MULTI-REGIONAL CLINICAL TRIALS

THE MRCT CENTER of BRIGHAM AND WOMEN'S HOSPITAL and HARVARD

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A Framework for AI Adoption and Oversight in Clinical Research

June 24, 2025

3:00 – 4:00 pm ET

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The Multi-Regional Clinical Trials Center (MRCT Center)

Our Vision

Improve the integrity, safety, and rigor of global clinical trials.

Our Mission

Engage diverse stakeholders to define emerging issues in global clinical trials and to create and implement ethical, actionable, and practical solutions.

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Building IRB Readiness for AI in Clinical Research:
A Framework for Adoption and Oversight

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MRCT Center

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AI is transforming research – and testing our readiness

- **AI is reshaping clinical research:** From diagnostics to clinical decision support, its use in studies involving human subjects is expanding rapidly.
- **Rising complexity for IRBs:** AI raises ethical and regulatory questions (e.g., privacy, transparency, potential for bias, and maintaining human autonomy).
- **Existing guidance lays ethical groundwork:** Agencies like the FDA, HHS, and NIST offer principles, but IRBs need practical tools for protocol-level review.
- **Oversight must evolve to keep pace:** IRBs are already seeing protocols involving AI, often missing sufficient details, causing delays in review.
- **This framework aims to fill a gap:** It offers structured, actionable steps to support consistent, thoughtful review of clinical research involving AI.

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Framework Development Process

- Task Force of experts convened by the MRCT Center and WCG in Spring 2024
  - IRB chairs, ethicists, AI technologists, and industry representatives
- Informed by:
  - Real-world clinical research involving AI under IRB review
  - Regulatory foundations (e.g., Common Rule, SACHRP, and NIST)
- Developed through:
  - Monthly meetings
  - Case examples
  - Internal review
  - External expert commentary

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Ethical research, regulatory alignment – our starting point

- The framework is built on core U.S. research ethics regulations, including the Common Rule (45 CFR 46)
- Ethical foundations from the Belmont Report:
  - Respect for Persons: Autonomy and Informed Consent
  - Beneficence: Maximize benefit, minimize harm
  - Justice: Fairness in access, burden, and benefit
- Applies existing definitions of research, human subjects, and minimal risk to studies involving AI
- Encourages IRBs to act within their remit – even when AI is unfamiliar
- Complements (not replaces) current regulatory and institutional policies

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A. Initial Questions to Guide Oversight

Question	Context and comments	Next Steps
1. Is the activity considered "research" under US federal definitions?[7]	Research is a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge [45 CFR § 46.102 (l)] The answer to this question may not be obvious. In general, activities intended to improve local processes (e.g., local QI/QA activities) are not typically considered research, but if the scope is to apply the lessons from such activities more broadly, then they may constitute research.	**Yes:** Proceed to question 2. • Consider reviewing questions in the Discovery stage for AI technology in early development. **No:** IRB review is not generally required.
2. Does the research involve human participants?	Human Subjects refer to living individuals about whom an investigator obtains **data** or biospecimens through intervention or interaction, or obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. [45 CFR § 46.102 (e)]	**Yes:** Proceed to question 3. • Consider additional questions for AI systems in the Translation or Deployment stage. **No:** IRB review is not generally required.
3. What is the intended use of the AI technology in the research study?[8]	Types of AI deployments include: **Administration of Research** (e.g., data analysis support, recruitment, transcribing interviews) **AI as the Intervention** (e.g., clinical decision-making or therapeutic intervention, AI-enabled medical devices)	**If for Administration of Research:** Refer to Part D of the framework **If AI is the Intervention** Proceed to question 4.

[7] 45 CFR 46 | HHS.org, see https://www.ecfr.gov/current/title-45/subtitle-A/subchapter-A/part-46
[8] Intended use is the purpose or purposes for which an AI health technology supplier specifies that they intend the technology to be used. It is usually specified by the manufacturer, person, or organization legally responsible (Alderman et al. 2025).

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4. What is known about the AI algorithm? (i.e., origins, and "marketed" or intended use)	Consider details in the protocol on whether the AI is a pre-existing tool (e.g., available commercially, open source, developed locally), and whether the current use is consistent with the study's intended use, or developed specifically for this research intervention.	**Sufficient Details in Protocol:** Proceed to question 5. **Insufficient Details in Protocol:** Request additional information about the AI system's developmental stage, intended use, and validation.[9] Refer to Part B for more information on AI developmental stages.
5. Has a risk analysis of the AI technology been conducted? Is there adequate evidence of risk considerations within the protocol?[10]	Risks could include impacts on clinical decision-making, amplification of bias, data confidentiality, identifiability, and privacy that could affect human participants.	**Minimal Risk:** Document risks and proceed to question 6. **Risks Identified:** Determine if they can be minimized or require further review. **More than minimal risk:** Full Board IRB review is required. Consider supplemental questions in Part C here.

[9] See Artificial Intelligence-Enabled Device Software Functions: Lifecycle Management and Marketing Submission Recommendations | FDA.gov for more information on AI Algorithm model cards.
[10] The FDA's Draft Risk-Based Credibility Assessment Framework outlines a process for determining risk across the research lifecycle.

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6. Does the research qualify for exemption under the Common Rule?	Exempt categories may include benign behavioral interventions, educational practice studies, or secondary research of identifiable or linkable data.[11] [45 CFR § 46.104]	**Yes:** Document the exemption. In cases where limited review[12] is conducted, refer to Part C, particularly information on Informed Consent. Otherwise, conclude the review. **No:** Proceed to question 7.
7. Does the research involve more than 'minimal risk' to human participants?	Minimal risk means the probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or routine exams. [45 CFR § 46.102(j)]	**Yes:** Full Board IRB review is required. • Consider supplemental questions in Part C. **No:** Consider eligibility for expedited review. [45 CFR § 46.110]

[11] Note that benign behavioral interventions "are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing." [45 CFR § 46.104 (d)(3)(ii)]
[12] See conditions for limited IRB review at § 46.104(d)(2)(iii), (d)(3)(i)(C), or (d)(7) or (8).

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A. Initial Questions to Guide Oversight

Part A: Initial Questions

Is it Human Subjects Research?

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What is the intended use of the AI technology?

↓

What is known about the AI algorithm?

↓

Is there adequate evidence of risk considerations within the protocol?

↓

Does the research involve more than minimal risk?

- Helps IRBs assess whether the research falls under Common Rule oversight
- Clarifies who the human subject is in AI-related research
- Asks: Is AI part of the intervention, or a tool being used for administrative purposes?

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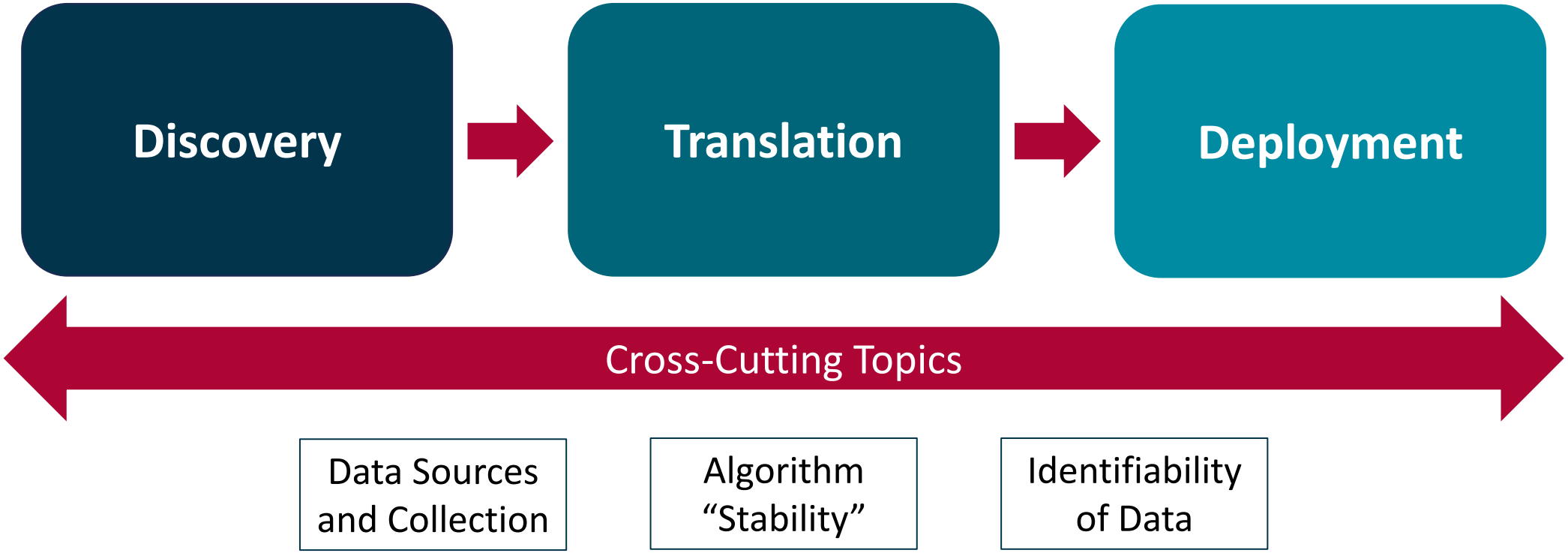
B. Review Considerations by AI Development Stage

- Assessing contextual risks across three stages[1]



1. AI Developmental Stages adapted from: Eto T, Lifson M, Vidal D. Pre-print: A novel, streamlined approach to the IRB review of artificial intelligence human subjects research (AI HSR). Whitepaper. September 2024. https://purl.stanford.edu/zj025zw1714

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C. Ethical Considerations

- Prompts IRBs to assess how the AI aligns with established ethical principles, including:

Human Agency and Oversight

Privacy, Confidentiality, and Data Governance

Technical Robustness and Safety

Transparency

Representation and Fairness

Informed Consent

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D. Artificial Intelligence Deployed in the Administration of Research

- Focus is on AI used to support research operations, not as the subject of the study intervention
  - Examples: Participant recruitment and matching, development of research materials, transcription, and analysis of interviews
- Prompts consideration of:
  - Impact on participants – direct or indirect
  - Institutional oversight
  - Transparency
- Considers areas of research that may fall outside the IRB's purview but should still be examined when they intersect with the protection of participants.

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Putting the Framework Into Practice

- The framework is publicly available on the MRCT Center website starting today
- Designed to be used by IRBs, researchers, and institutions
- Case examples are in development to further support real-world application
- We welcome feedback from those using the framework
- This is just the beginning: As AI continues to evolve, so must our oversight capacity

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Perspectives on AI Adoption and Building Oversight Capacity

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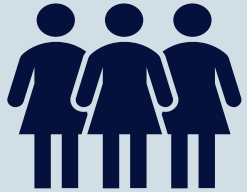
Applying the IRB Framework to an AI Research Protocol: A Case Study

Presented by:
Kevin Nellis, Executive Director,
Human Research Protections & Quality Assurance

Case Snapshot & Study Relevance

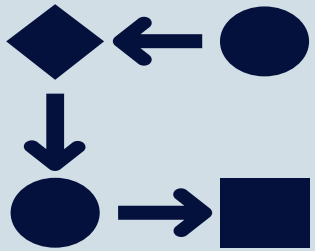
Study:

Wearable EEG + ML tool to support women with AUD in managing overeating



Participants:

Women 18–45, healthy and with AUD, recruited in Flatbush/NYC



Design:

Pilot study; real-time feedback using AI on eating behavior

Why It Matters:

Combines investigational device + AI + behavioral intervention

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Key Framework Touchpoints for IRB Review

AI Stage & Device Oversight
– Discovery/translation phase
– Includes 2 FDA-cleared & 1 investigational device
– IRB must evaluate NSR status

PHI Use & Data Security
– Accesses medical records plus questionnaires
– Stored securely; no PHI on portable devices
– Consent must disclose future data use and algorithm limits

Bias & Participant Equity
– Localized pilot (Flatbush/NYC): Is it representative?
– Equity in recruitment and future scalability

Ethical Guardrails & AI Exceptionalism
– Avoid bias from “Tech Halo” and “Horns Effect”
– Cleary explain AI’s role and limitations in consent forms
– Ensure investigators have appropriate AI expertise

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AI Exceptionalism: Believing AI bests humans

- Will transform
- Learning ever-advances
- Increases accuracy & speed
- Data-driven
- Advances humanity
- Communication elevated

- Fundamentally novel
- Inherently unknowable
- Requires more scrutiny
- Baseline bias
- Replaces humans
- Privacy lost