know the local legal context and which local and transnational entities are involved. Finally, it is always advisable in documentary research to rely for authenticity and accuracy on a primary documentary source if possible instead of a quotation or summary of it.

These Web sites have been useful direct or indirect sources for research into international law, foreign law, international health, international research, human subjects protections, and related human rights law, humanitarian law, and rule-of-law questions. Like most Web resources, they are of mixed quality, are not necessarily up to date, and are not equally authoritative. This list is not comprehensive.

Resources

Academic

Australian National University Asian Studies WWW Virtual Library
http://coombs.anu.edu.au/WWWVL-AsianStudies.html

Cornell Law School Legal Information Institute: Law by source: Global
http://www.law.cornell.edu/world/

Eubios Ethics Institute
http://www.biol.tsukuba.ac.jp/%7Emacer/index.html

Karolinska Institutet University Library - Links pertaining to Ethics
http://www.mic.ki.se/Diseases/K01.316.html

Michigan State University

African Studies Center, Research, Guidelines for Faculty, Student, and Institutional Collaboration in Africa
http://africa.msu.edu/EthicsII.htm

Asian Studies, Resources
http://www.isp.msu.edu/asianstudies/resources.htm

College of Human Medicine: Center for Ethics and Humanities in the Life Sciences
http://www.bioethics.msu.edu/

Global Access
http://www.msuglobalaccess.net/geo/

Human Research
http://www.humanresearch.msu.edu/

Stanford University Libraries & Academic Resources: Africa South of the Sahara: Health
http://www-sul.stanford.edu/depts/ssrg/africa/health.html

University of Michigan Documents Center: Foreign Government Resources on the Web
http://www.lib.umich.edu/govdocs/foreign.html

Governmental

Australia

National Health and Medical Research Council: Ethical Issues at the NHMRC
http://www.nhmrc.gov.au/issues/index.htm

United States

Advisory Committee on Human Radiation Experiments – Final Report
http://www.eh.doe.gov/ohre/roadmap/achre/report.html

Army, U.S. Military HIV Research Program, International Collaborations in Vaccine Development; and Royal Thai Army Command: joint Armed Forces Research Institute of Medical Sciences: Thailand
http://www.hivresearch.org/areas/thailand.html

National Bioethics Advisory Commission (archival mater)
http://www.georgetown.edu/research/nrcbl/nbac/

Department of Energy: Human Genome Project Information
http://www.doegenomes.org/

Department of Health and Human Services

Centers for Disease Control and Prevention: Public Health Law Program:
http://www.phppo.cdc.gov/od/phlp/

National Institutes of Health
Clinical Trials.Gov
http://www.clinicaltrials.gov/

National Institute of Allergy and Infectious Diseases:
Division of Microbiology & Infectious Diseases:
Malaria Vaccine Development, Status Report
http://www.niaid.nih.gov/dmid/malaria/malariavac.htm
NIAID's HIV Prevention Trials Network, Fact Sheet
http://www.niaid.nih.gov/factsheets/hvtn.htm
HIV Prevention Trials Network, Ethics Guidance
http://www.hptn.org/ResearchEthics/HPTN_Ethics_Guidance.htm

Office for Human Research Protections
http://www.hhs.gov/ohrp/

Department of State: Human Rights Reports
http://www.state.gov/g/drl/rls/hrrpt/2004/index.htm

Library of Congress: Law Library of Congress: Guide to Law Online, Index
http://www.loc.gov/law/guide/guideindex.html

Intergovernmental

African Union
http://www.africa-union.org/

Council of Europe: Legal Affairs: Bioethics
http://www.coe.int/T/E/Legal_Affairs/Legal_co-operation/Bioethics/

European Union: European Medicines Agency
http://www.emea.eu.int/

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
http://www.ich.org/

Efficacy Guidelines
http://www.ich.org/cache/compo/276-254-1.html

Organization for Security and Co-operation in Europe
http://www.osce.org/

United Nations

International Court of Justice
http://www.icj-cij.org/
http://www.lawschool.cornell.edu/library/International_Resources/icj.htm

International Vaccine Institute
http://www.ivi.int/lab/molecular_mb_development.html

Joint United Nations Programme on HIV/AIDS
http://www.unaids.org/en/default.asp

United Nations Educational, Scientific, and Cultural Organization: Bioethics
http://portal.unesco.org/shs/en/ev.php-URL_ID=1372&URL_DO=DO_TOPIC&URL_SECTION=201.html

World Health Organization
http://www.who.int/en/

International Health Regulations
http://www.who.int/csr/ihr/en/

WHO Ethics, trade, human rights, and health law
http://www.who.int/eth/en/

WHO International Digest of Health Legislation
http://www3.who.int/idhl-rils/frame.cfm?language=english

UNICEF-UNDP-World Bank-WHO Special Programme for Research and Training in Tropical Diseases
http://www.who.int/tdr/index.html

World Trade Organization: TRIPS and Public Health
http://www.wto.int/english/tratop_e/trips_e/public_health_e.htm

Non-governmental organizations

AfricaFocus
http://www.africafocus.org/healthexp.php

African Journals Online
http://www.ajol.info/

American Society of International Law:

Electronic Information System for International Law
http://www.eisil.org/index.php?sid=297648529&t=index

ASIL Insights
http://www.asil.org/insights.htm

Council for International Organizations of Medical Sciences
http://www.cioms.ch/

CIOMS: Texts of Guidelines and Other Normative Documents
http://www.cioms.ch/frame_menu_texts_of_guidelines.htm

CIOMS in cooperation with WHO and the Islamic Organization for Medical Sciences International Ethical Guidelines for Biomedical Research Involving Human Subjects *(An IslamicPerspective)*
http://www.islamset.com/ioms/Code2004/Islamic_vision1.html

Doctors Without Borders/Medicins Sans Frontieres
http://www.msf.org/

Indian Journal of Medical Ethics
http://www.issuesinmedicalethics.org/

International Commission of Jurists, ICJ Legal Resource Center
http://icj.org/news_multi.php3?lang=en

International Committee of the Red Cross: ICRC databases on international humanitarian law
http://www.icrc.org/web/eng/siteeng0.nsf/iwpList2/Info_resources:IHL_databases

Malaria Vaccine Initiative
http://malariavaccines.org/

Medical Association of Southeast Asian Nations
http://www.masean.org/

Nuffield Council of Bioethics
http://www.nuffieldbioethics.org/

Organization for Islamic Learning: Issues In Islamic Medical Ethics
http://www.people.virginia.edu/~aas/ismedeth.htm

Science and Development Network

http://www.scidev.net/

Wellcome Trust Biomedical Ethics: Specialist Site Guide
http://www.wellcome.ac.uk/doc_WTD003247.html

World Medical Association Declaration of Helsinki 2004
http://www.wma.net/e/policy/b3.htm

Private

LawMoose World Legal Resource Center Internet Law Library
http://www.lawmoose.com/internetlawlib/1.htm

LawMoose World Legal Resource Center Internet Law Library: Laws of Other Nations
http://www.lawmoose.com/internetlawlib/52.htm

Seminar procedures:

Class format: Lectures, discussions, mini-rounds, simulations.

Required reading: (1) From *Health and Human Rights: A Reader,* as assigned; (2) from journal articles and legal and policy documents, as assigned; these readings are available on the World Wide Web or on the course ANGEL sites or will be distributed. Students need not read *reference texts* (see next paragraph) in full but should be familiar with their origin, structure, and relevance to law and ethics of human subjects research. Much of this material will be used in more than one class session. Be prepared to discuss the readings.

Reference texts: Legal documents for reference. *Reference texts* will be analyzed in class discussions. These documents are available in *Health and Human Rights: A Reader,* on the World Wide Web, or on ANGEL. Students should at least skim these documents and then be able to find and use cited sections.

Mini-rounds: A portion of most class sessions will be devoted to mini-rounds on transnational human-subjects situations or proposals that raise ethical and legal issues. Mini-rounds should focus on specific factual situations, not general policy questions, although the situations may have implications for policy.

How it works: Responsibilities for mini-rounds will be assigned. The presenter chooses the problem, which may be hypothetical or drawn from experience, news reports, or current controversies, but not from existing case studies or textbook-type exercises. The problem should not be complex. Mini-rounds are not competitive. The presenter has three minutes in which to summarize the problem. The discussant has five minutes to suggest (1) the procedural setting in which the problem should be addressed or resolved,

and why, and (2) what ethical and legal considerations should apply, and why. Then seven minutes are devoted to open questioning and discussion.

These are analytical discussions, not readings or recitations. Presentation, commentary, and discussion should be analytical, not conclusory. Advance documentation: Avoid it if possible; otherwise keep it to an absolute minimum. For mini-rounds, there are no rewards for length, volume, or bibliography. Presenters should send a very short précis and any essential accompanying documentation (documents, not Web links) to the instructor and other students by e-mail at least two days in advance. Discussants should distribute any essential documentation (documents, not Web links) at least two days in advance by e-mail to the instructor and students.

Simulations: As assigned.

Grading: Based on written submissions (80%) and class participation (20%). Letter grades, numerical grades, or P-NP, depending on the school in which the student seeks credit.

Written assignments: One critical review of one of the articles or essays from among the assigned readings from each of four of the nine numbered Course Units; within these limits, students choose the materials they wish to review; a total of four critical reviews is required for the course. Each critical reviews is due no later than seven days after the unit on which it is based. Critical reviews based on other units are due one day prior to the class's beginning of the unit from which that reading is selected.

Format for critical reviews: Typed, 2-3 single-spaced pages each; send to instructor by e-mail (send to: schatzg@msu.edu). Write plainly, and make the order of argument clear. The form that a critical evaluation or an essay takes necessarily depends on the material. Generally, a critical review should include these elements:

For all critical reviews:

- Bibliographic citation for the selection reviewed, and, if possible, specific references (including page or section) for material quoted or summarized. In using quotations and paraphrases, make clear who is saying what.
- What is the author trying to say?
- Does the author say that?
- What facts and reasoning does the author use to support the position taken?
- Are there significant contrary facts and views?
- What relevant law, if any, is omitted?
- How does the author deal contrary facts and views and with relevant law? Is the author fair?
- On balance, is the author's position supportable?
- Do you agree? Why or why not?
- How do you deal with the significant facts and views contrary to yours?

- Your conclusion?

Reading tips:

For other materials, keep in mind:

News articles or series:

- What is being reported?
- Are the sources apparently authoritative? Are critically important texts or statements quoted, with context given? Or are they paraphrased?
- Is the relevant law, if any, reported accurately?
- Are there significant omissions in the reporter's account?
- How does the reporter deal with controversy? Is the account fair?
- Do you agree with the reporter's interpretation? Why or why not?
- What are the most important apparent implications of the situation reported?

Policy documents:

- Who wants what, why, how, and when?
- What interests are represented among the authors?
- What important interests are not represented?
- What important facts, background information, and relevant law are omitted?
- If legal issues or sources are mentioned, are they treated fairly and authoritatively?
- How do the authors deal with contrary views and law?
- Is the policy intended to be binding? Under what authority? On whom? By whom? How is it to be enforced? Remedies?
- If the document is in response to questions presented, were those questions fairly stated? How do the authors respond to those questions?
- Do the recommendations flow logically from the facts adduced by the authors?
- Irrespective of the recommendations, how do the authors contribute to clearer understanding of the issues addressed? Or do they?

Legal documents other than judicial opinions

- Source of authority?
- Is it consistent with existing international and local legal authority?
- If a bill, law, or regulation: How is it intended to work in practice? What protections is it supposed to provide? For whom? Who is obligated? What is supposed to be required? Does it bind governmental entities and

persons? How is it to be enforced? By whom? What remedies are provided?
- When is full compliance expected?
- What has been and what do you expect will be the effect of this document?
- Do you agree with this approach? Why or why not?

Judicial opinions

- Who are the parties? Who brought the original action? For what? Cause of action? What basic facts were alleged?
- Which court is ruling here?
- If an appellate decision: What happened in the courts below?
- What specific legal and factual issues are before this court?
- What did this court decide on these specific issues? What did this court order?
- What is the court's legal rationale? What is the court's policy rationale?
- Concurring and dissenting opinions?
- What does this decision imply for the parties? For society?
- Do you think this court decided these issues rightly? Why or why not?

Preparation for class participation:

Prior to each unit:
- Re-read the unit description.
- Read all assigned readings in Mann, et al., *Health and Human Rights: A Reader*.
- Read at least two of any additional readings listed.
- Familiarize yourself with the reference texts.
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Prior to each class session:
- Prepare for mini-rounds and simulation(s) as assigned.

Supplementary: On-campus and nearby events of possible interest will be announced. Students are encouraged but not required to attend.

Scheduling, attendance, cancellations: If you do not expect to attend, please notify instructor in advance. Classes canceled due to weather or other exigencies will be made up. Make-up sessions can be arranged for students who have to miss a class session. Cancellations due to weather: See MSU policy: http://keywords.msu.edu/viewpathfinder.asp?id=67#401

Religious observance: University policy is to permit students and faculty/academic staff to observe those holidays set aside by their chosen religious faith. It is the responsibility of those students who wish to be

absent to make arrangements in advance with their instructors. See MSU policy: http://www.hr.msu.edu/HRsite/Documents/Faculty/Handbooks/Faculty/Instruction/v-religiousobservance.htm

TOPICAL OUTLINE

(All units will be covered. Timing depends on semester calendar. Reading assignments may be updated.)

Unit 1 Week 1

Introduction to the interrelationships of international law and biomedical ethics. How civil law, common law, and religious legal cultures converge or diverge in public international law in the context of disease burden, health needs, research questions, and organizational imperatives. Medical ethical traditions. Classic and continuing concerns: inherent dignity of the human person; individual in society; natural rights; limitations on government power; ends v. means; utilitarianism, consequentialism, ethical relativism, coercion; humanitarian and human rights law. Bad examples. Legal and ethical responses.

What legal and ethical precepts bearing on human-subjects research arise from the same concerns?

Why are human rights arguments used both to encourage and to restrict research on human beings?

If a proposed act (or omission) is permissible, might it still be wrong? If it is impermissible, by ethical or legal standards, might it nevertheless be right? What moral precepts are universal?

Why do physicians have special obligations?

Why do all researchers have special obligations?

Readings:

In *Health and human rights: A reader:*

Mann, Jonathan M., Sofia Gruskin, Michael A. Grodin, and George J. Annas. Introduction. 1-3.

Mann, Jonathan M., Lawrence Gostin, Sofia Gruskin, Troyen Brennan, Zita Lazzarini, and Harvey Fineberg. Health and Human Rights. Ch.1; 7-20.

International Federation of Red Cross and Red Crescent Societies and François-Xavier Bagnoud. Human Rights: An Introduction. Ch. 2; 21-28.

International Federation of Red Cross and Red Crescent Societies and François-Xavier Bagnoud. Public health: An introduction. Ch. 3; 29-34.

Unit 2 Week 2

Contexts and ethical quandaries in international biomedical and behavioral research. Disease burdens, public health, research imperatives, institutional imperatives, therapeutic misconceptions, and confronting and bounding questions of cultural respect where law, ethical concerns, and tradition differ.

When we propose to or conduct or oversee research on human beings in other cultures, how might we determine what is right and wrong?

When is research on human beings beneficial? To whom?

Readings:

In *Health and human rights: A reader:*

Annas, George J. 1999. Questing for grails: Duplicity, betrayal, and self-deception in postmodern medical research. Ch. 21; 312-335.

Ijsselmuiden, Carel. Faden, Ruth. Research and Informed Consent in Africa—Another Look. Ch. 23; 363-372.

Appelbaum, Paul S. "Clarifying the Ethics of Clinical Research: A Path toward Avoiding the Therapeutic Misconception." *American Journal of Bioethics* 2, no. 2 (2002): 22-23. <Appelbaum-clinresmisconception.pdf>

Bhutta, Zulfiqar A. "Beyond Informed Consent." *Bulletin of the World Health Organization* 82 (2004): 771-777. <771_bhutta_beyondinformedconsent.pdf.pdf>

DeChambenoit, Gilbert. Ethics in the north and in the south: The african elites should not be silent. *African Journal of Neurological Sciences*, 24 June 2005. <dechambenoit2005africansshouldnotbesilentaboutunethicaltrials.r

tf>

Doumbo, Ogobara K. It Takes a Village: Medical Research and Ethics in Mali, *Science* 4 February 2005 vol. 307 pp. 679-681. <science2005feb4ittakesavillage.pdf>

C.S. Molyneux, D.R. Wassenaar, N. Peshua, K. Marsh, 'Even if they ask you to stand by a tree all day, you will have to do it (laughter)…!': Community voices on the notion and practice of informed consent for biomedical research in developing countries, Social Science & Medicine 61 (2005) 443–454. <consent-standbyatree-socscimed2005.pdf>

Simulation 1: <simulation-incidence.doc>

Unit 3 Weeks 3, 4, 5

Emerging state practice. Nuremberg Code. Continuing research abuses. Belmont Report: ethical principles for regulation and regulatory interpretation. U.S. regulatory structure for U.S. funding of international research and U.S. approval of research supporting applications for drug approval. Requirements include: just selection of subjects; benefits>burdens; ethics review; informed consent; special concern for vulnerable subjects; confidentiality; safety monitoring and oversight. Bioethical precepts (Belmont, Helsinki, Council for International Organizations of Medical Sciences). Roles of international organizations. World Health Organization programs and guidelines.

What do the ethical precepts for protection of human subjects of research provide in common? How do they differ?

How protective are ethical guidelines? Who enforces? How? How are violations remedied?

How do states' own regulatory practices have effect internationally?

Readings:

Faunce, T.A. "Will International Human Rights Subsume Medical Ethics? Intersections in the Unesco Universal Bioethics Declaration." *Journal of Medical Ethics* 31 (2005): 173-178. <faunce2005jme-unescohumanrightsbioethics>

Reference texts:

In *Health and human rights: A reader:*

Trials of War Criminals Before the Nuremberg Military Tribunals Under Control Council Law 10; 1947; excerpted. Judges Harold Walter Beals, and Johnson Crawford. "The Proof as to War Crimes and Crimes Against Humanity," and "Permissible Medical Experiments," 297-299.

Australia National Health and Medical Research Council. V*alues and Ethics: Guidelines for Ethical Conduct in Aboriginal and Torres Strait Islander Health Research*., 2003. <AustraliaNHMRC2003GuidelinesEthicalConductAboriginalTorres StraitIslanderHealthResearch.pdf>

Council for International Organizations of Medical Sciences (CIOMS). 1991. 1991 International Guidelines for Ethical Review of Epidemiological Studies. Geneva: Council for International Organizations of Medical Sciences (CIOMS). <cioms-epi-1991.doc>

Council for International Organizations of Medical Sciences (CIOMS). 2005. Draft International Guidelines for Ethical Review of Epidemiological Studies. Geneva: Council for International Organizations of Medical Sciences. <cioms-epi-draftrevision2005>

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: Council for International Organizations of Medical Sciences. <cioms.doc>

International Conferences on Harmonisation. 1996. E6: Good Clinical Practice: Consolidated guideline. <ICH-E6 GCP guideline.pdf>

International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use. 1997. ICH Harmonised Tripartite Guideline: General Considerations for Clinical Trials, E8. <ICH-E8 GCP guideline.pdf>

U.N. UNAIDS. *Ethical considerations in HIV preventive vaccine research, UNAIDS Guidance Document, UNAIDS/04.07E (English original, May 2000).* <jc072-ethicalcons_en_pdf.pdf >

U.N. United Nations Educational, Scientific and Cultural Organization. *First Intergovernmental Meeting of Experts Aimed at Finalizing a Draft Declaration on Universal Norms on Bioethics, 4-6 April*

2005, Final Report, Shs/Est/05/Conf.203/5, Paris, 6 April 2005. <unesco2005april-draftdeclaration-139593e.pdf>

U.N. World Health Organization. UNICEF-UNDP-World Bank-WHO Special Programme for Research and Training in Tropical Diseases. Operational Guidelines for Ethics Committees That Review Biomedical Research. TDR/PRD/ETHICS/2000.1. 2000. <tdrethics.pdf>

U.N. World Health Organization. UNICEF-UNDP-World Bank-WHO Special Programme for Research and Training in Tropical Diseases. Surveying and Evaluating Ethical Review Practices: a complementary guideline to the Operational Guidelines for Ethics Committees That Review Biomedical Research. TDR/PRD/Ethics/2002.1. 2002. <tdrethics2.pdf>

U.S. Alien Tort Claims Act and related statutes. <28usc1350etal>

U.S. Department of Health, Education and Welfare, Office of the Secretary, National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. Ethical Principles and Guidelines for the Protection of Human Subjects of Research (Belmont Report). 44 Fed. Reg. 23,192 (April 18, 1979). <Belmont Report.rtf>

U.S. Department of Health and Human Services, 45 C.F.R. pt. 46—Protection of Human Research Subjects. <45CFR46.pdf>

U.S. Department of Health and Human Services, Office for Human Research Protections. International Compilation of Human Subject Research Protections. June 20, 2005. <HSPCompilation.pdf>

U.S. Department of Health and Human Services, Food and Drug Administration. 21 C.F.R. pt. 50—Protection of Human Subjects. <21CFR50.pdf> 21 C.F.R. pt. 56—Institutional Review Boards. <21CFR56.pdf>

World Medical Association, Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects. September 10,2004. <wma declaration of helsinki 2004.pdf >

Simulation 2: <simulation-Dear.doc>

Unit 4 **Weeks 6, 7, 8**

International law defined and applied. Sources of law: International agreements and customary international law, as evidenced particularly in state practice. Enforceability. How law and guidelines differ. Nuremburg, humanitarian, and human rights law. Informed consent as a universal legal requirement.

How do international law and municipal (national) law differ?

How do we prove what the law is?

Readings:

Schatz, Gerald S. International Health Regulations: New Mandate for Scientific Cooperation, ASIL Insight, American Society of International Law (August 2, 2005) World Wide Web available: http://www.asil.org/insights/2005/08/insights050802.html; MSU ANGEL available: <ASILInsight-IHR-schatz-2005aug2.doc>

Schatz, Gerald S. International law and biomedical ethics. Published as diritto internazionale e bioetic (Giovanni Russo, trans.) In *Enciclopedia di bioetica e sessuologia*. Giovanni Russo, ed.:660. Rome: Elledici - CIC Edizioni Internazionali Leumann, 2004. <DICT1SCHATZpublished.rtf>

Schatz, Gerald S. Introductory Note to World Health Organization: Revision of the International Health Regulations, 44 International Legal Materials 1011 (2005). <IHR-ILM-2005.rtf>

Reference texts:

In *Health and human rights: A reader:*

U.N. Universal Declaration of Human Rights. 1948. App. A; 453-457.

U.N. International Covenant on Economic, Social, and Cultural Rights. 1966. App. B; 458-465.

U.N. International Covenant on Civil and Political Rights. 1976. App. C; 466-479.

Council of Europe, Convention on Human Rights and Biomedicine, Oviedo, April 4, 1997. <COEHRBiomedtext.doc>. Ratifications, as of July 5, 2005. <COEHRBiomedRatifications.pdf>.

U.N. Statute of the International Court of Justice. <ICJstatute.doc>

U.N. World Health Organization. International Health Regulations. Text approved May 23, 2005. <WHA58_3-en.pdf>

Vienna Convention on the Law of Treaties, May 22, 1969, 1155 U.N.T.S. 331. <Vienna Convention on the Law of Treaties.doc>

Schatz, Gerald S. 2005. International humanitarian and human rights law in war and other armed conflict. Center for Ethics and Humanities in the Life Sciences, College of Human Medicine, Michigan State University, March 14, 2005. <genevapoints.doc>

Unit 5 Weeks 9, 10

How legal and ethical concerns interrelate and apply in practice. Legal, political, societal contexts for regulatory efficacy; legal and ethical problems of human subjects research in unstable societies. Abuses, cultural sensitivity, cultural rationalization; critiques; renewed concerns for equivalent protections.

Is research on human beings in Uzbekistan currently internationally legal and ethical if intended to benefit the society by way of building health delivery systems capacity and if prospective research subjects agree to sign consent forms? Why or why not?

Readings:

Angell, Marcia. "The Ethics of Clinical Research in the Third World." *New England Journal of Medicine* 337, no. 13 (1997): 847-849. <nejm1997angell.doc>

Appelbaum, Paul S. "Abuses of Law and Psychiatry in China,." *Psychiatric Services* 52, no. 10 (2001): 1297-1298. <abuses of law and psychiatry in china.pdf>

Cyranoski, David. "Chinese Clinical Trials: Consenting Adults? Not Necessarily...,." *Nature* 435 (2005): 138. <nature2005maychinaabuses.doc>

People's Republic of China. PRC Regulations on Informed Consent and Protection of Human Subjects in Biomedical Studies, Informed Consent and Privacy in China's Laws and Other Documents, excerpts from Interim Measures for the Administration of Human Genetic Resources, promulgated by the Ministry of Science and Technology and the Ministry of Health, entered into effect on June 10, 1998, and excerpts from Guidelines on Ethical Review of Medical Research, promulgated by the Committee on Research Involving Human Subjects, promulgated by the Ministry of Health

and enforced on December 1, 1998, but with the establishment of a new Ethics Committee of the Ministry of Health; unofficial translations. <PRCpatient-protection.html.>

Préziosi, Marie-Pierre, Ablaye Yam, Malick Ndiaye, Aminata Simaga, François Simondon, and Steven G.F. Wassilak. "Practical Experiences in Obtaining Informed Consent for a Vaccine Trial in Rural Africa." *New England Journal of Medicine* 336, no. 5 (1997): 370-373. <nejm1997-Practical Experiences in Obtaining Informed Consent for a Vaccine Trial in Rural Africa.rtf>

Tomlinson, Tom, et al., submission to Office for Human Research Protections, May 6, 2005, In re: Notice, Protection of Human Subjects, Proposed Criteria for Determinations of Equivalent Protection, 70 Fed. Reg. 15,322 (2005). <ohrpecmt2005may.rtf>

U.S. Embassy Beijing, Human Research Subject Protection in China: Implications for U.S. Collaborators: A November 2000 report from U.S. Embassy Beijing. <Human Research Subject Protection in China.doc>

Washington Post. "Body Hunters" series. December 2000. <Body Hunters-Washington Post-Dec 2000.doc>

Simulation 3:
<Simulation-WHO research in developing countries hypothetical.doc>

Unit 6 Week 11

Developing regional and national bioethics law: European Union, Asia, Latin America, Africa, Middle East. Commonalities.

What ethical and legal precepts are shared in emerging regional international law concerning research on human subjects? How do the regional legal approaches differ?

Reference texts:

E.U. Directive 2001/20/EC OF the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use (Official Journal L 121, 1/5/2001 p. 34 - 44). <2001-20-EC.pdf>

Pan-African Bioethics Initiative (PABIN) Good Health Research Practices in Africa, Third Conference, 28-30 April 2003, United Nations Conference Hall, Addis Ababa, Ethiopia, report. <pabin3rd.pdf>

Pan American Health Organization, Area of Information and Knowledge Management, Research Promotion and Development Unit, Research Grants Program (dd/ikm/rc/rgp). Ethical guidelines for research involving human subjects (24/may/2002). <paho-ethics_guide.doc >

South Africa Medical Research Council. 2003. Guidelines for Ethics for Medical Research: Book 5: Guidelines for HIV Preventive Vaccine Research. <southafricaethicsbook5.pdf>

Unit 7 Weeks 12, 13

Major controversies: Vaccine trials; behavioral research; studies in nature; commercial drug testing.

What questions have the major international human-subjects research controversies commonly posed for law and ethics

Readings:

In *Health and human rights: A reader:*

Annas, George J. and Michael A. Grodin. 1999. Human Rights and Maternal-Fetal HIV Transmission Prevention Trials in africa. Ch. 24; 373-379.

Abdullahi v. Pfizer, No. 01 Civ. 8118, 2002 U.S. Dist. LEXIS 17436 (defendant's motion to dismiss complaint for failure to state claim den'd, defendant's motion to dismiss complaint on forum non conveniens grounds granted). <abdullahi-sdny-2002.doc>

Abdullahi v. Pfizer, Nos. 02-9223(L), 02-9303(XAP), slip op. (2d Cir. Oct. 8, 2003) (vacating, remanding). <abdullahi-2dcir-02-9223_so.pdf>

Andrews, Jason. 2005. U.S. Military Sponsored Vaccine Trials and La Resistance in Nepal. *American Journal of Bioethics* 5, no. 3: W1. <vaccine-us-nepal-ajob-2005.rtf>

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Medicine 351, no. 1: 6-8. <nejm2005jul7-blochemarks-doctorsandinterrogatorsatgtmo.pdf>

Brown, David. "U.S.-Backed Aids Vaccine Trial in Thailand Is Questioned." *Washington Post*, January 19, 2004 2004, A2. <U.S.-Backed AIDS Vaccine Trial in Thailand Is Questioned>

Burton, Dennis R., Ronald C. Desrosiers, Robert W. Doms, Mark B. Feinberg, Robert C. Gallo, Beatrice Hahn, James A. Hoxie, Eric Hunter, Bette Korber, Alan Landay, Michael M. Lederman, Judy Lieberman, Joseph M. McCune, John P. Moore, Neal. Nathanson, Louis Picker, Douglas Richman, Charles Rinaldo, Mario Stevenson, David I. Watkins, Steven M. Wolinsky, and Jerome A. Zack. "A Sound Rationale Needed for Phase Iii Hiv-1 Vaccine Trials." *Science* 303 (2004): 316. <sound rationale needed for phase iii trials sci 2004.pdf>

Nundy, Samiran & Chandra M. Gulhati, A New Colonialism? — Conducting Clinical Trials in India, *New England Journal of Medicine* April 21, 2005, 352;16: 1633-1636. <NEJM2005apr21NundyNewColonialismClinTrials-16331.pdf>

U.S. Department of Health and Human Services, Office of Inspector General (Janet Rehnquist, Inspector General). *The Globalization of Clinical Trials: A Growing Challenge in Protecting Human Subjects, OEI-01-00-00190.* September 2001. <a542_dhhsigglobalizationofclin.pdf.pdf>

Simulation 4: <simulation-j-adapt.rtf>

Unit 8 Week 14

Emerging issues: Intellectual property, distributional justice controversies, genetic information, biological samples, big-project imperatives.

International law and research ethics touch on distributional-justice issues relating to human-subjects research, but with what effect?

What does distributional justice mean in these contexts? Do research subjects have a right to distributional justice? Why or why not?

In what settings might distributional-justice issues relating to human-subjects research be addressed? By whom?

Should a government have the right to sell its people's individual genetic information?

How should the international market in human tissues for research be regulated?

How does the TRIPS public-health provision actually play out?

Readings:

Angell, Marcia. "Investigators' Responsibilities for Human Subjects in Developing Countries." *New England Journal of Medicine* 342, no. 13 (2000): 967-969. <nejm2000angellinvestigatorsresponsibilitiesforhumansubjectsindevelopingcountries.doc>

Lie, R.K., E. Emanuel, C. Grady, and D. Wendler. 2004. The standard of care debate: The declaration of helsinki versus the international consensus opinion. *Journal of Medical Ethics* 2004, no. 30: 190-193. <emanuelhelsinkibestcarecare2003.pdf>

Reference texts:

World trade Organization. Agreement on Trade-Related Aspects of Intellectual Property Rights [TRIPS], Annex 1C to the Final Act Embodying the Results of the Uruguay Round of Multilateral Trade Negotiations, and Agreement Establishing the World Trade Organization, Marrakesh, April 1994. <27-trips.pdf>

World Trade Organization. Ministerial Declaration on the TRIPS agreement and public health. November 14, 2001. <wto-doha2001-trips.rtf>

Unit 9 Week 15

Review. Critiques of applicable law and ethical precepts. Continuing student concerns. Reconciling ethical, legal, medical concerns.

What elements of human-subjects protection are universal requirements in international law?

If a proposed or actual course of conduct is illegal, can it still be ethical? Why or why not? If a proposed or actual course of conduct is legal, is it therefore ethical? Why or why not?

Where do international law and the ethics of human-subjects research coincide? Where do they conflict? Should these conflicts be reconciled? Why? How?

Readings:

Benatar, Solomon R. "Towards Progress in Resolving Dilemmas in International Research Ethics." *Journal of Law, Medicine & Ethics* 32, no. 4 (2004): 574-582. <benatar-2004-jlme-TowardsProgressinResolvingDilemmasinInternationalResearchEthics.pdf>

Berlin, Isaiah. 1958. Two concepts of liberty. In *Isaiah berlin: The proper study of mankind, an anthology of essays*, ed. Henry Hardy and Roger Hausheer:191-242 (1997). <berlin-2conceptsofliberty.doc>

Emanuel, E., D. Wendler, and Grady C. 2000. What makes clinical research ethical? *Journal of the American Medical Association* 283, no. 20: 2701-2711. <emanuel-whatmakesresearchethical-jama2000.pdf>

Emanuel, Ezekiel J., David Wendler, Jack Killen, and Christine Grady. 2004. What makes clinical research in developing countries ethical? The benchmarks of ethical research. *Journal of Infectious Diseases* 2004, no. 189: 930-937. <Benchmarks. EE,DW,JK,CG in JID.pdf>

Fluss, Sev S. "Research Ethics: The Current International Configuration." *Journal of Law, Medicine & Ethics* 30, no. 4 (2004): 596-603. <fluss2004-jlme-researchethics-currentinternationalconfiguration.pdf>

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