Ethical and Regulatory Aspects of Clinical Research

October 1, 2025 – November 12
8:30-11:30 am
All material to be delivered by NIH Videocast and CANVAS
8.21.25- DRAFT
SYLLABUS

Session	Date	Topics	Faculty
1	10/1/25	Introduction/Framework/History/Institutional Review Boards	Taylor
2	10/8/25	Informed Consent/Decision Making/Capacity Assessment	*Dickert*, Kim, Brintnall-Karabelas (NIMH)
3	10/15/25	Study Design/Risk-Benefit/Social Value/Inclusion of Children in Research	Taylor, Wendler, *Shah*
4	10/22/25	Equity/Subject Selection/Recruitment and Retention	*Asada*, Taylor**,** *Langford*
5	10/29/25	International/Standards of Care/Post-trial Obligations/Community Engagement	Rid, *Millum, Kamuya*
6	11/5/25	Genomic Sequencing, Return of Results from Field, Conducting Genetic Research with Indigenous Communities	Berkman, Sapp (NHGRI), *Claw*
7	11/12/25	FDA, *TBA* , Xenotransplantation	*Lynch, TBA, Maschke*

Guest Lecturers (unaffiliated with the NIH) noted in ***Italics***

Overall Course Objectives

Upon completion of this course, you should be able to:

- Utilize a systematic framework for evaluating the ethics of a clinical research protocol.
- Identify, define, and consider ethical issues in the conduct of human subject research.
- Apply appropriate codes, regulations, and other documents governing the ethical conduct of human subject research to their own research.
- Describe the purpose, function, and challenges of IRBs.
- Identify the critical elements of informed consent and strategies for implementing informed consent for clinical research.
- Identify and apply relevant considerations for assessment of research risks and benefits
- Explore the ethical requirement of fair subject selection and its application.
- Identify challenges and opportunities related to genetics research and research with stored samples
- Appreciate ethical challenges with conducting international collaborative research in low- and middle-income countries
- Understand the role of the Food and Drug Administration in the oversight of the drug development process
- Explore the scientific and ethical challenges in the development, review and oversight of novel interventions

Session 1: *October 1* - Introduction/Framework/History/Institutional Review Boards

Objectives:

- Identify and describe the ethical principles and historical basis that provide guidance for the ethical conduct of research.
- Describe important cases in the history of research and how cases shaped current ethical considerations, and regulations for clinical research.
- Describe ethical framework to be applied throughout course
- Understand the basis of the role and responsibilities of an Institutional Review Board

Time	Topic	Faculty
8:30-8:45	Introduction to Course	Holly Taylor, PhD MPH NIH Clinical Center Department of Bioethics
8:45-9:30	Framework for Ethical Conduct of Research	
9:30-9:40	Discussion	
9:40-10:25	History of Research Ethics	
10:25-10:35	Discussion	
10:35-10:50	Break	
10:50-11:20	Institutional Review Boards	Holly Taylor, PhD MPH NIH Clinical Center Department of Bioethics
11:20-11:30	Discussion	

Readings and Resources

Emanuel EJ, Wendler D, Grady C. What makes clinical research ethical? *JAMA*. 2000 May 24-31;283(20):2701-11.

Emanuel EJ, Wendler D, Killen J, Grady C. What makes clinical research in developing countries ethical? The benchmarks of ethical research*. Journal of Infectious Diseases*. 2004 Mar 1;189(5):930-7.

Part I: Scandals and Tragedies of Research with Human Participants: Nuremberg, the Jewish Chronic Disease Hospital, Beecher and Tuskegee. Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary (2003) Edited by EJ Emanuel, RA Crouch, JD Arras, JD Moreno, Grady C. Johns Hopkins University Press: Baltimore (Overview and Chapters 1-4; pp. 1-25).

Public Responsibility in Medicine and Research (PRIM&R) History of Research Ethics Interactive Timeline https://primr.org/timeline/

Beecher HK. Ethics and clinical research. *NEJM.* 1966 Jun 16;274(24):1354-60.

Jones DS, Grady C, Lederer S. **"**Ethics and Clinical Research" — The 50th Anniversary of Beecher's Bombshell**.** *NEJM* 2016; 374(24): 2393-2398.

Grady C. Institutional Review Boards: Purpose and Challenges. *Chest*. 2015; 148(5):1148-55.
Strauss DH, White SA, Bierer BE. Justice, Diversity, and Research Ethics Review. *Science* 2021;371(6535):1209-1211.

Strauss DH, White SA, Bierer BE. Justice, Diversity, and Research Ethics Review. *Science* 2021;371(6535):1209-1211.

Core Research Ethics Codes

Nuremberg Code (1949) as published in the British Medical Journal (1996) 313:1448 https://www.bmj.com/content/313/7070/1448.1

Declaration of Helsinki (also known as World Medical Association Declaration Of Helsinki – Ethical Principles For Medical Research Involving Human Subjects) (2013) https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/

National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research **Belmont Report** (also known as Ethical Principles and Guidelines for the Protection of Human Subjects of Research) (1979) https://www.hhs.gov/ohrp/regulations-and-policy/belmont-report/read-the-belmont-report/index.html

Council for International Organization of Medical Sciences (CIOMS). **International Ethical Guidelines for Health-related Research Involving Humans** (2016): https://cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/

US Federal Regulations

HHS Common Rule, Protection of Human Subjects 45 CFR 46 (2018) https://www.hhs.gov/ohrp/regulations-and-policy/regulations/45-cfr-46/revised-common-rule-regulatory-text/index.html

FDA, Protection of Human Subjects 25 CFR 50 (2012) https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-50

FDA, Institutional Review Board 25 CFR 56 (1981) https://www.ecfr.gov/current/title-21/chapter-I/subchapter-A/part-56

Session 2: *October 8* - Informed Consent/Decision Making/Capacity Assessment

Objectives:

- Describe the ethical basis of and elements of informed consent, strategies for implementation, and areas for improvement.
- Identify the ethical challenges of including persons in research who have decreased capacity to consent, and discuss the implementation of appropriate additional safeguards
- Understand the practice of implementing appropriate safeguards to assess capacity

Time	Topic	Faculty
8:30-9:20	Informed Consent	Neal Dickert, MD PhD Associate Professor Thomas R. Williams Professor of Medicine Emory University School of Medicine, Division of Cardiology, ECCRI Co-Director, Emory Health Services Research Center Emory University Rollins School of Public Health, Department of Epidemiology Emory Center for Ethics
9:20-9:30	Discussion	
9:30-10:20	Research Involving Persons at Risk for Impaired Decision-Making	Scott Kim, MD PhD NIH Clinical Center Department of Bioethics
10:20-10:30	Discussion	
10:30-10:40	Break	
10:40-11:20	Capacity Assessment in Practice	Julie Brintnall-Karabelas, MSW LCSW-C Human Subjects Protection Unit National Institute of Mental Health
11:20-11:30	Discussion	

Readings and Resources

Part V: Informed Consent in Research Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary (2003) Edited by EJ Emanuel, RA Crouch, JD Arras, JD Moreno, Grady C. (Johns Hopkins University Press: Baltimore) (Overview and Chapters 30-32; pp. 189-210; Chapters 36-37; pp. 216-223)

Dickert NW, Eyal N, Goldkind SF, Grady C, Joffe S, Lo B, Miller FG, Pentz RD, Silbergleit R, Weinfurt KP, Wendler D, Kim SYH. Reframing Consent for Clinical Research: A Function-Based Approach. *American Journal of Bioethics*. 2017 Dec;17(12):3-11

Dickert NW, Scicluna VM, Adeoye O, Angiolillo DJ, Blankenship JC, Devireddy CM, Frankel MR, Goldkind SF, Kumar G, Ko YA, Mitchell AR, Nogueria RG, Parker RM, Patel MR, Riedford M, Silbergleit R, Speight CD, Spokoyny I, Weinfurt KP, Pentz RD. Emergency Consent: Patients' and Surrogates' Perspectives on Consent for Clinical Trials in Acute Stroke and Myocardial Infarction. *J Am Heart Assoc.* 2019 Jan 22;8(2):e010905.

Grady C. Enduring and Emerging Challenges of Informed Consent, *NEJM* 2015; 372(9):855-62.

FDA. Informed Consent Guidance for IRBs, Clinical Investigators, and Sponsors (2023) https://www.fda.gov/regulatory-information/search-fda-guidance-documents/informed-consent

Kim SYH. Chapter 8: Capacity to Consent to Research, from Evaluation of Capacity to Consent to Treatment and Research. Oxford University Press 2010

Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation 2021 https://policymanual.nih.gov/3014-403

National Institute of Mental Health, Human Subjects Research Protections Toolkit https://www.nimh.nih.gov/sites/default/files/documents/research/research-conducted-at-nimh/scientific-director/office-of-clinical-director/administrative-research-support/NIMH_human_subjects_research_protections_toolkit.pdf

Session 3: *October 15* - Study Design/Risk-Benefit/Inclusion of Children in Research

- Identify ethical issues in the design and conduct of clinical trials
- Identify and apply relevant considerations for assessment of research risks and benefits
- Consider the unique aspects of the inclusion of children in research

Time	Topic	Faculty
8:30-9:00	Introduction to Study Design	Holly Taylor, PhD MPH NIH Clinical Center Department of Bioethics
9:00-9:10	Discussion	
9:10-10:00	Risk/Benefit/Social Value	David Wendler, PhD NIH Clinical Center Department of Bioethics
10:00-10:10	Discussion	
10:10-10:25	Break	
10:25-11:20	Ethical Inclusion of Children in Research	Seema Shah, JD Founders' Board Professor of Medical Ethics Professor, Pediatrics Director of Research Ethics at Lurie Children's Hospital Feinberg School of Medicine Northwestern University
11:20-11:30	Discussion	

Readings and Resources

Part III: The Ethics of Trial Design. Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary (2003) Edited by EJ Emanuel, RA Crouch, JD Arras, JD Moreno, Grady C. (Johns Hopkins University Press: Baltimore) (Chapter 11; pp. 103-107, Chapters 13-15; pp. 113-126; Chapters 20-21 pp. 144-149)

Part VIII: The Behavior of Clinical Investigators: Conflicts of Interest. Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary (2003) Edited by EJ Emanuel, RA Crouch, JD Arras, JD Moreno, Grady C. (Johns Hopkins University Press: Baltimore) (Chapter 74; pp. 378-381)

World Health Organization. Guidance for best practices for clinical trials. https://www.who.int/publications/i/item/9789240097711

Rid A, Emanuel EJ, Wendler D. Evaluating the risks of clinical research. JAMA. 2010 Oct 6;304(13):1472-9.

Rid A. Judging the Social Value of Health-Related Research: Current Debate and Open Questions. *Perspectives in Biological Medicine*. 2020;63(2):293-312.

Shah S. The Ethics of Pediatric Research. Chapter 34 in The Oxford Handbook of Research Ethics Edited by AS Iltis, D MacKay. 2024. Oxford University Press: New York. 683–698.

Mintz K, Jardas E, Shah S, Grady C, Danis M, Wendler D. Enrolling Minors in COVID-19 Vaccine Trials. Pediatrics. 2021 Mar;147(3):e2020040717.

For those less familiar with drug/vaccine development process

Food and Drug Administration. Drug Development Process. https://www.fda.gov/patients/learn-about-drug-and-device-approvals/drug-development-process

National Institutes of Health. NIH Clinical Research Trials and You. The Basics. https://www.nih.gov/health-information/nih-clinical-research-trials-you/basics

Session 4: *October 22* - Equity/Subject Selection/ Recruitment and Retention

Objectives:

- Consider what a commitment to equity can mean in the design, implementation and reporting of clinical research
- Explore the ethical requirement of fair subject selection and its application
- Identify ethical issues and strategies in the recruitment and retention of subjects

Time	Topic	Faculty
8:30-9:15	Equity in Clinical Research	Yukiko Asada, PhD Adjunct Professor Department of Health, Aging & Society McMaster University
9:15-9:25	Discussion	
9:25-10:10	Subject Selection	Holly Taylor, PhD MPH NIH Clinical Center Department of Bioethics
10:10-10:20	Discussion	
10:20-10:35	Break	
10:35-11:20	Recruitment and Retention	Aisha T. Langford, PhD, MPH, FSBM Associate Professor Department of Family Medicine and Public Health Sciences, Division of Behavioral Sciences Wayne State University School of Medicine
11:20-11:30	Discussion	

Readings and Resources

Part IV: The Ethics of Research Participant Recruitment. Ethical and Regulatory Aspects of Clinical Research: Readings and Commentary (2003) Edited by EJ Emanuel, RA Crouch, JD Arras, JD Moreno, Grady C. Johns Hopkins University Press: Baltimore. (Chapters 24-25; pp. 166-188)

Jull J, Whitehead M, Petticrew M, Kristjansson E, Gough D, Petkovic J, Volmink J, Weijer C, Taljaard M, Edwards S, Mbuagbaw L, Cookson R, McGowan J, Lyddiatt A, Boyer Y, Cuervo LG, Armstrong R, White H, Yoganathan M, Pantoja T, Shea B, Pottie K, Norheim O, Baird S, Robberstad B, Sommerfelt H, Asada Y, Wells G, Tugwell P, Welch V. When is a randomised controlled trial health equity relevant? Development and validation of a conceptual framework. *BMJ Open*. 2017 Sep 25;7(9):e015815.

R Cookson, M Robson, I Skarda, T Doran. Equity-informative methods of health services research. *Journal of Health Organization and Management.* 2021; 35(6): 665-681.

Langford AT, Orellana KT, Buderer N. Correlates of knowledge of clinical trials among U.S. adults: Findings from the 2020 Health Information National Trends Survey. *Contemporary Clinical Trials.* 2022; 114:1-6.

Langford AT. Health Communication and Decision Making about Vaccine Clinical Trials during a Pandemic*. Journal of Health Communications.* 2020; 25(10):780-789.

Scott E, McComb B, Trachtman H, Mannon L, Rosenfeld P, Thornton R, Bougrab N, Sherman S, Langford A. Knowledge and use of recruitment support tools among study coordinators at an academic medical center: The Novel Approaches to Recruitment Planning Study*. Contemporary Clinical Trials Communication.* 2019 Jul 22;15:100424

Dickert N, Grady C. What's the price of a research subject? Approaches to payment for research participation. *NEJM*. 1999 Jul 15;341(3):198-203.

NIH Guidelines on The Inclusion of Women and Minorities as Subjects In Clinical Research
https://grants.nih.gov/grants/guide/notice-files/not94-100.html

NIH Policy and Guidelines on the Inclusion of Individuals Across the Lifespan as Participants in Research Involving Human Subjects
https://grants.nih.gov/grants/guide/notice-files/NOT-OD-18-116.html

FDA, Division of Pediatrics and Maternal Health - Clinical Trials in Pregnant Women
https://www.fda.gov/drugs/development-resources/division-pediatrics-and-maternal-health-clinical-trials-pregnant-women

Session 5: *October 29* - International/Standards of Care/Post-trial Obligations/Community Engagement

Objectives:

- Appreciate ethical challenges with conducting international collaborative research in low- and middle-income countries
- Understand ethical considerations for defining an appropriate standard of care in clinical trials in international collaborative research
- Understand the obligations investigators and sponsors have to research participants after the conduct of a trial (e.g. post-trial access to any proven effective treatments)
- Consider and identify challenges and opportunities related to community engagement in the design and implementation of research

Time	Topic	Faculty
8:30-9:15	Introduction and Standards of Care	Annette Rid, MD PhD NIH Clinical Center Department of Bioethics and Fogarty International Center
9:15-9:25	Discussion	
9:25-10:10	Post-trial Obligations	Joseph Millum, PhD Senior Lecturer Department of Philosophy St. Andrews University Scotland, UK
10:10-10:20	Discussion	
10:20-10:35	Break	
10:35-11:20	Community Engagement in Health Research: Why it Matters and Different Approaches	Dorcas Kamuya, PhD, MSc Head of Health Systems and Research Ethics KEMRI-Wellcome Trust Research Programme Associate Professor Nuffield Department of Medicine, Centre for Tropical Medicine, University of Oxford
11:20-11:30	Discussion	

Reading and Resources

Council for International Organization of Medical Sciences (CIOMS). International Ethical Guidelines for Health-related Research Involving Humans (2016): https://cioms.ch/publications/product/international-ethical-guidelines-for-health-related-research-involving-humans/

- Guideline 2. Research conducted in low-resource settings
- Guideline 5. Choice of control in clinical trials
- Guideline 6. Caring for participants' health needs

Wendler D, Emanuel EJ, Lie RK. The standard of care debate: can research in developing countries be both ethical and responsive to those countries' health needs? *American Journal of Public Health*. 2004 Jun;94(6):923-8.

Millum J. Post-trial access to antiretrovirals: who owes what to whom? *Bioethics*. 2011 Mar;25(3):145-54.

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.

Gobat N, Slack C, Hannah S, Salzwedel J, Bladon G, Burgos JG, Purvis B, Molony-Oates B, Siegfried N, Cheah PY, Conway M, Kamuya D, Davies A, Johnson T, Tholanah M, Mugamba S, Mutengu NL, Machingaidze S, Schwartz L, Rägo L, von Harbou K. Better engagement, better evidence: working in partnership with patients, the public, and communities in clinical trials with involvement and good participatory practice. *Lancet Global Health*. 2025 Apr;13(4):e716-e731.

Marsh VM, Kamuya DK, Parker MJ, Molyneux CS. Working with Concepts: The Role of Community in International Collaborative Biomedical Research. *Public Health Ethics*. 2011 Apr;4(1):26-39

Barsdorf N, Maman S, Kass N, Slack C. Access to treatment in HIV prevention trials: perspectives from a South African community. *Developing World Bioethics.* 2010 Aug;10(2):78-87.

Nuffield Council on Bioethics Workgroup. Workshop report: global expert group highlights need for better community engagement during global health emergencies. 2019.

UN Community Engagement Guidelines on Peacebuiling and Sustaining Peace
https://www.un.org/peacebuilding/content/un-community-engagement-guidelines-peacebuilding-and-sustaining-peace-0

Session 6: *November 5* - Genomic Sequencing/Return of Results/Inclusion of Native Populations

- Identify challenges and opportunities related to genetics research and research with stored samples
- Understand how the rapid development and diffusion of genetic technology influence the conduct of human subject research
- Understand the difference between research findings and incidental findings and the relevant ethical considerations for each
- Appreciate the complexity of conducting genetics research with native populations
- Understand the concept of group harms

Time	Topic	Faculty
8:30-9:15	An Overview of Research on Genomic Sequencing and Related Ethical Issues	Ben Berkman, JD MPH NIH Clinical Center Department of Bioethics and National Human Genome Research Institute
9:15-9:25	Discussion	
9:25-10:10	Outcomes Associated with Opportunistic Screening for Secondary Findings	Julie Sapp, ScM, CGC Precision Genomics Section Genomics Services Research Program National Human Genome Research Institute
10:10-10:20	Discussion	

10:20-10:35	Break	
10:35-11:20	Genetics and Inclusion of Indigenous Populations	Katrina Claw, PhD Associate Professor Department of Biomedical Informatics Colorado Center for Personalized Medicine University of Colorado Anschutz Medical Campus
11:20-11:30	Discussion	

Readings and Resources

National Academies of Sciences, Engineering, and Medicine. 2023. Using Population Descriptors in Genetics and Genomics Research: A New Framework for an Evolving Field. Washington, DC: The National Academies Press. https://doi.org/10.17226/26902.

President's Commission for the Study of Bioethical Issues. Anticipate and Communicate: Ethical Management of Incidental and Secondary Findings in the Clinical, Research, and Direct-to-Consumer Contexts. 2013. Executive Summary, pages 1-20, available at https://bioethicsarchive.georgetown.edu/pcsbi/node/3183.html

Wolf SM, Green RC. Return of Results in Genomic Research Using Large-Scale or Whole Genome Sequencing: Toward a New Normal. 414 *Annual Review of Genomics and Human Genetics*. 2023 Aug 25;24:393- 2023; 24:393-414.

Schupmann W, Miner SA, Sullivan HK, Glover JR, Hall JE, Schurman SH, Berkman BE. Exploring the motivations of research participants who chose not to learn medically actionable secondary genetic findings about themselves. *Genetics in Medicine*. 2021 Dec;23(12):2281-2288.

Bombard Y, Brothers KB, Fitzgerald-Butt S, Garrison NA, Jamal L, James CA, Jarvik GP, McCormick JB, Nelson TN, Ormond KE, Rehm HL, Richer J, Souzeau E, Vassy JL, Wagner JK, Levy HP. The Responsibility to Recontact Research Participants after Reinterpretation of Genetic and Genomic Research Results. *American Journal of Human Genetics*. 2019 Apr 4;104(4):578-595.

Claw KG, Dorr CR, Woodahl EL. Implementing community-engaged pharmacogenomics in Indigenous communities. *Nature Communications*. 2024 Jan 31;15(1):920.

Claw KG, Anderson MZ, Begay RL, Tsosie KS, Fox K, Garrison NA; Summer internship for indigenous peoples in Genomics (SING) Consortium. A framework for enhancing ethical genomic research with Indigenous communities. *Nature Communications*. 2018 Jul 27;9(1):2957.

Tsosie KS, Claw KG, Garrison NA. Considering "Respect for Sovereignty" Beyond the Belmont Report and the Common Rule: Ethical and Legal Implications for American Indian and Alaska Native Peoples. *American Journal of Bioethics*. 2021 Oct;21(10):27-30

Barton KS, Porter KM, Mai T, Claw KG, Hiratsuka VY, Carroll SR, Burke W, Garrison NA. Genetic research within Indigenous communities: Engagement opportunities and pathways forward. Genet Med. 2024 Jul;26(7):101158.

Session 7: *November 12* FDA

Objectives TBA

Time	Topic	Faculty
8:30-9:15	ABCs of the Food and Drug Administration (FDA)	Holly Fernadez Lynch, JD MBe Associate Professor of Medical Ethics and Health Policy University of Pennsylvania
9:15-9:25	Discussion	
9:25-10:10	TBA	
10:10-10:20	Discussion	
10:20-10:35	Break	
10:35-11:20	Xenotransplantation	Karen Maschke, PhD Senior Research Scholar Hastings Center for Bioethics
11:20-11:30	Discussion	

Readings and Resources

Food and Drug Administration. What We Do. https://www.fda.gov/about-fda/what-we-do

Lewis-Kraus, L. When Dying Patients. *New Yorker.* June 19, 2023 https://www.newyorker.com/magazine/2023/06/26/relyvrio-als-fda-approval

Lynch HF, Lurie P, Cohen IG. Checks and Balances on FDA's Authority. *JAMA*. 2024 Sep 3;332(9):705-706.

[hold for gene therapy]

Maschke KJ, Gordon EJ, Gusmano MK. Executive Summary Informing Ethical Translation of Xenotransplantation Clinical Trials https://www.thehastingscenter.org/wp-content/uploads/Xeno-Executive-Summary-6-23-25.pdf

Gordon EJ, Maschke KJ, Gacki-Smith J, Brooks HL, Matthews MM, Traboulsi K, Manning D, Leventhal J, Gusmano MK. Transplant Patients' Perceptions About Participating in First-in-Human Pig Kidney Xenotransplant Clinical Trials: A Mixed Methods Study. *Xenotransplantation*. 2025 Jan-Feb;32(1):e70013.