Ethical and Regulatory Aspects of Clinical Research

September 21 to November 9, 2022
8:30-11:30 am
All material to be delivered by NIH Videocast and CANVAS

8.2.22

Overview

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<tr>
<th>Session</th>
<th>Date</th>
<th>Topics</th>
<th>Faculty</th>
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<tr>
<td>1</td>
<td>9/21/22</td>
<td>Introduction/Framework/History/Institutional Review Boards</td>
<td>Taylor, Grady, Lederer</td>
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<tr>
<td>2</td>
<td>9/28/22</td>
<td>Study Design/Risk-Benefit/Perspectives from the Field</td>
<td>Taylor, Wendler, Ledgerwood, Arlen</td>
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<td>3</td>
<td>10/12/22</td>
<td>Subject Selection/Recruitment and Retention/Inclusion of Children</td>
<td>Taylor, Wendler, Shah</td>
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<td>4</td>
<td>10/19/22</td>
<td>Equity and Inclusion</td>
<td>Asada, Taylor, Langford</td>
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<td>5</td>
<td>10/26/22</td>
<td>Informed Consent/Decision Making/Capacity Assessment</td>
<td>Grady, Kim, Todman, Taylor</td>
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<td>6</td>
<td>11/2/22</td>
<td>Incidental Findings/Return of Results/Inclusion of Native Populations</td>
<td>Berkman, Jamal, Claw</td>
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<td>7</td>
<td>11/9/22</td>
<td>International/Standards of Care/Post-trial Obligations/Community Engagement</td>
<td>Rid, Millum, Kamuya</td>
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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 and apply relevant considerations for assessment of research risks and benefits.
- Explore the ethical requirement of fair subject selection and its application.
- Identify the critical elements of informed consent and strategies for implementing informed consent for clinical research.
- Appreciate ethical challenges with conducting international collaborative research in low- and middle-income countries.
Session 1: Introduction/Framework/History/Institutional Review Boards  September 21

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

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<tr>
<th>Time</th>
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<tbody>
<tr>
<td>8:30-8:45</td>
<td>Introduction to Course</td>
<td>Holly Taylor, PhD MPH NIH Clinical Center Department of Bioethics</td>
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<tr>
<td>8:45-9:30</td>
<td>Framework for Ethical Conduct of Research</td>
<td>Christine Grady, RN PhD NIH Clinical Center Department of Bioethics</td>
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<tr>
<td>9:30-9:40</td>
<td>Discussion</td>
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<td>9:40-10:25</td>
<td>History of Research Ethics</td>
<td>Susan E. Lederer, Ph.D. Robert Turell Professor of History of Medicine and Bioethics Chair, Department of Medical History and Bioethics University of Wisconsin School of Medicine and Public Health</td>
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<td>10:25-10:35</td>
<td>Discussion</td>
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<td>10:35-10:50</td>
<td>Break</td>
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<tr>
<td>10:50-11:20</td>
<td>Institutional Review Boards</td>
<td>Holly Taylor, PhD MPH NIH Clinical Center Department of Bioethics</td>
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<td>11:20-11:30</td>
<td>Discussion</td>
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Readings Assignment

Textbook

Part I: Scandals and Tragedies of Research with Human Participants: Nuremberg, the Jewish Chronic Disease Hospital, Beecher and Tuskegee (Overview and Chapters 1-4; pp. 1-25)

Part II: Ethical and Regulatory Guidance for Research with Humans (Overview and Chapters 5-7; pp. 25-38)

Part X: Challenges to the Institutional Review Board System (Chapter 85; pp-436-440)
**Journal Articles**


**US Federal Regulations**


**Optional**


**Session 2: Study Design/Risk-Benefit/Perspectives from the Field** September 28

- Identify ethical issues in the design and conduct of clinical trials
- Identify and apply relevant considerations for assessment of research risks and benefits
- Consider unique ethical issues related to the design and conduct of Phase I trials.

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<tr>
<td>8:30-9:00</td>
<td>Study Design</td>
<td>Holly Taylor, PhD MPH&lt;br&gt;NH Clinical Center Department of Bioethics</td>
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<tr>
<td>9:00-9:10</td>
<td>Discussion</td>
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<tr>
<td>9:10-9:55</td>
<td>Risk/Benefit</td>
<td>David Wendler, PhD&lt;br&gt;NH Clinical Center Department of Bioethics</td>
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<tr>
<td>9:55-10:05</td>
<td>Discussion</td>
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<td>10:05-10:20</td>
<td>Break</td>
<td></td>
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<tr>
<td>10:20-11:20</td>
<td>Phase I Research Roundtable</td>
<td>Julie Ledgerwood, DO&lt;br&gt;<em>Most recently</em>&lt;br&gt;Chief Medical Officer and Deputy Director&lt;br&gt;Vaccine Research Center&lt;br&gt;National Institutes of Allergy and Infectious Disease, NIH&lt;br&gt;<em>Currently</em>&lt;br&gt;Chief Medical Officer&lt;br&gt;Vaccine Company, Inc.</td>
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Readings Assignment

Textbook

Part III: The Ethics of Trial Design (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 (Chapter 74; pp. 378-381)

Archived Lecture
https://videocast.nih.gov/watch=42671 (first 60 minutes)

Randomized Clinical Trials: Clinical Equipoise (September 29, 2021)
Robert Truog, MD
Director, Harvard Center for Bioethics
Frances Glessner Lee Professor of Legal Medicine, Professor of Anaesthesia (Pediatrics) Harvard Medical School

Articles


Web Resources (for those less familiar with drug/vaccine development process)


Coronavirus Resource Center, Johns Hopkins University. Vaccine Research and Development. https://coronavirus.jhu.edu/vaccines/timeline

YOM KIPPUR October 5 – No class
Session 3: Subject Selection/ Recruitment and Retention/Inclusion of Children— October 12

Objectives:
- Explore the ethical requirement of fair subject selection and its application
- Identify ethical issues and strategies in the recruitment and retention of subjects
- Review ethical challenges and strategies for conducting ethical research involving children

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<tr>
<td>8:30-9:10</td>
<td>Fair Subject Selection</td>
<td>Holly Taylor, PhD MPH NIH Clinical Center Department of Bioethics</td>
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<tr>
<td>9:10-9:20</td>
<td>Discussion</td>
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<tr>
<td>9:20-10:00</td>
<td>Recruitment and Retention</td>
<td>Dave Wendler, PhD NIH Clinical Center Department of Bioethics</td>
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<td>10:10-10:20</td>
<td>Discussion</td>
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<td>10:20-10:35</td>
<td>Break</td>
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<tr>
<td>10:35-11:20</td>
<td>Ethical Inclusion of Children in Research</td>
<td>Seema Shah, JD Founders' Board Professor of Medical Ethics Associate Professor of Pediatrics Feinberg School of Medicine Northwestern University</td>
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<td>11:20-11:30</td>
<td>Discussion</td>
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Reading Assignment

Textbook

Part IV: The Ethics of Research Participant Recruitment (Chapter 22; pp. 155-161, Chapter 27; pp. 179-183, Chapter 29; pp. 185-188)

Part VI: Clinical Research with Special Populations (Chapters 42; pp. 247-252)

Journal Article

Shah SK, When to start paediatric testing of the adult HIV cure research agenda? Journal of Medical Ethics 2017 43: 82-86.
Session 4: Equity and Inclusion – October 19

Objectives:
- Identity the difference between inequality and inequity
- Review Federal Policy intended to diversify those enrolled in clinical research
- Explore the practical implications of diversifying enrollment in clinical research

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<tr>
<td>8:30-9:15</td>
<td>When are Health Inequalities Unfair?</td>
<td>Yukiko Asada</td>
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<td></td>
<td>NIH Clinical Center Department of Bioethics</td>
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<tr>
<td>9:15-9:25</td>
<td>Discussion</td>
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<td>9:25-9:45</td>
<td>Federal Inclusion Policy</td>
<td>Holly Taylor, PhD MPH</td>
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<td>NIH Clinical Center Department of Bioethics</td>
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<tr>
<td>9:45-10:00</td>
<td>Break</td>
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<tr>
<td>10:00-10:50</td>
<td>What does Commitment to Diversity in Clinical Research Look Like in practice: Protocol Design, Patient, and Staffing Considerations</td>
<td>Aisha Langford, PhD MPH</td>
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<td>Department of Population Health</td>
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<td>Co-Director, CTSI Recruitment and Retention Core</td>
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<td>NYU Grossman School of Medicine</td>
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<td>10:50-11:00</td>
<td>Discussion</td>
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<tr>
<td>11:00-11:30</td>
<td>Case: What does genetics have to say about diversity?</td>
<td>Holly Taylor, PhD MPH</td>
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<td>NIH Clinical Center Department of Bioethics</td>
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Reading Assignment

**Textbook**

Part IV: The Ethics of Research Participant Recruitment (Chapters 24-25; pp. 166-175)

**Journal Articles**


**NIH Inclusion Policies**


**Optional**


**Session 5: Informed Consent/Decision Making/Capacity Assessment** October 26

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

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<tr>
<td>8:30-9:15</td>
<td>Informed Consent</td>
<td>Christine Grady, RN PhD NIH Clinical Center Department of Bioethics</td>
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<tr>
<td>9:15-9:25</td>
<td>Discussion</td>
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<tr>
<td>9:25-10:10</td>
<td>Research Involving Persons at Risk for Impaired Decision-Making</td>
<td>Scott Kim, MD PhD NIH Clinical Center Department of Bioethics</td>
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<td>10:10-10:20</td>
<td>Discussion</td>
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<td>10:20-10:35</td>
<td>Break</td>
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### Capacity Assessment in Practice

Katherine Todman MSW, LCSW-C  
Human Subjects Protection Unit  
National Institute of Mental Health

### Nuts and Bolts of Consent

Holly Taylor, PhD MPH  
NIH Clinical Center Department of Bioethics

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**Reading Assignment**

**Textbook**

Part V: Informed Consent in Research (Overview and Chapters 30-32; pp. 189-207; Chapters 36-37; pp. 216-223)

**Journal Articles**


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

**NIH Clinical Center Policy**


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**Session 6: Incidental Findings/Return of Results/Inclusion of Native Populations** November 2

- 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

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<th>Time</th>
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| 8:30-9:15 | Ethics of Genetics Incidental and Secondary Findings | Ben Berkman, JD MPH  
NIH Clinical Center Department of Bioethics and NHGRI |
| 9:15-9:25 | Discussion                                |                                             |
9:25-10:10  | Returning Research Results in the Context of Evolving Science | Leila Jamal, PhD ScM, CGC NIH Clinical Center Department of Bioethics and NCI
10:10-10:20  | Discussion |
10:20-10:35  | Break |
10:35-11:30  | Genetics and Inclusion of Indigenous Populations | Katrina Claw, PhD Assistant Professor Medicine and Bioinformatics University of Colorado Denver Anschutz Medical Campus
11:20-11:30  | Discussion |

**Reading Assignment**

*President’s Commission*


*Journal Articles*


*Optional*


Session 7: International/Standards of Care/Post-trial Obligations/Community Engagement - November 9

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 related to community engagement in the design and implementation of research

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<tr>
<th>Time</th>
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| 8:30-9:15 | Introduction and Standards of Care             | Annette Rid, MD PhD
NIAID Clinical Center Department of Bioethics and NIAID                  |
| 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, MPH
Head of Health Systems and Research Ethics KEMRI-Wellcome Trust Research Programme Nairobi, Kenya |
| 11:20-11:30| Discussion                                     |                                                                         |
**Reading Assignment**

World Medical Association (WMA). Declaration of Helsinki (2013):
https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-
medical-research-involving-human-subjects/

Council for International Organization of Medical Sciences (CIOMS). International Ethical

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

Barsdorf N, Maman S, Kass N, Slack C. "Access to treatment in HIV prevention trials:

Wendler D, Emanuel EJ, and 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; 94 (6): 923-928.

Marsh VM, Kamuya DK, Parker MJ, Molyneux CS. Working with Concepts: The Role of
Community in International Collaborative Biomedical Research. *Public Health Ethics*

**Optional:**


Wertheimer A. Exploitation. Chapter 20 in E. Emanuel et al (eds). The Oxford Textbook of

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