
CURATING CONNECTION
2025
IRB Member
Retreat
Innovations Interlude

WELCOME!

Welcome & Opening Remarks

Innovative Refrain: Exploring AI Across our HRPP

- What is AI and Why it Does and Doesn't Matter
- Streamlining IRB Review of AI HSR: The 3 Phase Approach
- Strengthening the HRPPP

SIMPLIFYING THE IRB REVIEW PROCESS: AI HSR IN 3 PHASES

Tamiko Eto, M.S., M.A., CIP
Director, Research Operations
Mayo Clinic

Disclaimers

Laws, regulations, and guidance documents are subject to change – especially the latter, given the dynamic environment in the innovative digital health technologies space.

The materials contained herein are for general informational purposes only to promote discussion and are not legal advice.

Tamiko Eto has no real or apparent conflicts of interest to report.

CURIOSITY PRIMER

How do we protect human subjects during the development and testing of this tool?

GenAI-enabled tool that provides real-time monitoring of patients admitted to the hospital to create individual risk-of-sepsis scores, which are updated continuously

ℹ Sepsis is a life-threatening condition that occurs when the body's immune system has an extreme response to an infection or injury

Agenda

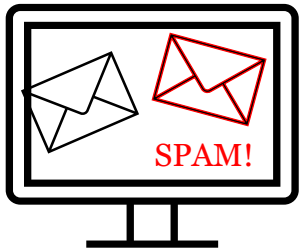
1. **What is AI and Why it Does and Doesn't Matter – 5 minutes**
2. **Streamlining IRB Review of AI HSR: The 3-Phase Approach | 15 Mins**
3. **Strengthening the HRPP | 5 Mins**

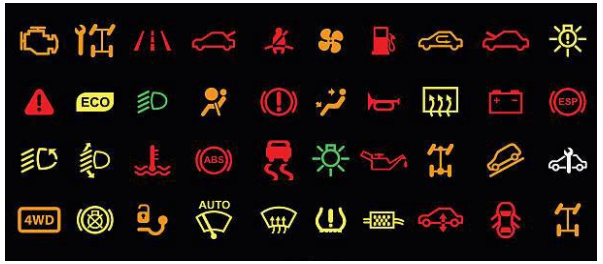
Artificial Intelligence

*Machine-based system that, for **explicit** or **implicit** objectives, infers, from the input it receives, how to generate outputs such as predictions, content, recommendations, or decisions that can influence physical or virtual environments.* -OECD

EXPLICIT (knowledge based):

- *Clear goals*
- *Directly programmed in the system by a human developer.*

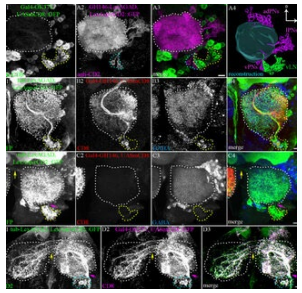




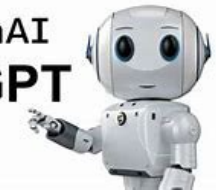
IMPLICIT (ML and Deep Learning):

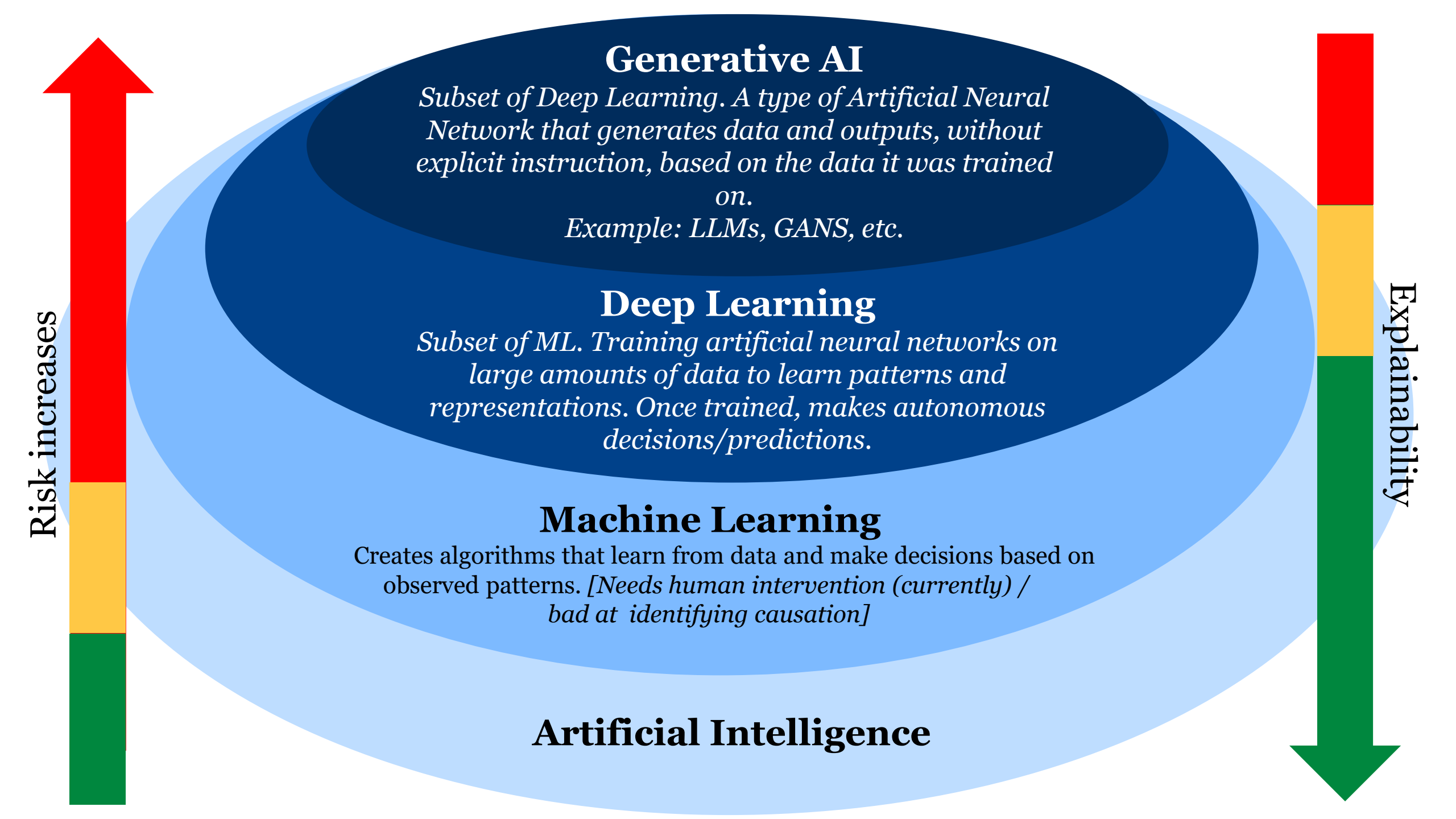
- *"hidden goals" the AI figures out on its own while working.*
- *Creates algorithms based on identified patterns; makes decisions based on those patterns.*
- *Initially programmed by a set of rules specified by a human, BUT programming changes as system "learns" new objectives.*

TESLA



OpenAI
ChatGPT

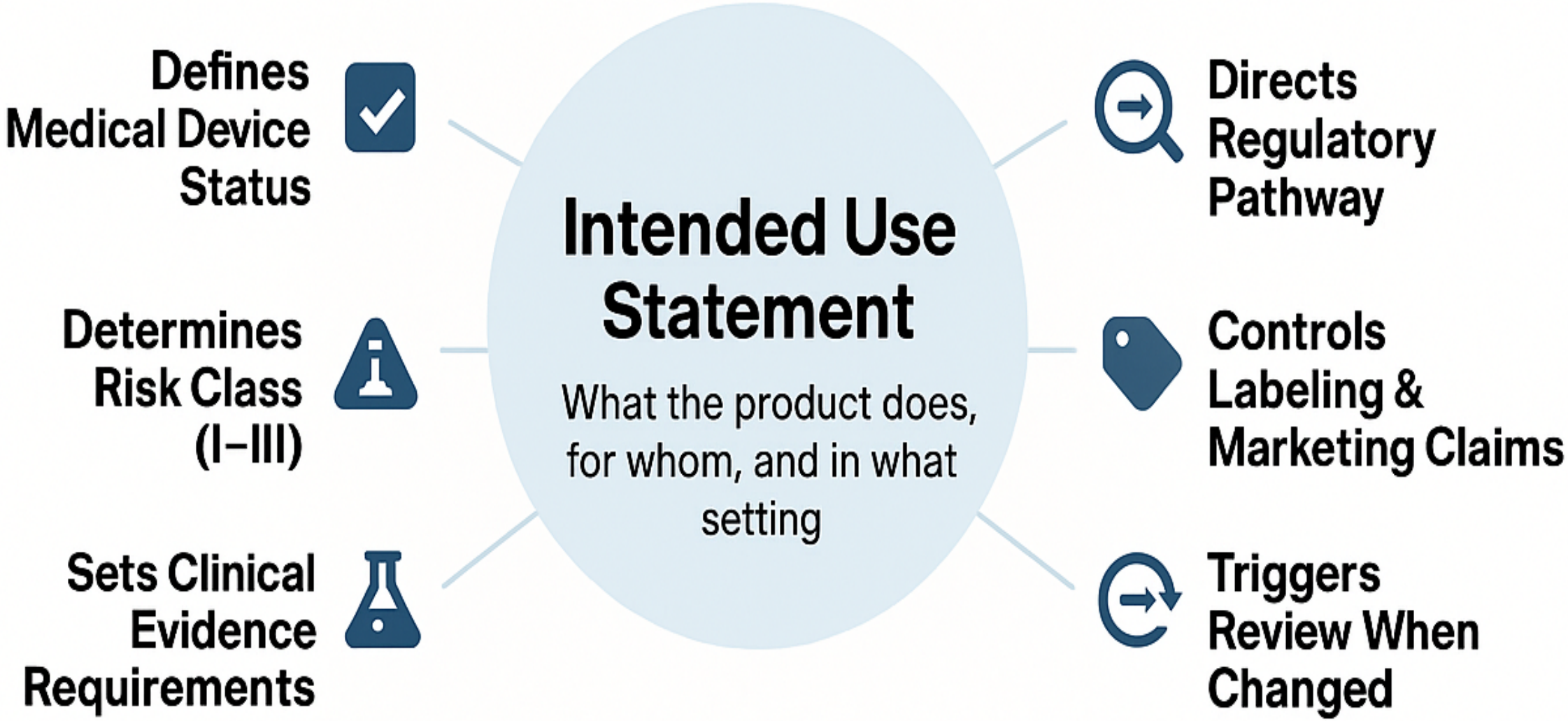



Generative AI
Subset of Deep Learning. A type of Artificial Neural Network that generates data and outputs, without explicit instruction, based on the data it was trained on.
Example: LLMs, GANS, etc.
Deep Learning
Subset of ML. Training artificial neural networks on large amounts of data to learn patterns and representations. Once trained, makes autonomous decisions/predictions.
Machine Learning
Creates algorithms that learn from data and make decisions based on observed patterns. [Needs human intervention (currently) / bad at identifying causation]
Artificial Intelligence
Risk increases
Explainability

Agenda

1. What is AI and Why it Does and Doesn't Matter – 5 minutes
2. **Streamlining IRB Review of AI HSR: The 3-Phase Approach | 15 Mins**
3. Strengthening the HRPP | 5 Mins

The Intended Use Statement: One Sentence That Drives It All



LEVELS OF CLINICAL EVIDENCE:

Clinical Evaluation

Clinical Association
between software output and clinical condition:
Literature searches, original clinical research, professional society guidelines, ***secondary data analysis****, past clinical trial findings*

Product Performance Verify & Validate

Analytical / Technical Validation	**Clinical Validation**
Accuracy, Reliability, Precision…	*Sensitivity, Specificity, Odds Ratio… (near final)*

Clinical Investigation

Clinical Trial (pre-approval)

Pilot: Small study to determine preliminary safety and performance
Pivotal: Larger study to determine efficacy and adverse effects

Clinical Trial (post-approval)

Collection of long-term data on effectiveness, safety & usage

(usually non-interventional)

Phase 1:
Exploratory/ Discovery/ Ideation
(pre-clinical)

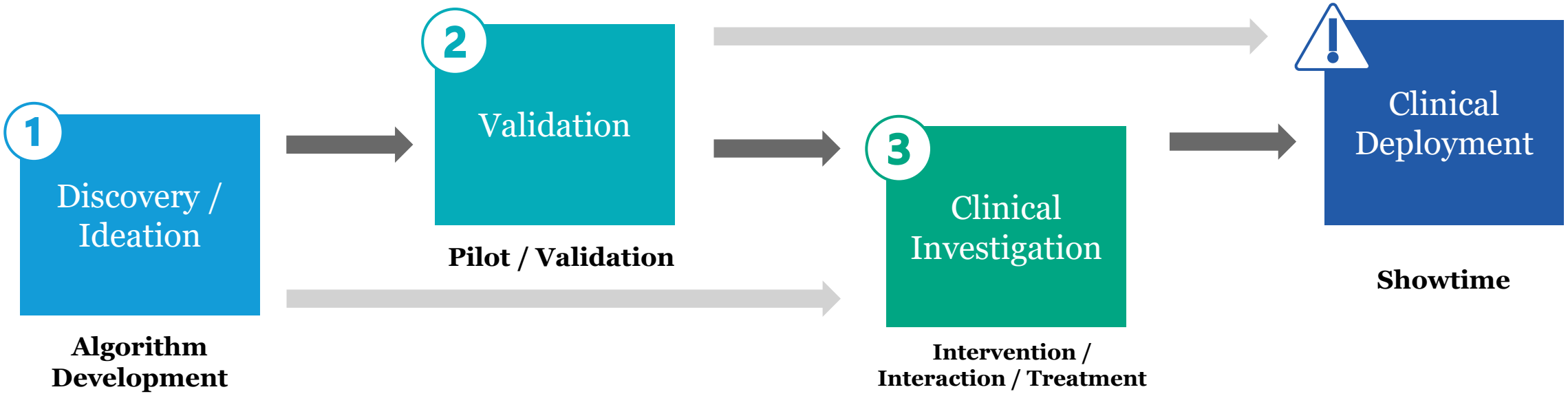
Phase 2:
Pilot/Validation
(early feasibility, preliminary safety & performance; NO IMPACT ON CARE/TREATMENT)

Phase 3: Intervention/Treatment
(Confirms clinical efficacy, safety & risks; Potentially impacts patient health, care, or treatment)

A SIMPLIFIED IRB REVIEW PROCESS
FOR AI HUMAN SUBJECTS RESEARCH

Risk-Based **Three-Phased Approach**

- Level of risk and stage of development determine degree of oversight and design controls
- Evidence to support clinical deployment builds across each phase



1. Discovery / Ideation
2. Validation
3. Clinical Investigation

WHAT IS PHASE 1?

- ☑ Discovery & Ideation (“Clinical Association”)
- ☑ Via Algorithm Development and Training

DISCOVERY AND IDEATION

Establishing Data Needs

"Clinical evidence is all the scientific data and information generated and held by the manufacturer that supports the scientific validity, analytical validity, and clinical performance of a SaMD."

IMDRF Section 6.0: Clinical Evidence, Page 12

Preparing Study Design

Requesting Data Access for Clinical Evaluation

"The clinical evaluation of a SaMD is a systematic and planned process to continuously generate, collect, analyze, and assess the clinical data pertaining to a SaMD in order to generate clinical evidence verifying the clinical association and the performance metrics of a SaMD when used as intended."

IMDRF Section 7.0: SaMD Clinical Evaluation Process Flow Chart, Page 13

Analyzing Approved Secondary Data

Extracting Clinical Patterns from Secondary Data

"Valid clinical association can be demonstrated through multiple forms of evidence, including but not limited to:
- Existing clinical studies or literature demonstrating the relationship between input data and the SaMD output
- Retrospective secondary data analysis using high-quality datasets
- Expert consensus or established clinical practice that supports the association"

IMDRF Section 7.1: Considerations for Generating and Assessing Evidence, Page 15

Discovering Novel AI Models

Developing and Validating Clinical Associations

"Novel clinical association: These SaMD may involve new inputs, algorithms, or outputs, new intended target populations, or new intended use. An example may include the combination of non-standard inputs... using novel algorithms to detect early onset of a deterioration of health or diagnosis of a disease."

IMDRF Section 7.1: Considerations for Generating and Assessing Evidence, Page 15

PHASE 1 – DISCOVERY & IDEATION

GenAI-enabled tool that provides real-time monitoring of patients admitted to the hospital to create individual risk-of-sepsis scores, which are updated continuously

- ☑ Clinical association
- ☑ Narrow focus
- ☑ Status quo clinical decision making and standard of care
- ☑ Study risk determination

ℹ Sepsis is a life-threatening condition that occurs when the body's immune system has an extreme response to an infection or injury

1 Discovery / Ideation

2 Validation

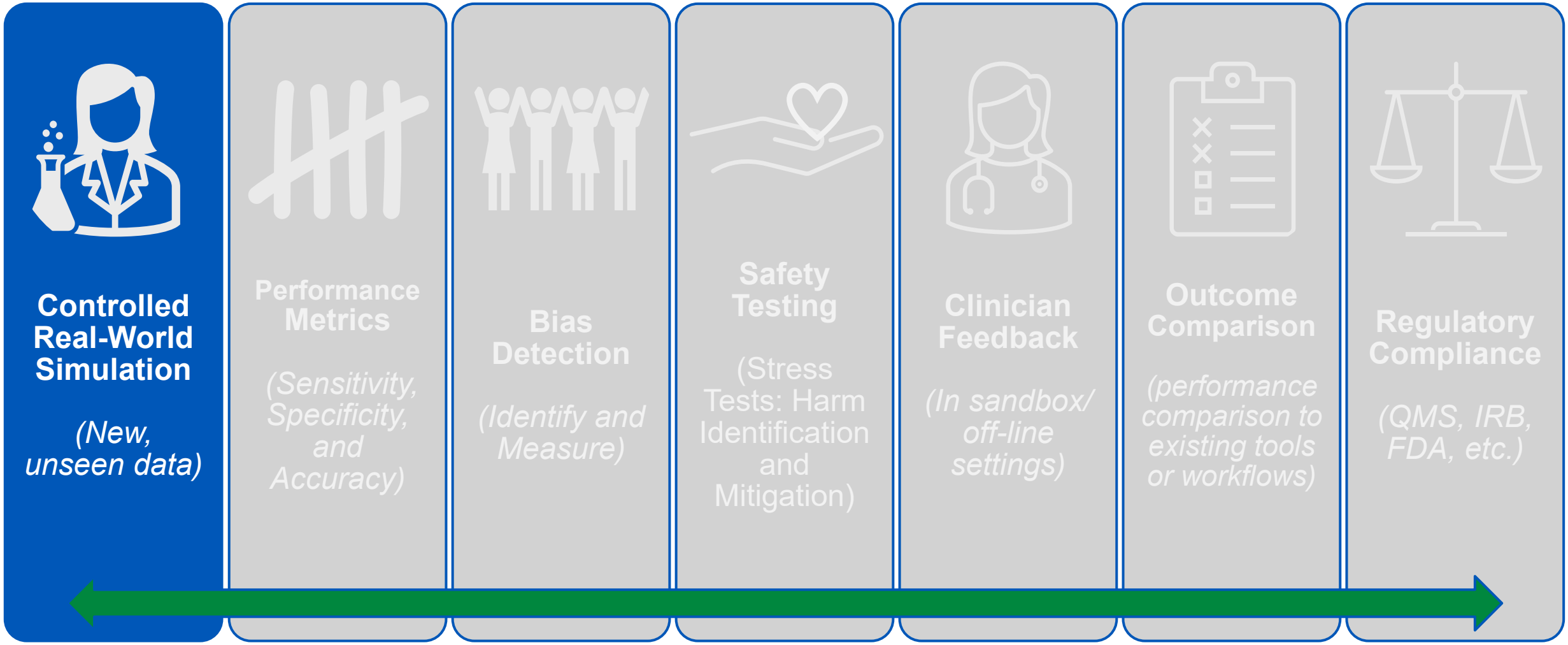
3 Clinical Investigation

WHAT IS PHASE 2?

- ☑ Clinical Validation (“Pilot”) of Intended Use
- ☑ Via Evaluation of Performance and Confirmation that Output is as Expected on Unseen Data

PHASE 2: VALIDATION & TESTING

(WHAT TO LOOK FOR IN PHASE 2 PROTOCOLS)



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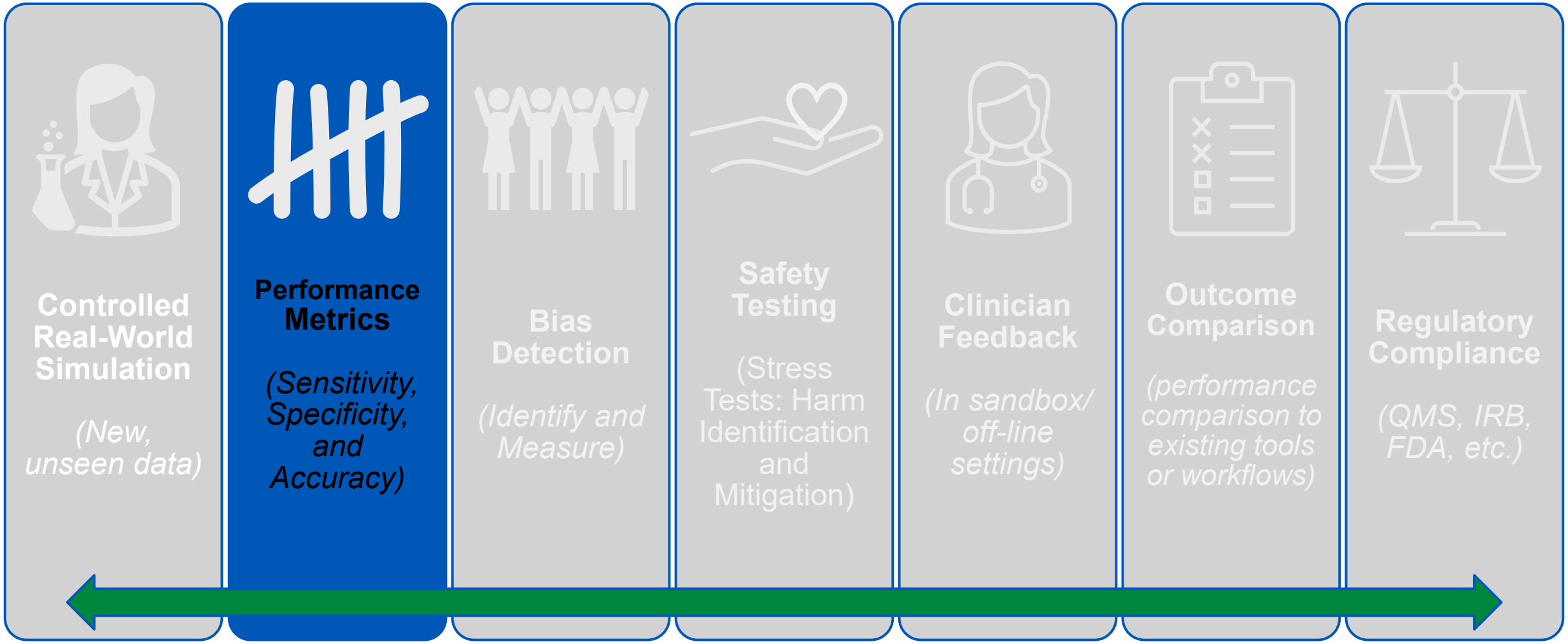

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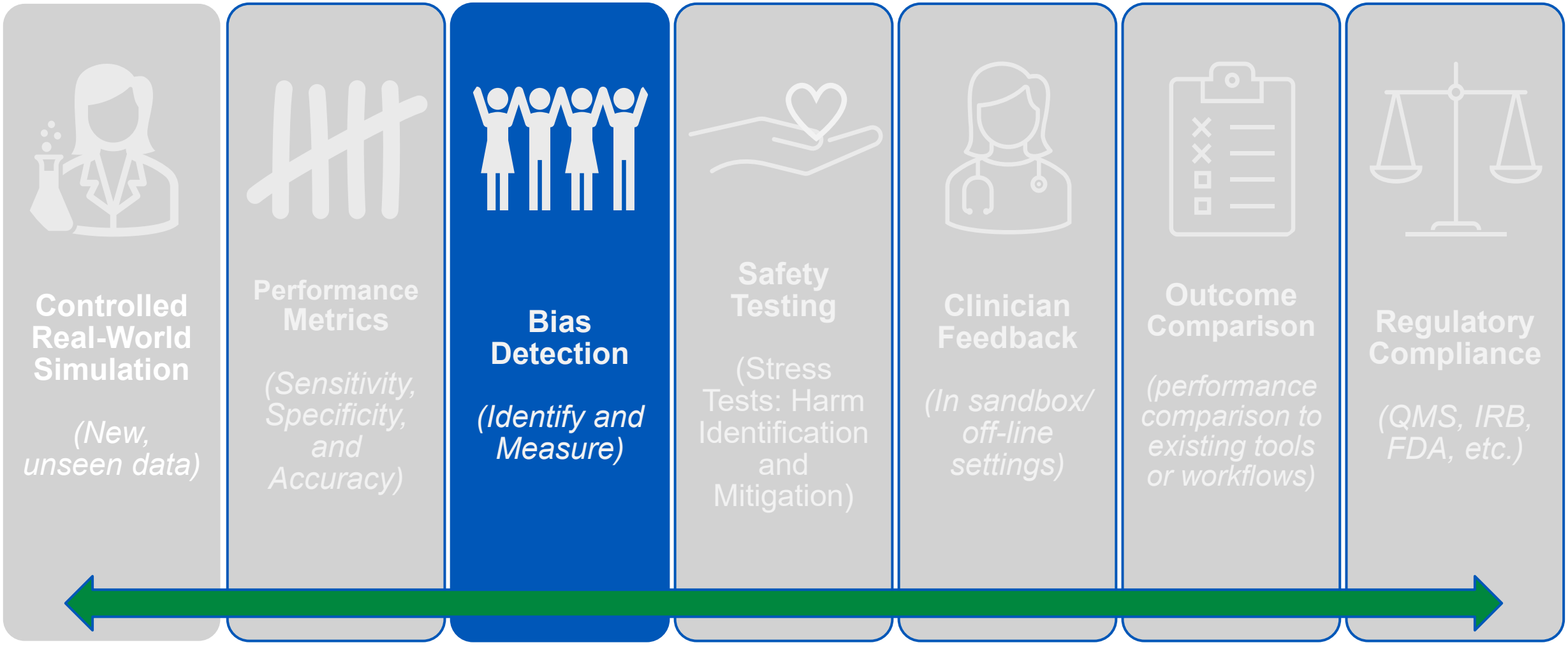

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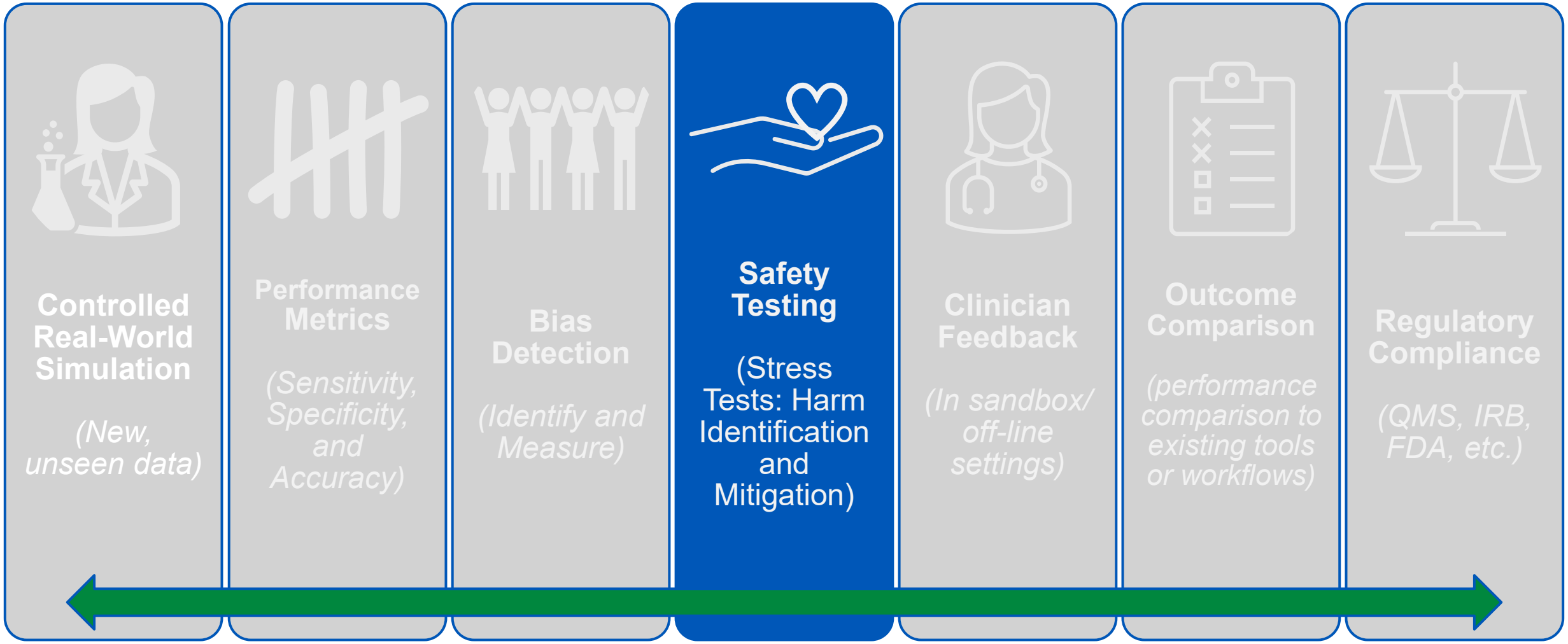

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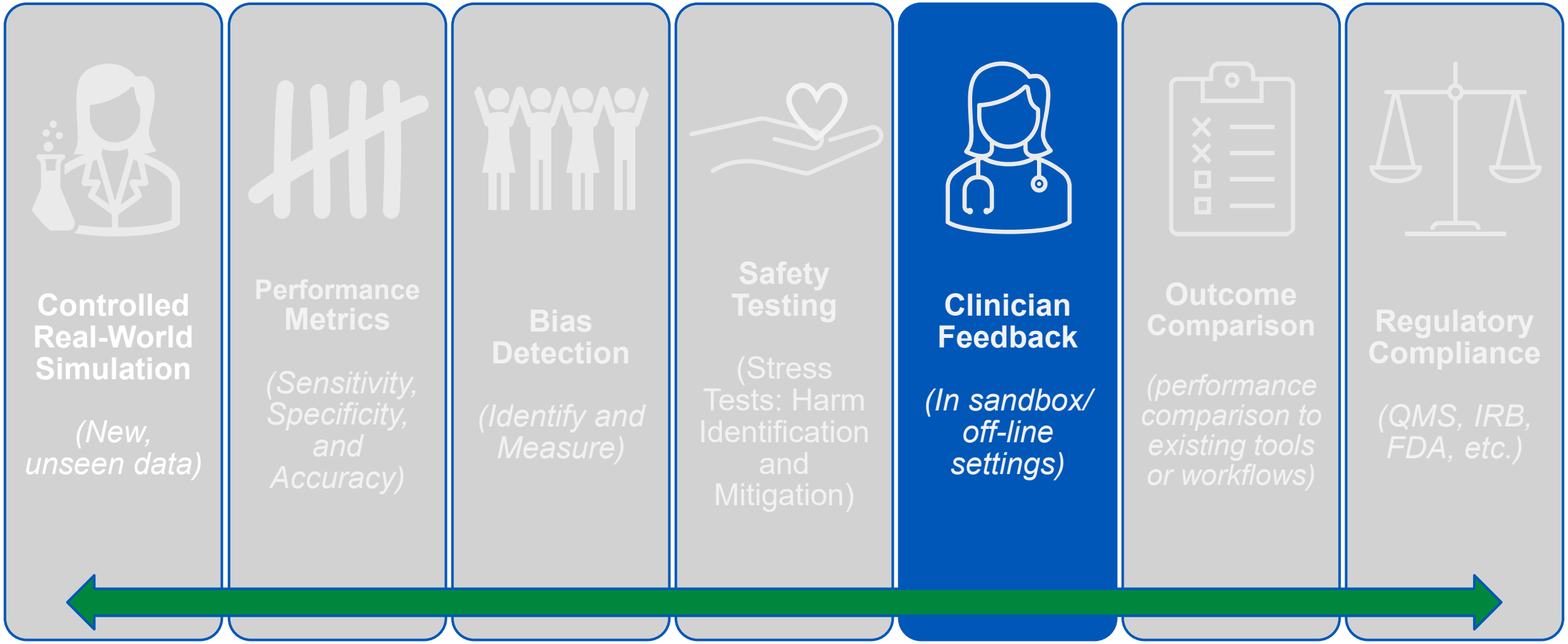

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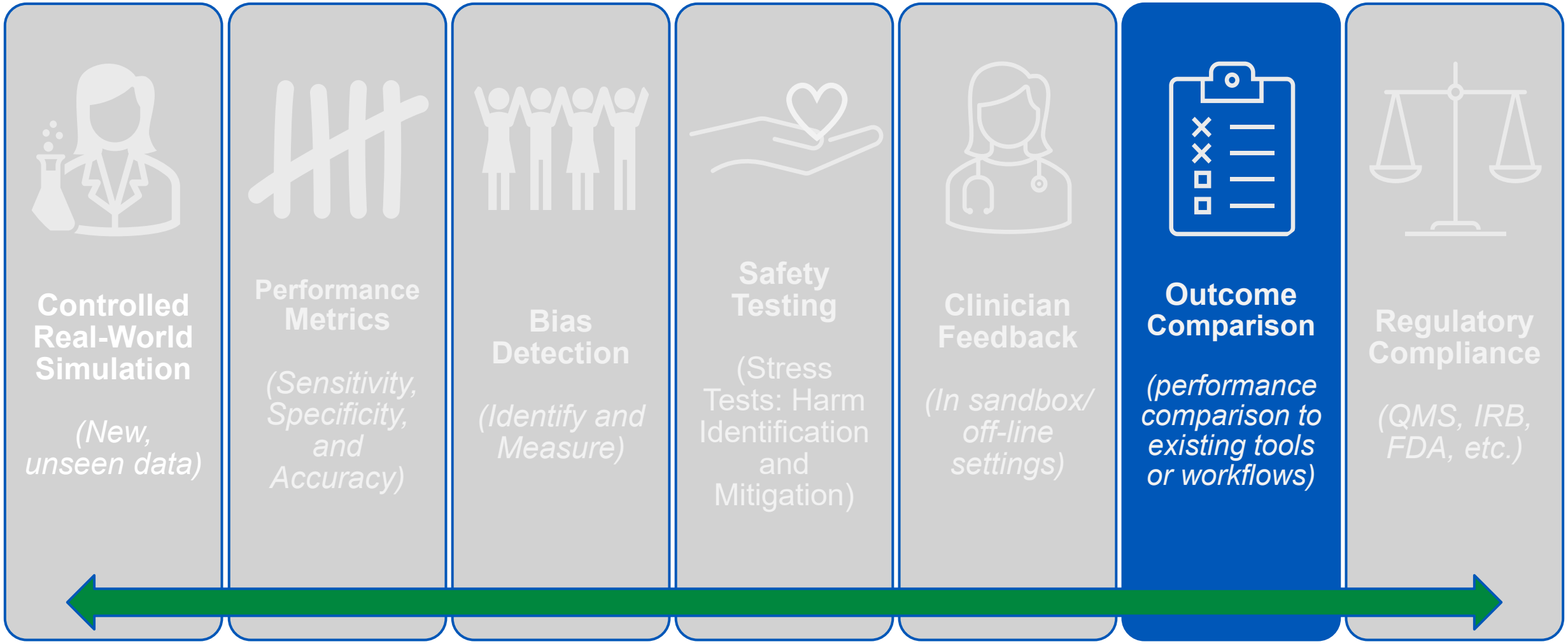

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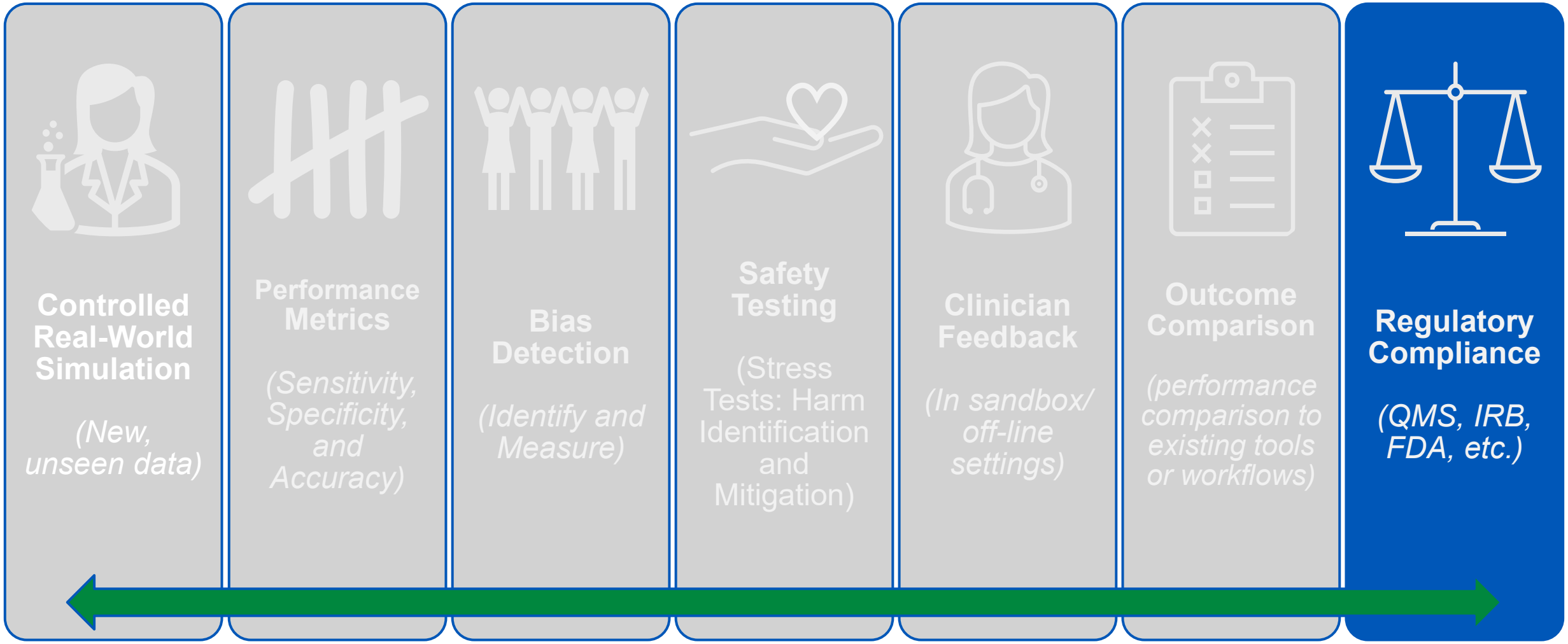

EXAMPLE AI RISKS AND MITIGATION STRATEGIES

Misuse & Improper Training:

- Proper labeling (RUO, IUO, etc) and Instructions for Use (IFU)
- Ongoing Education/Training (model's purpose, proper use, and result interpretation).
- Accessible documentation and support resources

Data Shift/Drift:

- Input validation and error-checking.
- Monitor ongoing performance on equity/fairness
- Update model regularly with new data, perform security assessments

Incorrect Outputs:

- Validate EHR inputs and limit erroneous outputs
- Designate a clinical proponent and implement a monitoring and decommissioning plan

Use Over-Reliance (Automation Bias):

- Disclaimers in the user interface
- Require user training and document acknowledgment of AI limitations

Hallucination:

- Rigorous validation and verification of AI outputs
- Require human-driven decision-making
- Retrain model on diverse datasets
- Implement guidelines for interpreting AI outputs

PHASE 2 – PILOT & VALIDATION

GenAI-enabled tool that provides real-time monitoring of patients admitted to the hospital to create individual risk-of-sepsis scores, which are updated continuously

- ☑ New data
- ☑ Off-line
- ☑ Additional risk controls
- ☑ Study risk determination; Device determination; Device Risk determination

1 Discovery / Ideation

2 Validation

3 Clinical Investigation

WHAT IS PHASE 3?

- ☑ Clinical Investigation
- ☑ Via Collection of Real-World Evidence Demonstrating Safe and Effective Use of AI tool

PHASE 3 – CLINICAL INVESTIGATION

GenAI-enabled tool that provides real-time monitoring of patients admitted to the hospital to create individual risk-of-sepsis scores, which are updated continuously

- ☑ Safety and efficacy data
- ☑ Real-world setting; Potential impact to clinical care
- ☑ Additional risk controls
- ☑ Study risk determination; Device determination; Device risk determination

PHASE 3: INVESTIGATION IN REAL-WORLD SETTINGS

Why would or should a study team conduct a Phase 3 Clinical Investigation?

- **Output from investigational AI tool to be entered into medical record**
- **Study aims include intervention or treatment**
- **Collection of pre- or post-deployment safety and efficacy evidence for AI tool that meets FDA's definition of a medical device**
- **Generation of evidence to substantiate claims (i.e., advertising and promotional content) about AI tool**
- **Demonstration of real-world use to satisfy local governance and oversight bodies**
- **Advancement of state-of-the-art clinical care**
- **Recognition and funding**

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ADOPTION AND APPLICATION

How can we successfully adopt and apply this 3 Phase approach?

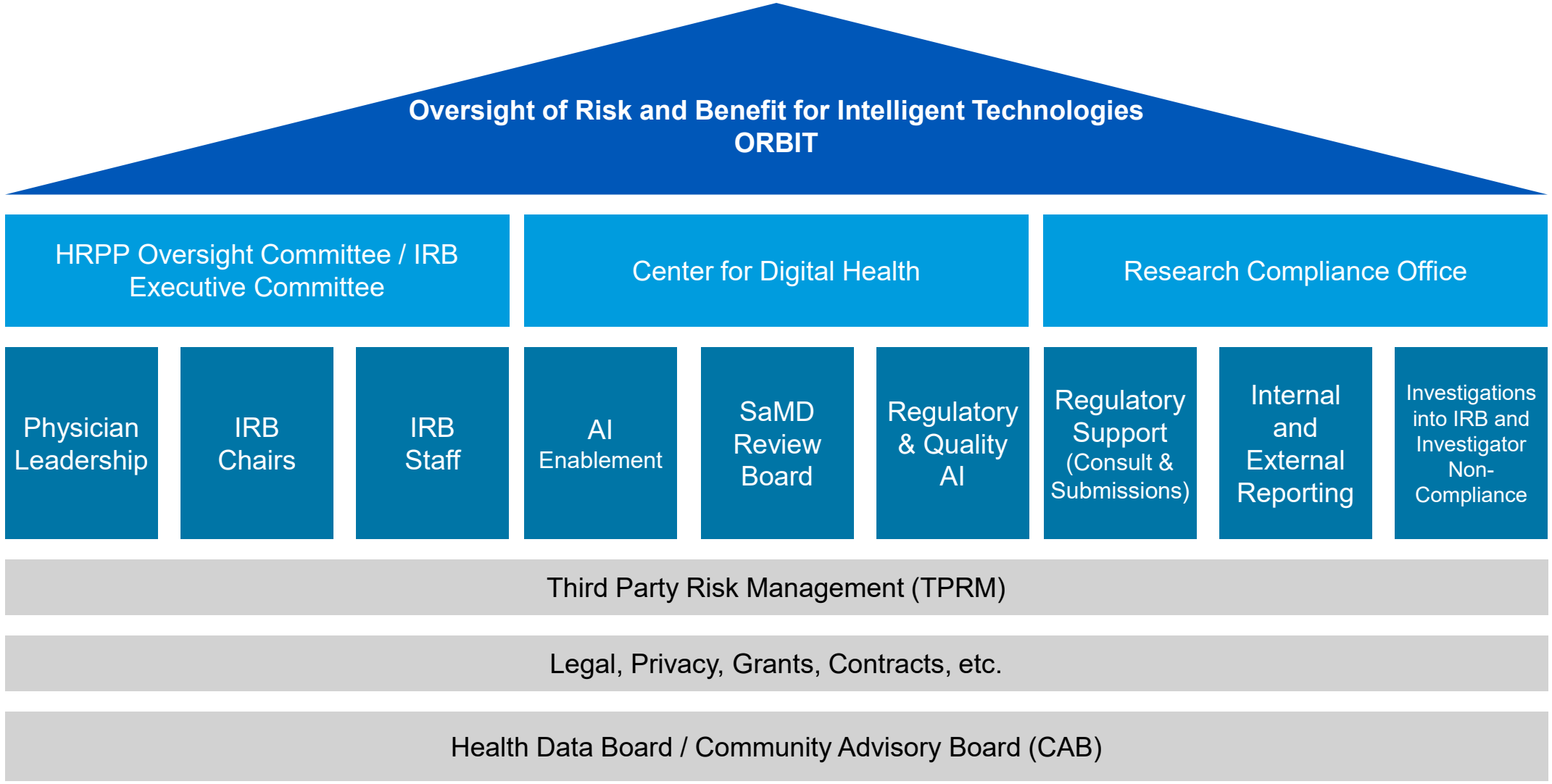
- Establish internal policies, procedures, and templates
- Obtain stakeholder buy-in from key organizational leaders and influencers
- Educate innovators and other frequent collaborators

"IRBS ARE JUST ONE PART OF A MUCH LARGER FRAMEWORK OF STAKEHOLDERS RESPONSIBLE FOR HUMAN SUBJECT PROTECTIONS.

RESEARCH OVERSIGHT IS A SYSTEM OF INTERDEPENDENT ELEMENTS AND MULTIPLE ENTITIES."

-GAO REPORT, 2023

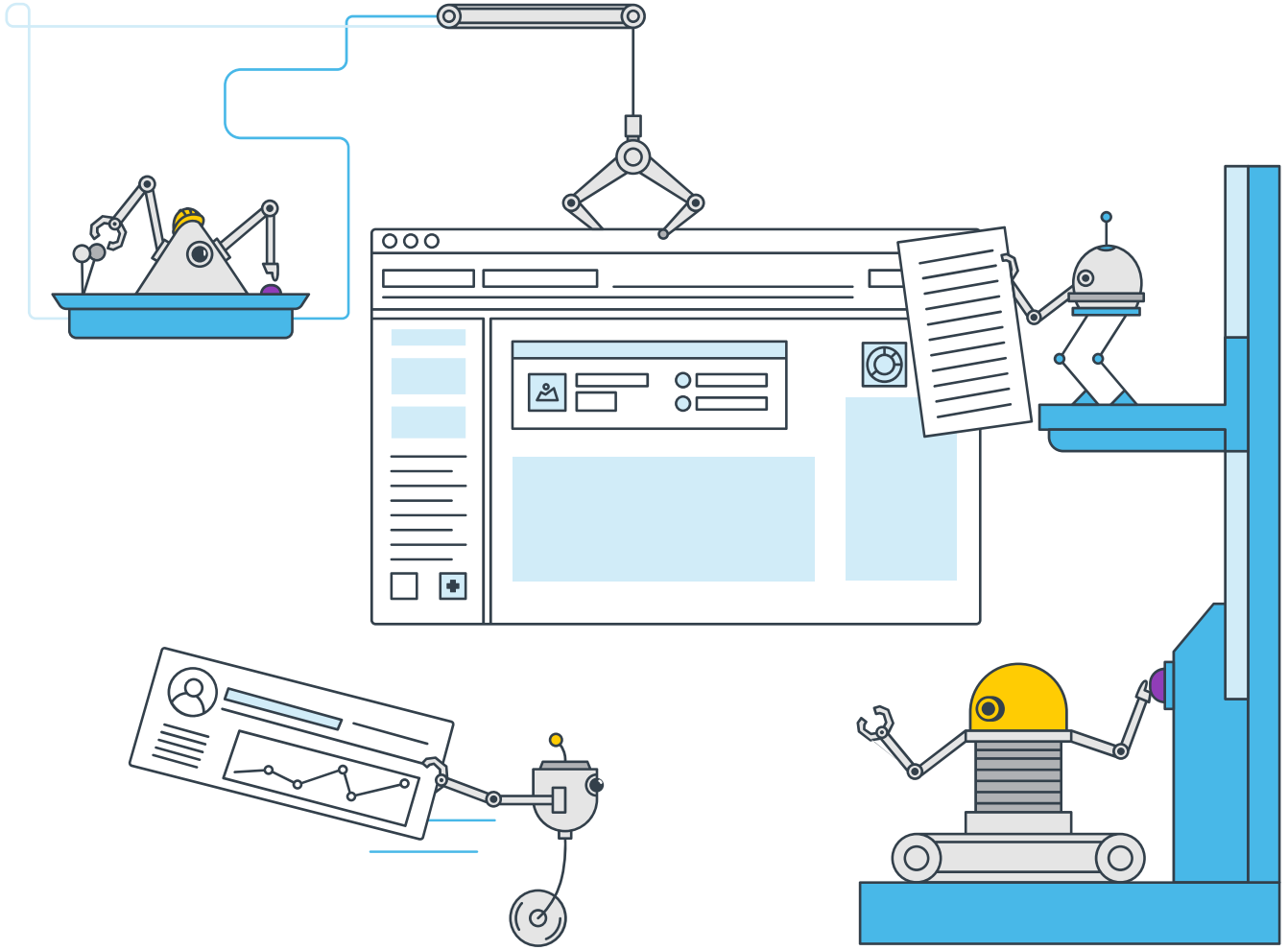
MAYO CLINIC HRPP



Let's Discuss!

Contact info

Eto.Tamiko@mayo.edu



DAVID WAYNE

Joined UM on October 28th 2024

PhD - University of Colorado, Boulder

- Pure Mathematics, Algebraic Geometry

Led Data Science and AI teams at multiple organizations

- Ad Tech
- Fashion Tech
- HR Tech
- Most recently at UKG as the Head of Data Science

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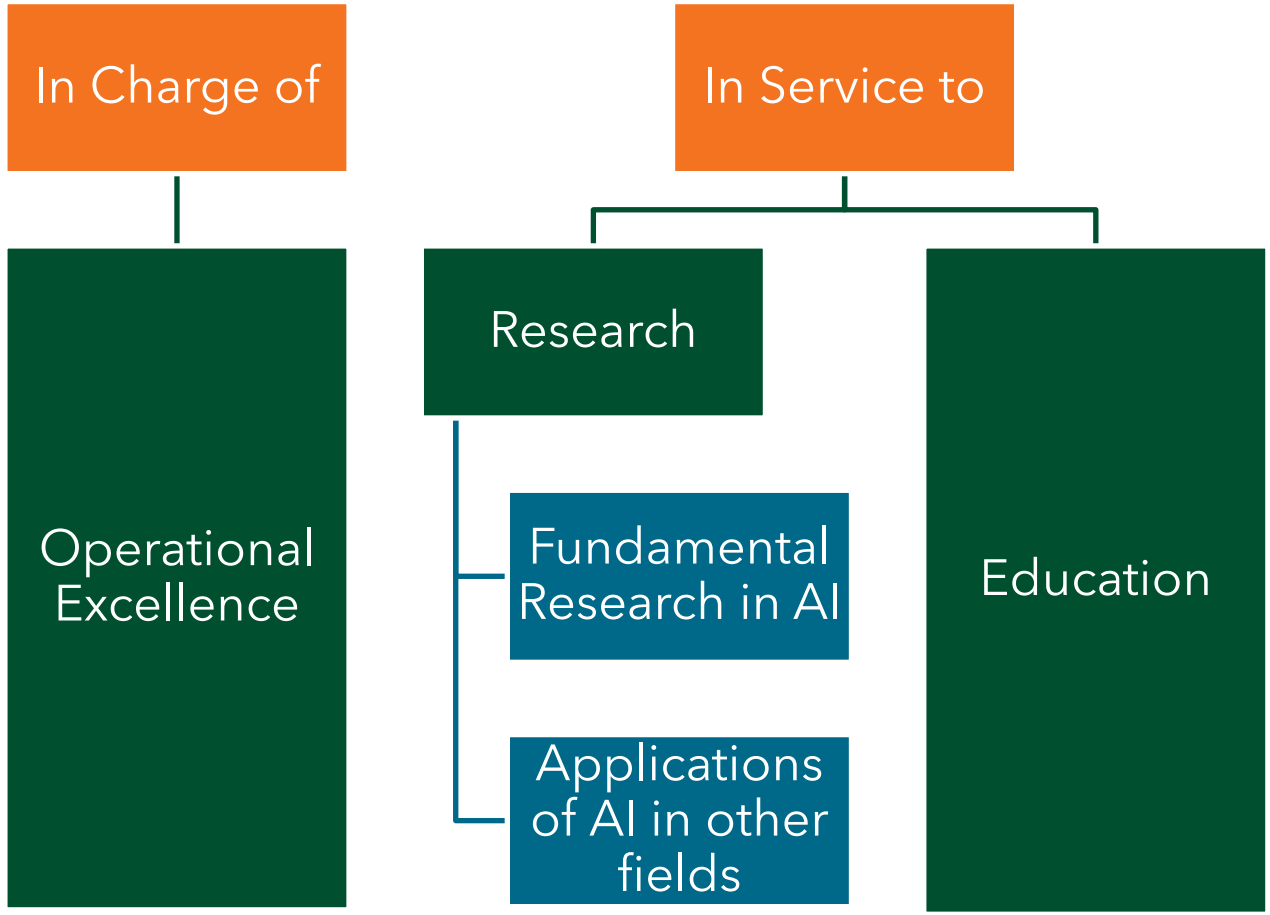
INTRODUCTION – AI CENTER OF EXCELLENCE

Who we are

- AI COE is a team of AI practitioners in IT
- Data Scientists, AI Solution Engineers, Product Managers, Innovators

Role of the AI COE:

- Provide equitable access to AI tools and services
- Development and Implementation of AI for the UM community
- Enhance our operational excellence with the use of AI



SUPPORTING RESEARCH – AI TOOLS AND TECHNOLOGY

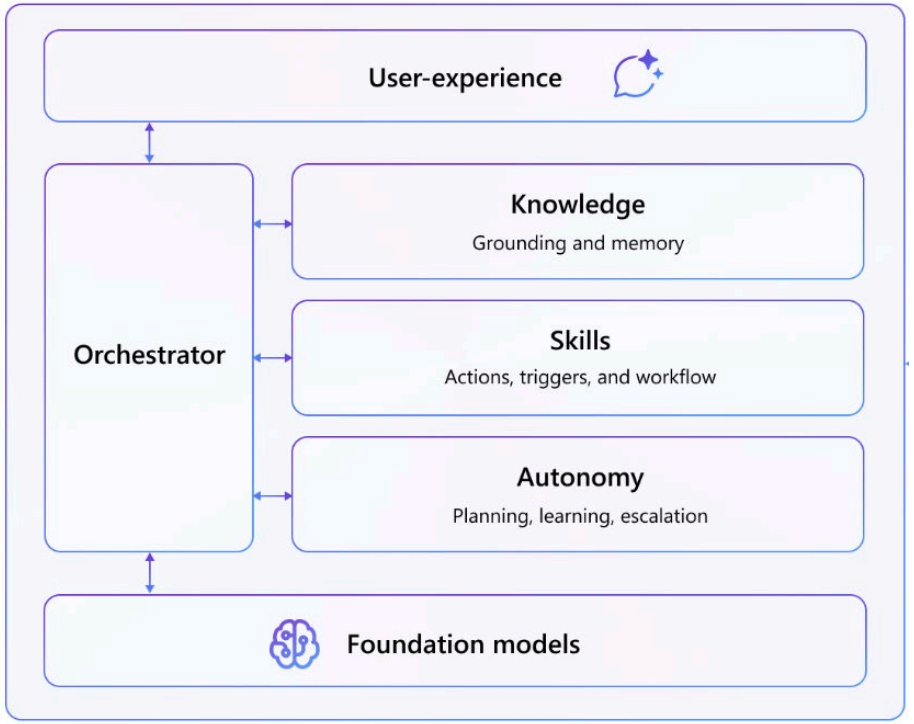
Standard set of AI tools and technology

Aware of the latest advancements in AI

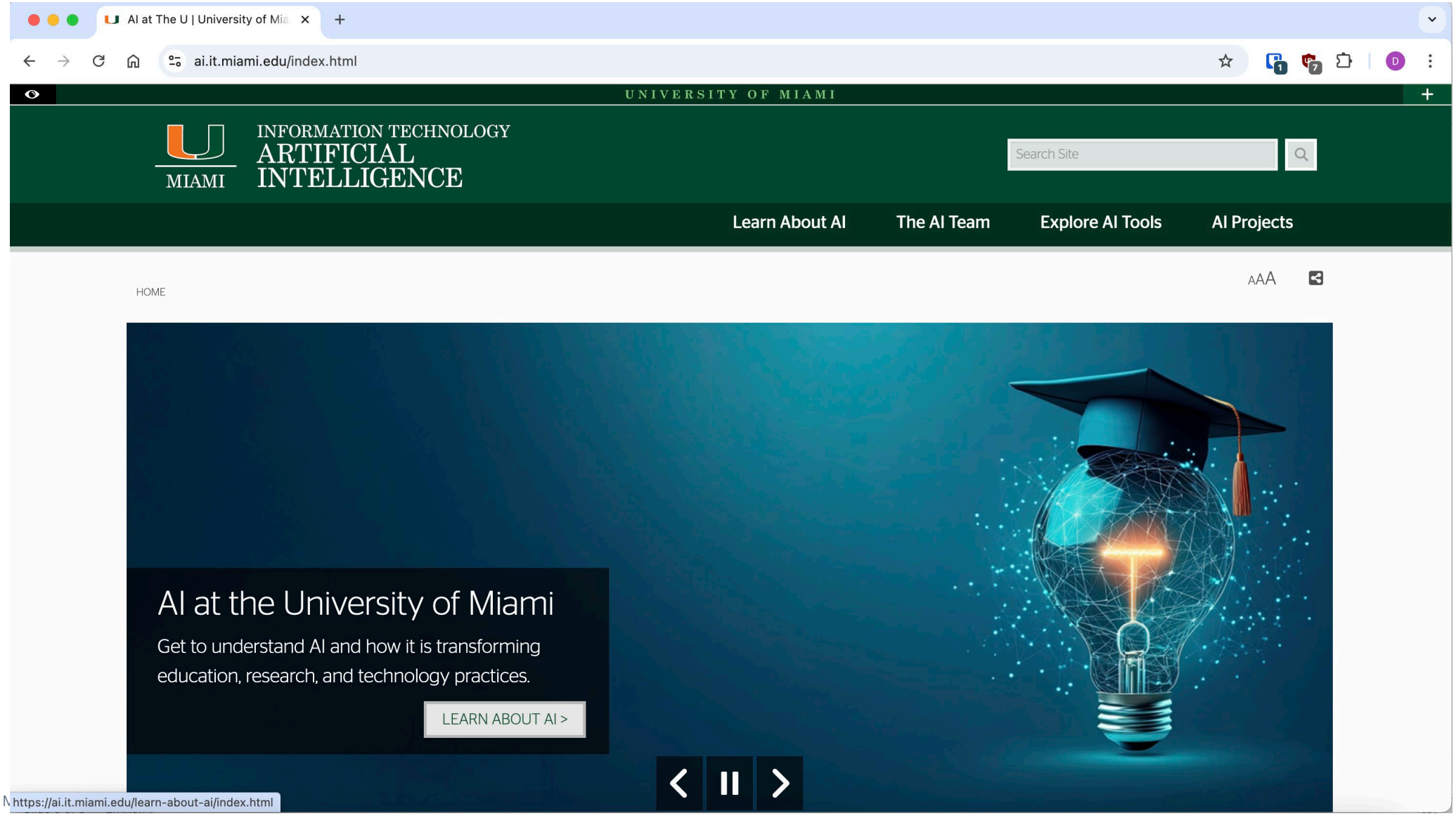
Identify trends in research and augment standard offerings to support emerging research needs

COPILOT FOR MICROSOFT 365 (+AGENTS)

Anatomy of an agent



AI AT THE U – AI.MIAMI.EDU

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Morning Break

HRPP Harmony: Effective Strategies for a Successful Submission

- Highlight the roles and responsibilities of varying groups within the HRPP
- Explore ways to ensure a complete & compliant submission and seamlessly help champion it through the entire workflow
- Describe best practices in grant/contractual & regulatory compliance

HRPP Harmony: Effective Strategies for a Successful Submission

Stewart MacIntyre, Office of Research Administration, Office of the Vice Provost for Research & Scholarship

Lory Hayes, Disclosures & Scholarly Activities Management, Office of the Vice Provost for Research & Scholarship

Nicole McCullough, Investigator Initiated Trial Services at the U, Office of the Executive Dean for Research, MSOM

Ashley Kaufman, Research Quality Assurance, Office of the Vice Provost for Research & Scholarship

Katuzka Barbery, Clinical Trials Office, Jackson Health System

Session objectives

- Highlight the roles and responsibilities of varying groups within the HRPP, be it regulatory and/ or institutional requirements
- Explore ways to ensure a complete & compliant submission and seamlessly help champion it through the workflow
- Describe best practices in grants/contracts & regulatory compliance

Relevant Conflicts

- The following individuals DO NOT have an actual or potential conflict of interest in relation to this program/presentation:
  - Stewart MacIntyre
  - Lory Hayes
  - Nicole McCullough
  - Ashley Kaufman
  - Katuzka Barbery

ORA Submission-Industry Sponsored

- **Simultaneous Submission to IRB and ORA is required**. (Effective July 29, 2024)
  - ORA and IRB submissions must be linked using the “Manage Relationships” functionality in either the FP or IRB workspace.
  - Studies submitted to ORA must be submitted to IRB within the latter of either
    - two weeks, or
    - when ORA starts to work on the coverage analysis (MCA) and budget.
- **Protocol Modifications**:
  - CTA, Budget and MCA need to align with current version of Protocol approved in IRB.
  - Protocol Amendments may require an amendment to the CTA (modified clinical research protocols, modified ICFs, Change of PI and other changes may warrant revision of MCA).
- **If JHS is involved**:
  - JHS must be included as a Resource in the applicable FP (Funding Proposal) in IBIS
    - JHS CTO Application
    - JHS Calendar

ORA Submission-Industry Sponsored

Use ORA Resources!

https://www.ora.miami.edu/about-ora/clinical-research/engaging-clinical-research/index.html

- Has information on some Institutional fees.
- F&A Rate for Industry Clinical Trials (36%)
- Checklists:
  - Clinical Trial Checklist
  - Budget Checklist

Pre-Award Guidance

https://www.ora.miami.edu/about-ora/pre-award/contracts/pre-award-guidance/index.html

TIPS!

- When in doubt. Ask.
- Try to avoid the cart before the horse.
  - i.e. ORA cannot begin review of a CTA before the protocol is finalized.

Pre-Award Guidance

Form	Description	Date Revised
IBIS Submission Guidance-Advance Account	Please follow this guidance document on how to submit an Advance Account to ORA through IBIS.	New
IBIS Submission Guidance-Award Mod Request	Please follow this guidance document when submitting an Award Modification Request (AMR) to ORA through IBIS.	New
IBIS Submission Guidance-CDA	Please follow this guidance document on how to submit a new Confidentiality Agreement to ORA through IBIS.	New
IBIS Guidance-Collaboration Agreement	Please follow this guidance document on how to submit a new Collaboration Agreement to ORA through IBIS.	New
IBIS Submission Guidance-CTA	Please follow this guidance document on how to submit a new Clinical Trial Agreement to ORA through IBIS.	New
IBIS Submission Guidance - DUA	Please follow this guidance document on how to submit a Data Use Agreement to ORA through IBIS.	New
IBIS Submission Guidance-MTA	Please follow this guidance document on how to submit a new Material Transfer Agreement to ORA through IBIS.	New
IBIS Submission Guidance-OS (New)	Please follow this guidance document on how to submit a new Outbound Subcontract to ORA through IBIS.	New

INVESTIGATOR INITIATED TRIAL SERVICES AT THE U (IITSU)
OVERVIEW OF SERVICES

Regulatory Services & Support

- FDA submission support for Investigational New Drug (IND) and Investigational Device (IDE) applications
- Study document review (protocols, CRFs, ICFs, DSM plans)
- Clinical trial regulatory guidance & consultations.
- Managing the Trial Master File when UM is the sponsor

Clinical Trial Monitoring Services

- Monitoring services for UM Investigator Initiated Trials (IITs)
- Central monitoring for multi-site IITs

Project Management Services (for multi-site IITs)

Data Management Services (for multi-site IITs)

Safety Monitoring (when UM has sponsor role for multi-site IITs)

Clinical Research Education

MIAMI MILLER SCHOOL of MEDICINE

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IITSU ancillary review (formerly CRORS ancillary review)

Investigator Initiated Trial Services at the U (IITSU) ancillary review is required for new studies involving a UM investigator-held IND or IDE for the studies to ensure that the PI has either contracted with a monitor, CRO or would like to engage IITSU monitoring services.

Before the initial ancillary approval, the PI should contact IITSU to discuss any services that they may need.

For IITSU services:
Nicole S. McCullough, MS, CCRP
Director, Regulatory Support
Investigator Initiated Trial Services at the U
University of Miami, Miller School of Medicine
Don Soffer Clinical Research Center, Rm. 1238
Ph: 305-243-0493
E-mail: nshank@med.miami.edu

For training of new PIs:
Alina Gjerpen
Project Manager
Investigator Initiated Trial Services at the U
Ph: 305-243-0492
E-mail: arg136@med.miami.edu

IBIS IRB submission – best practices

Basic Study Information

8. * **Who initiated this study?**

- ○ UM Investigator
- ● Industry
- ○ Cooperative Group
- ○ Non-UM Investigator
- ○ Other Institution

Clear

Answer should reflect the regulatory sponsor of the study (typically shown on the protocol title page or contacts list)

Drugs Q3 or Devices Q3 – IND, IDE or HDE number

3. * **Identify each IND:**

+ Add

IND Number	IND Holder	Other Holder
123456	Investigator	

IND Holder

If this study is being conducted under any IND numbers, please list each IND here.

Please indicate the IND Holder as follows:

- If the IND is held by the PI for this study OR any other UM investigator/faculty member, select **Investigator**
- If the IND is held by the drug manufacturer or study's sponsor (not a UM investigator), select **Sponsor**
- If the IND is held by a non-UM investigator, select **Other** and enter the name of the IND holder in the "If other, identify the IND Holder" box

Protocol Development Resources – Coming Soon!!

ProtocolBuilder® cloud-based software solution

- 16 different protocol templates (increase regulatory compliance & help w/ IRB review)
- Guidance for what to write in protocol sections, some boilerplate starter text
- User friendly, easy to navigate
- Formatting similar to Microsoft Word, shows tracked changes
- Automatic version control, automatically creates summary of changes
- Export to Microsoft Word or Adobe PDF (working on possible integration with IBIS IRB submission)
- Upload references library
- Collaboration - automatic formatting, ensure all working on same version, email notifications
- Complimentary access to CITI “Research Study Design” & “Observational Prospective Protocols” courses

CommUnIITy

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ProtocolBuilder

INTERVENTIONAL

- NIH and FDA Protocol Template for Phase 2 and 3 IND/IDE Clinical Trials
- Interventional FDA Approved Drug/Biologic
- Interventional Investigational New Drug/Biologic
- Interventional Non-Significant Risk Device
- Interventional Significant Risk Device
- Interventional Combination
- Behavioral Intervention (incl. benign behavioral intervention)

OBSERVATIONAL

- Chart Review
- QA/QI
- Repository with the use of Broad Consent
- Repository without the use of Broad Consent
- Observational study of a FDA regulated product
- Observational study of individual or group characteristics or behavior, or human factor evaluation

SOCIAL BEHAVIORAL

- NIH Protocol Template for Behavioral and Social Sciences Research Involving Humans
- Social Behavioral

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UM policies related to clinical research

- HRP-103 - UM Investigator Manual
- Clinical Trial Management and Participant Enrollment and Tracking (under UMHC location in PolicyStat)
- Certified Copies in Human Subjects Research
- Confidential Audit Reports
- Corrective Action Preventative Action Plans in Human Subjects Research
- Clinical Trial Disclosure: Determination and Protocol Registration
- Electronic Medical Record Access by External Parties
- HIPAA Privacy - HP 57.0 - Document Retention
- HIPAA Privacy - HP 9.0 - Accounting of Disclosures
- Hosting External Governmental Audits of Clinical Research
- Research Study/Clinical Trial Patients (under UM Laboratories location in PolicyStat)
- Responsibilities of an IND/IDE Holder
- Responsibilities of Researchers Using Electronic Signatures
- Use of Electronic Regulatory Binders in FDA-Regulated Research

Contact Info

Investigator Initiated Trial Services at the

Website: https://med.miami.edu/research/clinical-research/iitsu
E-mail: iitsu@miami.edu

Nicole McCullough, MS, CCRP, Director, Regulatory Support
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MIAMI MILLER SCHOOL of MEDICINE

CURATING CONNECTION 2025 IRB Member Retreat Innovations Interlude

Conflict of Interest (COI) Committee

UNIVERSITY OF MIAMI

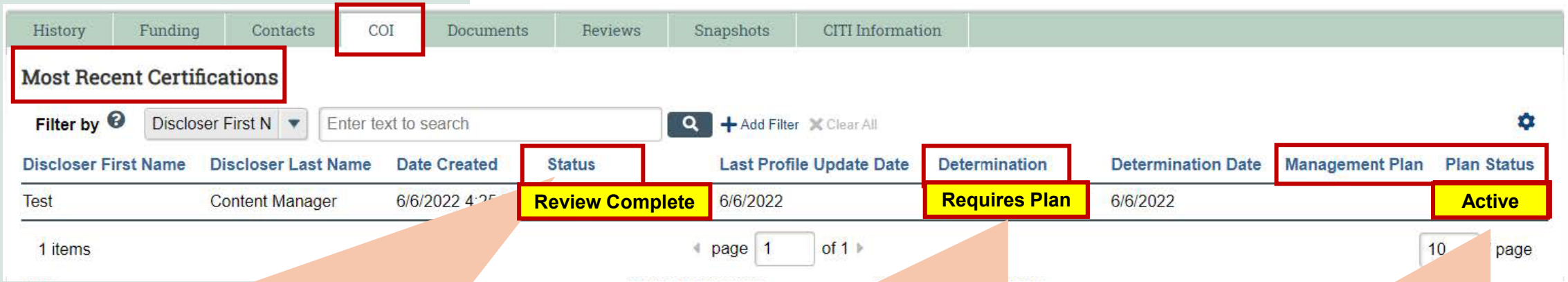
- **UM's COI policy requires all team members (TMs) complete before participating and annually:**
  - *COI training*
  - *Disclosure process*

- **Non-UM team members (TMs) must complete UM's Interest Disclosure Form (IDF) process**
  - *Process includes COI training and disclosure of related interests*
  - *Must be completed before TMs can participate on project*
  - *Notify DSAM via Ancillary Review (AR) submission listing the investigator's name and email address*
  - *DSAM contacts non-UM TMs via Redcap, and will contact the PI if no response*
  - *DSAM will close the AR in eProst when the TMs are cleared to participate*
  - *If additional TMs are added, must be noted in the AR*

- **UM's COI policy requires that *ANY* relationship to a HSR study must be disclosed to participants**
  - *Consulting/teaching/ad board (irrespective of compensation), ownership (equity/shares/options)*
  - *Sponsor/funder/manufacturer of a drug/device used in the study*
  - *ETC*
  - *Method of disclosure is at the purview of the IRB*

Contact us anytime! DSAM@miami.edu or 305-243-0877

Review Process: Does a TM need to disclose in ICF?



Status:

1. No Review Required
2. Under Review
3. Review Complete

Determination

(*AKA: Does the TM need to disclose in ICFs?**)

No disclosure required

1. No Review Required
2. Unrelated

Disclosure is required*

3. No Conflict (related interest, no plan)
4. Requires Management Plan

Plan Status:

Disclosure is required*

1. Drafting (by DSAM)
2. Pending Discloser Acceptance
3. Active (AKA study can move forward)

Creating a Successful CAPA Plan:

Finding the Perfect Balance of Compliance & Comfort

Ash Kaufman, MA, CCRP
Sr. Quality Assurance Auditor
Research Quality Assurance (RQA)

Relevant Conflicts

- I DO NOT have an actual or potential conflict of interest in relation to this program/presentation.

Corrective and Prevetive Action (CAPA) Plans:
What Are They & Why Do We Need Them?

- Quality management system used to:
  - Identify the research-related problem (understand the root cause(s) of the non-compliance; if you don't know what's causing the problem, how can you fix it?)
  - Fix/**CORRECT** the problem (immediate vs. long-term solutions)
  - Create actions to **PREVENT** the problem from recurring (examine potential risks and areas that need improvement, break patterns, develop new processes, enact change)

- A successful CAPA Plan
  - Is factual, realistic and measurable
  - Stands the test of time and can be implemented/applied across similar situations effectively
  - Improves overall efficiency and quality of the study

- Compliance Creates Confidence & Comfort within a study team

Creating a Successful CAPA Plan is Like Creating the Perfect Hamburger

All You Need are the Right Ingredients:

The "Patty"	Your **Root Cause** is the main/core reason(s) that caused the problem
Seasoning	What **techniques** will you use to identify the root cause(s)? Ex: 5 Whys vs. Fishbone Diagram
Toppings & Condiments	What actions will you implement to **correct** the problem and **prevent** it from happening again? Reactive vs. Proactive
The Bun	Does your CAPA hold up? Was it **Effective**? Things to consider: Were timelines and responsibilities met? Were you able to implement all your changes/actions? Does your documentation for these actions meet regulatory & UM standards?

Ask yourself, "is the issue still occurring?"

The CAPA Plan “Secret Sauce”

Empathy

Engagement

Empowerment

Effectively employing these skills during the creation of a CAPA Plan:

- Can create a sense of comfort within the study team
- Helps instill confidence within them that issues will be addressed, compliance will be obtained, and future problems will be mitigated

Example #1: The CAPA Process

- Issue: Specific bloodwork was not being collected at subject study visits
- Background:
  - PI amended protocol to include a specific lab at *all* study visits
  - All study team members trained on the updated protocol, according to Complion
  - All 3 study sites experienced the same issue

Why was this not being collected? Find the Root Cause(s)

- CRCs & RNs: Didn't know this lab was required at every study visit

  Why? I didn't see it in the updated protocol; I thought it was only required at screening; I wasn't notified

- PI: Not aware of the issue

  Why? External Monitor never reported this was missing

Assembling the CAPA Plan: Team Effort

Study Team + Auditor

<u>Corrective Actions</u>:

- Record the Deviation
- Determine if there are additional corrective measures?

Study Team + Auditor

<u>Preventive Actions</u>

- Increasing communication: Discuss protocol updates in future PI oversight and team meetings
- Having any new, future labs featured more prominently in the protocol vs. in the middle of a footnote

Ask: What Else Can We Do As A Team to Prevent the Issue from Recurring?

Example #2: A CAPA Plan in Progress

- Issue: Study Medication not being administered as per protocol and pharmacy manual timeframe

- Background:
  - The study medication must be administered within 1.5 to 2 hours
  - Protocol notes that any medical staff administering IP must be trained
  - Numerous examples of nurses exceeding administration times at all 3 sites

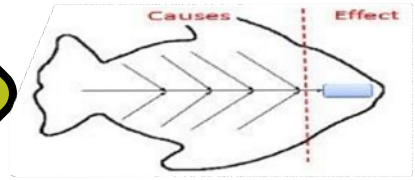
Why are Infusion times exceeding 2 hours ?

Brainstorm as a Team to Identify the Root Cause(s) and Create Effective Corrective & Preventive Actions

Focus on the Root Causes…

The Treatment Plan did not include infusion time instructions; only featured infusion rate and calculated dose

#1 **#2** **#3**



The in-service training provided to nurses did not contain/discuss infusion timeframes

PI and study team were unaware that nurses were exceeding infusion times; issue was never addressed during any external monitoring visits

Final Thoughts:
Creating and Maintaining CAPA Confidence

- A CAPA Plan is an opportunity to:
  - Learn from research-related mistakes and work together to implement effective solutions that will prevent issues from recurring
  - Support and Protect the UM Research Community

- A Successful CAPA Plan:
  - Creates Corrective and Preventive Actions/Measures that are factual, realistic measurable and sustainable
  - Empowers teams to find *their* perfect balance of compliance and comfort

Thank You!

Ash Kaufman
RQA
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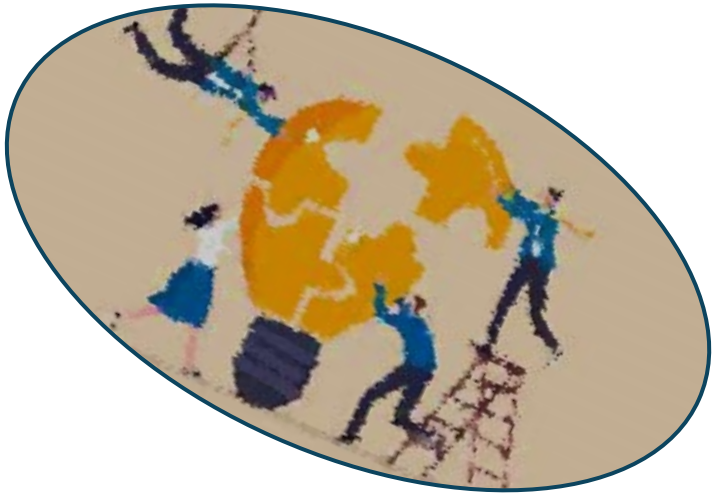
https://www.research.miami.edu/about/admin-areas/roi/rqa/index.html

EFFECTIVE STRATEGIES FOR A SUCCESSFULL SUBMISSION



KATUZKA BARBERY FMD, EMBA

DIRECTOR

OFFICE OF RESEARCH ADMINISTRATION

JACKSON HEALTH SYSTEM

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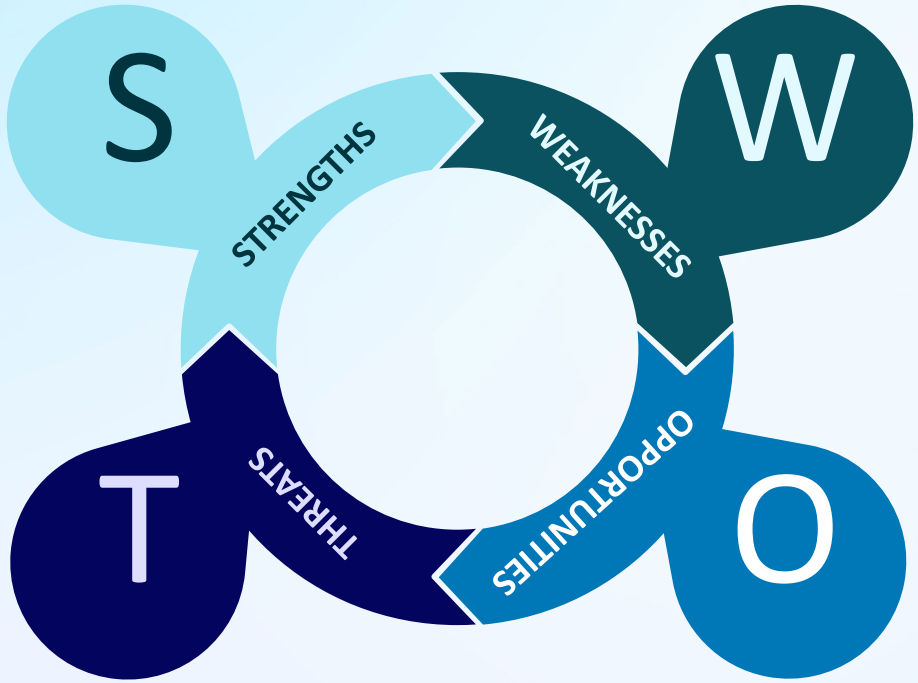
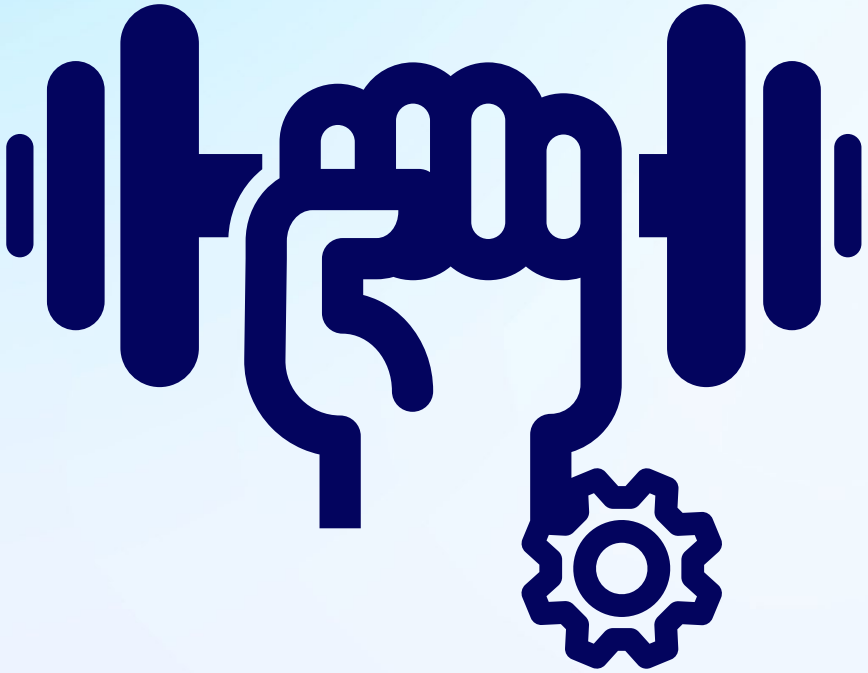
INTRODUCTION



- Jackson Health System does not have an IRB and relies on other IRB's including the University of Miami
- § 46.112 Review by institution: Research covered by this policy that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB
- JHS ORA at the pre-approval stage ensures that there is financial, and operational feasibility to conduct research decreasing risks and billing compliance errors to the institution in the post-approval stage.
- Understand how we can do better in all areas by learning how to do a SWOT analysis

STRENGTHS



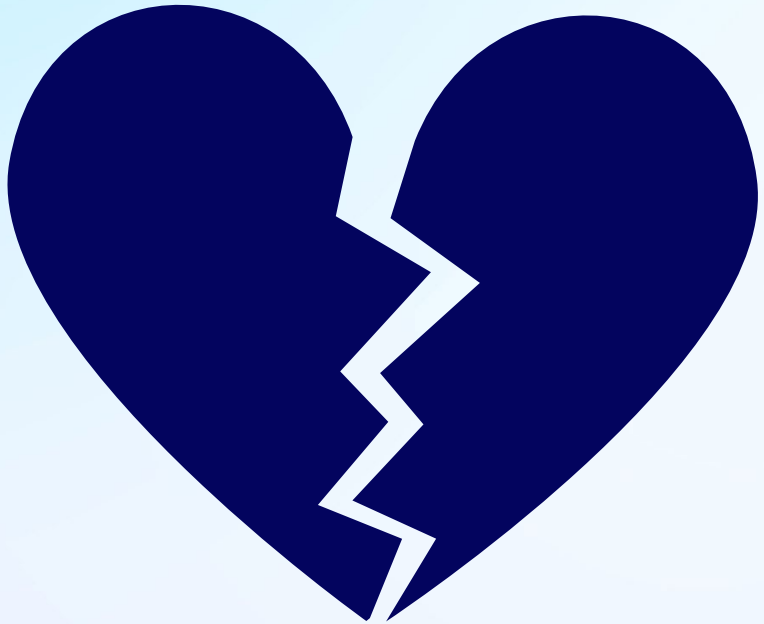
Collaborations

- Between UM IRB and JHS ORA
- Between UM ORA and JHS ORA
- Between Study teams and JHS ORA
- Between UM business services and JHS

Tools & Resources

- Ancillary Committees
- Oneness Research Solution
- JHS ORA
- UM Research Navigator
- JHS ClickUp study updates

WEAKNESSES



IRB Submission

- JHS is not added as a Site and Ancillary Reviewer at time of submission

Communication

- JHS clarifications via IBIS or via email are not addressed

Missing Documentation

- JHS application, study calendar, workflow not submitted timely or uploaded in the IBIS (if applicable) or when requested

- Missing HIPAA waiver for recruitment purposes when using External IRB

OPPORTUNITIES

Review the Tools and Resources Available

- JHS ORA website
- FAQs and Compliance Checklist

IRB Submission Requirements

- Don’t forget to add JHS as a site and ancillary reviewer
- Submit the JHS Application at time of submission

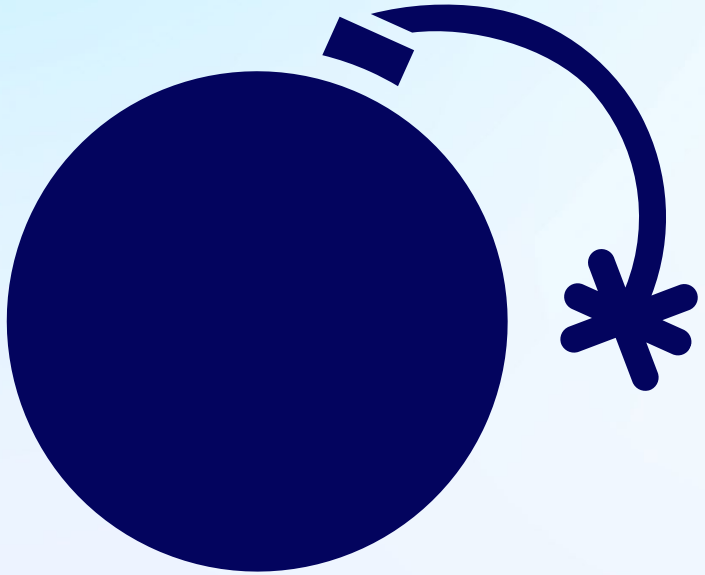
UM/JHS ORA Requirements

- Submit the JHS Application at time of submission
- Submit the JHS study calendar completed to JHS ORA when requested or directly to JHS for non-industry studies
- Submit the completed JHS Workflow to JHS ORA when requested
- Ensure to review the instructions provided by UM business services for service agreements

Communication

- Ensure to answer all questions timely to prevent additional delays

THREATS



- Unclear documentation and data requests submitted
- Not following protocol template guidelines
- Lack of response from study teams
- Lack of personnel
- Non-parallel submissions
- Not reviewing all resources available

ACTION PLAN

1. **Submit in parallel**
2. **Add JHS from Start**
3. **Use Tools & Resources**
4. **Respond Timely**
5. **Collaborate**
6. **Contact us in Advance**

CONTACT US

General Inbox

- JHS-CTO-Submissions@jhsmiami.org

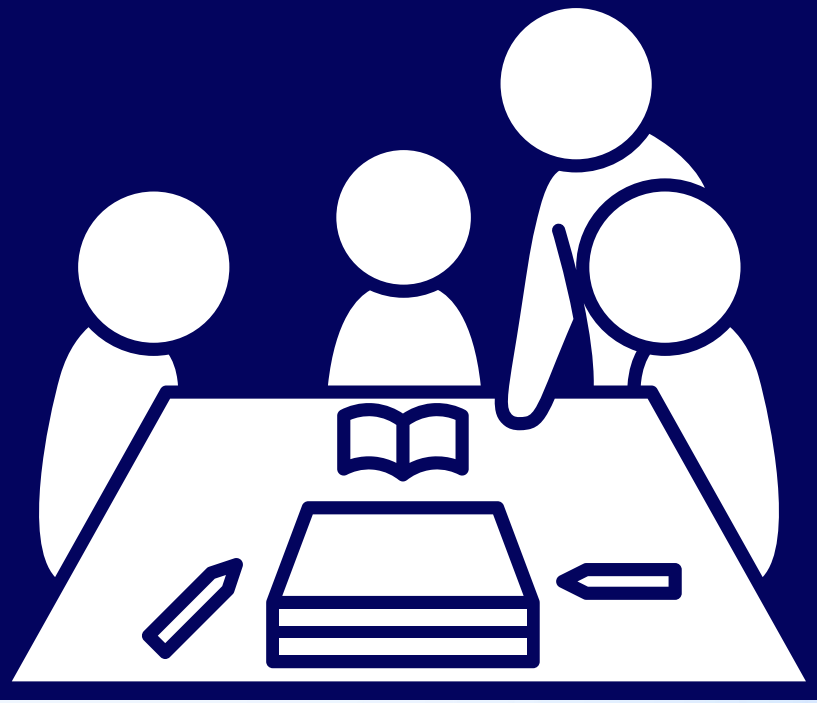
Data Requests and EMR Access

- Office of Research | Jackson Health System
- JHS-CTO-Research-Tickets@jhsmiami.org
- Oneness Research Solution

Informed Consent, Enrollment Form Submissions and Research P&P Training

- ClinicalTrialsOffice@jhsmiami.org

LET'S DISCUSS



THANK YOU

OVPR+S Pragmatic Compilation: Best Practices & Trending Topics in IRB Review

- Discuss IRB QI trends to help ensure more streamlined submissions
- Explore proactive measures to avoid bottlenecks
- Review innovative approaches in assessing effectiveness

Requirements and **Actions** When a Reportable New Information (**RNI**) is Identified as a **Noncompliance** Report

Denise Dimitriu, IRB Regulatory Analyst, HSRO

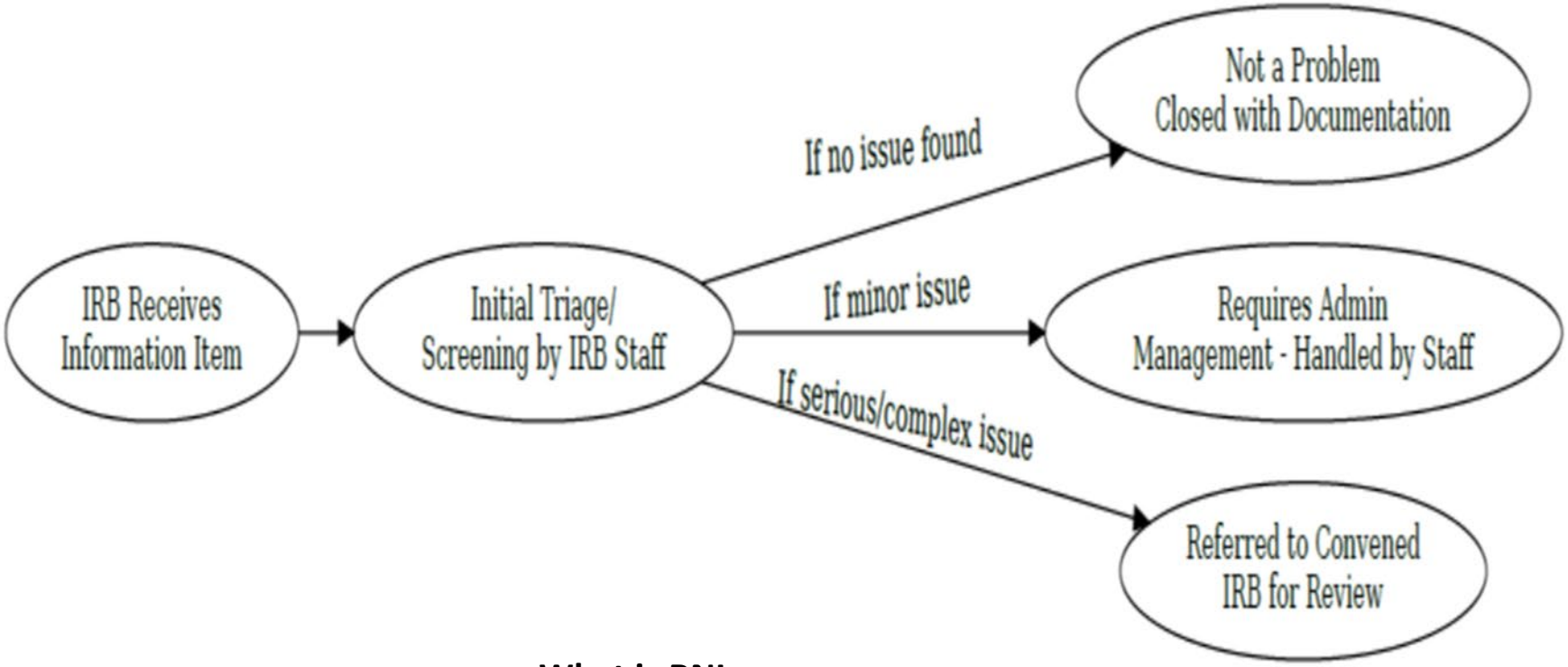
05/15/2025

Relevant Conflicts

I DO NOT have an actual or potential conflict of interest in relation to this program/presentation.

Objective Overview

1. Describe Noncompliance
2. Outline IRB Review and Determination Process
3. Required Institutional and Regulatory Actions



Introduction to RNI

What is RNI:

Reportable New Information includes but is not limited to any information that may affect the **rights, safety, or welfare** of research participants or others.

Essentially, it's a mechanism for informing the IRB about events or discoveries that could affect ongoing research (SOP: HRP-024).

This **process** starts when the IRB receives an information item and ends when the information item is determined not to represent a problem that requires management, is managed administratively, or referred to the convened IRB for review.

Introduction to RNI - Continued

What is RNI used for:

- Identifying and reporting issues
- Protecting participants
- Ensuring ethical conduct
- Making necessary adjustments

Examples of RNIs:

- Allegations of non-compliance,
- Noncompliance,
- Serious non-compliance,
- Unanticipated problems involving risks to subjects or others,
- Adverse events,
- Audit findings,
- New risk or safety information,
- Suspension of IRB approval,
- Termination of IRB approval.

1. Detailed Description of Noncompliance

What is Noncompliance:
Failure to follow applicable laws, IRB requirements, or approved protocol (SOP: HRP-001).

Required Elements:

- **What occurred** (facts only, no judgment),
- **When it happened** (date and approximate time),
- **Who was involved** (e.g., subject ID, staff, monitors), redact any identifiable information.
- **Where it happened** (clinic, remote visit, lab, etc.),
- **What was supposed to happen** according to protocol.
- **How the issue was identified** (during what process was the deviation(s) discovered (e.g., self-identified, monitoring visit, data QC, PI review, internal review, etc.)
- State whether the **subject's safety** was affected and provide a detailed explanation for your evaluation,
- Clarify the **subject's current status,** including enrollment status,
- Clarify whether the **subject has been notified** (if needed).

Regulatory and Data Impact (Worksheet: HRP-321)

- Study validity/ data integrity,
- Whether the sponsor was notified.

1. Detailed Description of Noncompliance

Corrective and Preventive Actions (CAPA) (Investigator Manual)
Explain in detail what is done to address the issue:

- **Root cause analysis** (why it happened, ask why 5 times until the root cause is revealed),
- **Corrective actions**, and immediate fix taken (if any),
- **Preventive actions**, ex: training, process updates, other system changes, etc.

Supporting Documentation:
Attach or reference:

- **Redacted** source documents (make sure no identifiable information is listed)
- Screenshots,
- Email communication,
- Any corrective action, training log, etc.

1. Detailed Description of Noncompliance

Submission Method:

- Institutional RNI submission portal through IBIS Research suite: IRB10 System

*** If the study is under the oversight of an external IRB, please review the requirements from the external IRB and report accordingly. UM requirements can be found in the Investigator Manual (HRP-103, Section 4.1)

Prompt Reporting:

At UM 10 business days of knowledge for all non-compliance reports, Investigator Manual: (HRP-103).

2. IRB Review Process

Step 1: Preliminary Review by IRB Staff (SOP: HRP-031)

- Prepare for a Non-Committee Review or Committee Review
- Provides the materials to the Designated Reviewer, who in turn might determine to assign it to a convened committee review.

Step 2: Referral to Full Board for (SOP: HRP-052):

IRB potential determinations:

- Unanticipated problems involving risks to subjects or others
- Serious **noncompliance**
- Continuing **noncompliance**
- Suspension or termination of IRB approval.

2. IRB Review Process

IRB potential determinations:

Serious Noncompliance

- Puts subjects at increased risk
- Compromises data integrity
- Violates ethical principles (Belmont Report)

Continuing Noncompliance

- Recurring incidents
- Failure to implement corrective actions

3. Required Institutional and Regulatory Actions

Institutions must document rationale for **determination**.

- All determinations and required actions are documented in the IRB meeting minutes.

Documentation should Include:

- Description of event
- Determination outcome
- Actions taken
- Date of IRB review and determinations

Reporting of **the following** to outside agencies, per our SOP: HRP-052 is to take place within 30 business days from the determination of a reportable problem:

- Serious Non-Compliance;
- Continuing Non-Compliance;
- Suspension of IRB Approval;
- Termination of IRB Approval;
- Unanticipated Problem Involving Risks to Subjects or Others.

3. Required Institutional and Regulatory Actions

Notification Requirements (when a reportable event is determined):
(SOP: HRP-024-3.5-3.5.2)

- Participants (re-consent or withdrawal)
- Principal Investigator
- Institutional Officials
- Sponsors

Reporting to Federal Agencies (when applicable)

- OHRP (Office for Human Research Protections): 45 CFR 46
- FDA (Food and Drug Administration): 21 CFR 56

Consequences of Non-Reporting:

- Federal enforcement action
- Potential loss of Federal wide Assurance (FWA) status
- Suspension of research activities
- Loss of federal funding

Summary and Best Practices

- Establish a robust RNI reporting and tracking system
- Train research staff on definitions and timelines
- Engage IRB early when potential issues arise
- Ensure corrective actions are documented and monitored

References

- 45 CFR 46: Protection of Human Subjects
- 21 CFR 56: Institutional Review Boards (FDA)
- OHRP Guidance on Reviewing and Reporting Unanticipated Problems and Noncompliance: OHRP Guidance Documents
- Belmont Report
- Institutional Policies (Investigator Manual HRP-103, chapter 8), Worksheet (HRP-321), and SOPs (HRP-001, HRP-024, HRP-052).

Q&A

- For more information, please visit our HSRO website or contact us at hsro@miami.edu and 305-243-3195.

- Thank you!

UNIVERSITY OF MIAMI
OFFICE of the VICE PROVOST
for RESEARCH & SCHOLARSHIP

Single IRB Reliance at UM

Angel Gallusi, B.A.

IRB Regulatory Analyst, Human Subjects Research - Reliance

Relevant Conflicts

I DO NOT have an actual or potential conflict of interest in relation to this program/presentation.

The Basics of sIRB

Single IRB (sIRB, Central IRB, Reviewing IRB, IRB of Record)

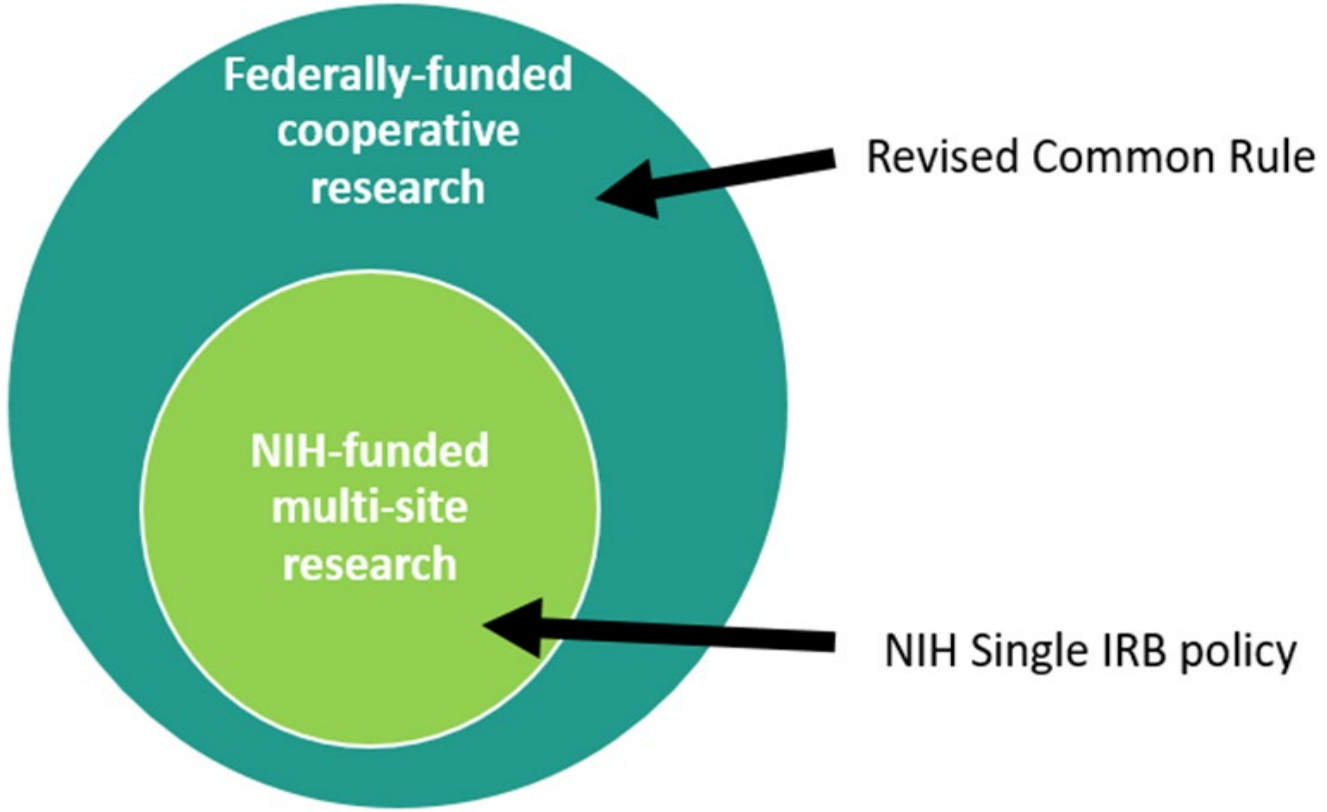
- IRB of one site provides IRB oversight for other relying sites
- IRB of record
- Usually identified by the federal department funding the research

Relying site

- A site that agrees to rely on the Reviewing IRB and comply with their requirements

Benefits

- Eliminate administrative burden for PIs
- Avoid duplication of efforts
- Consistency in the review process
- Enhance research partnerships
- Accelerate approval



Responsibilities of Each Institution

Relying Institution

- Provide local context (applicable state or local laws, regulations, institutional policies, local factors, etc.)
- Provide study documents with the local/institutionally required language (compensation for injury, payment, etc.)
- Perform ancillary reviews such as conflict of interest review.
- Review study personnel's education, training and qualifications.
- Comply with the determinations of the Reviewing IRB.
- Notify the Reviewing IRB of unanticipated problems, potential noncompliance, suspension or restriction, significant subject complaints.
- Submit any change in research in a timely manner

Reviewing Institution

- Making IRB determinations for all types of review (initial, amendments, continuing, reportable events, etc.)
- Review of findings and actions related to reportable issues (unanticipated problems, serious or continuing noncompliance, suspension or termination, subjects' complaints)
- Report to federal, state or funding agencies.
- Audits (Investigating and determining potential corrective and preventive actions in the event of non-compliance)

Shared Responsibilities

- Sign an IRB Authorization Agreement (IAA).
- Establish a plan for sharing of information between the site and the IRB. A crucial one is as establishing a **Coordinating Center** or **Coordinating Center Liaison**.

UM as the Single IRB

Requirements

- Study is federally funded
- Relying site must be engaged in the human subject research
- The Lead PI is a UM PI or study is conducted in collaboration with a UM PI.
- The engaged site does not have an IRB.
- The relying site must be domestic.
- Case by case determination.

HSRO Consultation

- Set up a reliance consultation with the HSRO to discuss the study plan, expectations, review fees associated with Single IRB review, negotiate the agreement, etc…
- Site eligibility is determined by the HSRO through the HRP-217 form. Please consult the reliance team if unsure of site engagement.

Exemptions

- International sites
- Exempt studies
- The federal department supporting the research determines that sIRB review is not appropriate.
- Prohibited by tribal or state laws so some sites may not be required to comply.

Coordinating Center

- The UM PI will serve as the Coordinating Center for the research or designate a Coordinating Center Liaison.
- The Coordinating Center will be responsible for coordinating the submissions from each site and submitting information into the UM HSRO's electronic system, IBISResearch.

Process for Onboarding Relying Sites

Reliance Agreement

- An Institutional Authorization Agreement that allows an IRB to rely on another IRB as the IRB of record and outlines the specific provisions and responsibilities for each of the parties entering the agreement.
- Types of Institutional Authorization Agreement:
  - **UM IRB Reliance agreement template**
  - **Master Reliance agreements**
  - **Smart IRB:** a flexible, national IRB reliance agreement that UM and many other institutions have used to cede review.

Site Localization

- The relying site must complete the Relying site Information Questionnaire form HRP-218.
- The relying site must provide a version of the consent document(s) that includes the relying site's institutionally required language and meets their institutional and local requirements.

IRB Submission

- The HSRO reliance coordinator will create the site submission for the relying site in the IBIS system upon completion of the reliance agreement.
- The Coordinating Center will submit all site materials including the relying site's local language documentation for IRB review on behalf of the relying site.
- The Coordinating Center will act as liaison to ensure any pending items are addressed to secure IRB approval for the relying site.

Reducing Your Burden for Onboarding Relying Sites

Ensure that the relying site completes the HRP-218 Relying site Information Questionnaire in coordination with their local IRB.

- This document lists research personnel involved in the research at the site, the role of the site in the research, confirmation that all ancillary reviews, training and financial disclosures have been completed, and important local context.
- The local study team **alone** will likely not be able to complete this without assistance from their local IRB.

Develop a protocol that clearly defines the responsibilities of each participating institution including data collection, subject recruitment, adverse event reporting, and communication with the reviewing IRB.

- Ensure that the core elements in the study protocol are included as they pertain the UM **and** the relying sites in general or specific terms as applicable.
- This will reduce the need for revision, and, after study approval, this will help ensure that review of site submissions and modifications are not delayed until the protocol can be adequately revised.

Ensure that the relying site(s) provides a documentation of their institutionally required language and local requirements before submitting to the IRB for review.

- This documentation from the relying site must be provided to validate that the revisions made to the consent documents are consistent with their institutional requirements.
- If the documents submitted deviate from the relying site's language requirements, we will send the submission back for confirmation.

Develop Template versions of Consent Documents and Recruitment Materials.

- Templates for these essential documents will help streamline the review process for the relying sites by significantly simplifying the document localization process.

Reducing Your Burden for Onboarding Community Centers as Relying Sites

Consider if they have an administrative body to identify and manage conflicts of interest.

- The HRP-218 will indicate if the Community Partner does or does not have an administrative body to identify and manage conflicts of interest.
- If the relying site does **not** have an administrative body to identify and manage conflicts of interest, the UM's office of Disclosures & Scholarly Activities Management (DSAM) will need to conduct these reviews on their behalf.
- This is a manual process where each individual team member will need to disclose to DSAM via Qualtrics.

Consider the community partner's access to CITI training.

- If the community center does not have access to CITI training, the relying study team will need to complete Miami CTSI's Community Involvement in Research Training course. (CIRTification)

UM as the External IRB

Eligibility

- Federally-funded and external review is required per single IRB mandate.
- Industry funded, multi-site study and the sponsor is requiring the UM to rely on an external IRB as a condition of participation. Sponsor must provide a statement requiring external IRB review.
- Other extenuating circumstances considered on a case-by-case basis.
- The University of Miami reserves the right to determine if the use of an external IRB for a specific project is appropriate for the institution.

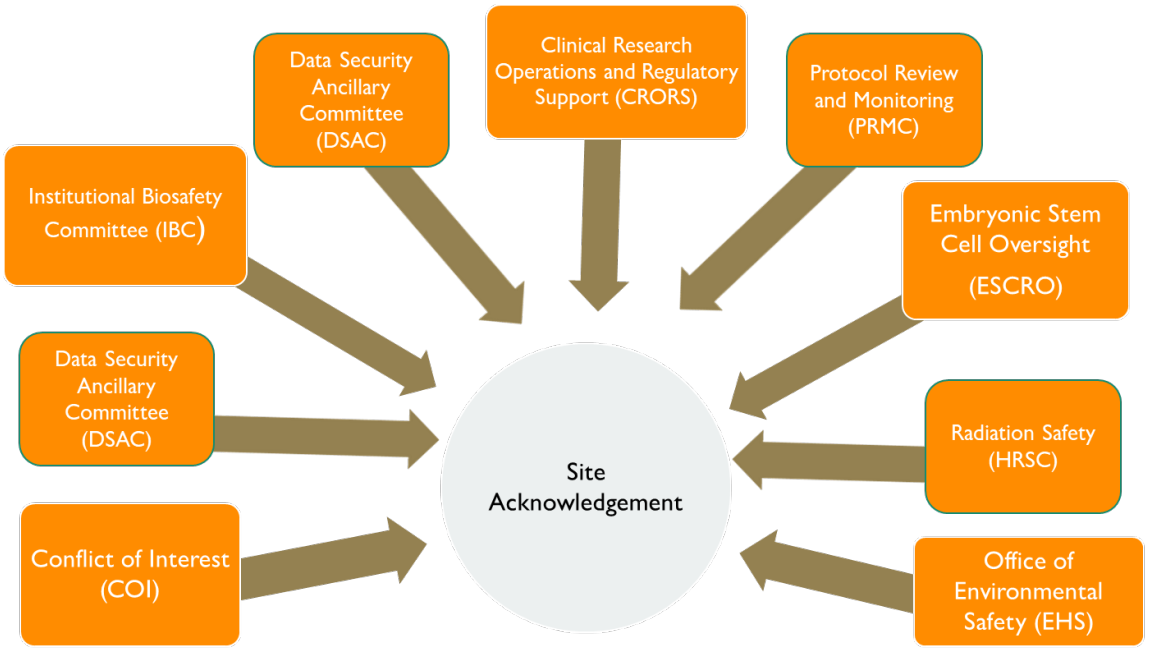
Administrative Review

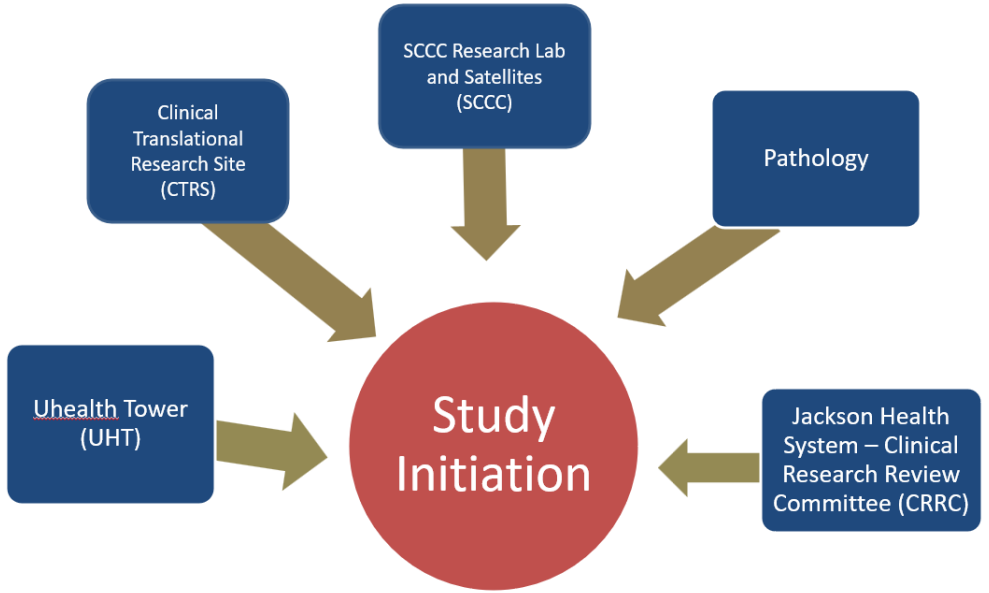
- The study is submitted in IBISResearch along with an HRP-216 Reliance Application. The UM consent document(s) must include UM's Institutionally Required Site-Specific language.
- After review of local documents has been completed, an IRB Authorization Agreement is signed.
- Once the Reviewing IRB has approved the UM as a participating site, an approval letter/notice must be submitted in IBISResearch along with the approved study documents.
- The HSRO Acknowledges the IRB approval and research at the UM site can commence.

UM as the External IRB

Ancillary Reviews and Study Team Training

- The UM is responsible for reviewing the financial interests of the study team for Conflicts of Interest. A study cannot be released for external review until all financial interest reviews have been completed.
- The PI must ensure that CITI Training credentials are not expired.
- The Ancillary Review process is largely unchanged from the process as it applies to single-site studies with the exception that a Conflict of Interest Committee (COIC) review must be completed **before** the study is released for external review.





Thank You!

Angel Gallusi, B.A.
IRB Regulatory Analyst
axg1966@miami.edu

Best Practices for Data Integrity

(Harmony, Harmony, Harmony)

Kanchan Sakhrani
Supervisor, Business Systems Analyst

Relevant Conflicts

- I DO NOT have an actual or potential conflict of interest in relation to this program/presentation.

Learning Objectives

By the end of this session, the attendee should be able to:

- Evaluate the structure and organization of a project
- Understand data validation techniques
- Aim for data consistency and timeliness of updates
- Identify what “harmonious” data means in the research life cycle.


PERFORMANCE
DOMAIN
REFERENTIAL
TECHNIQUES
DATA
MAINTAINING
DATABASE
ACCURACY
CHECK
INTEGRITY
REDUNDANCY
PHYSICAL
STABILITY
CONSTRAINTS
CONSISTENCY
RECORD
ASSURING
COMPUTING
LOGICAL
ENTITY
LIFE CYCLE
ERROR DETECTING

Types of Information collected

booleans,

text/string values,

multiple choice variables,

data sets/lookup tables

PHI/PII

Types of Systems available

Data Repositories

EMR/EDC systems

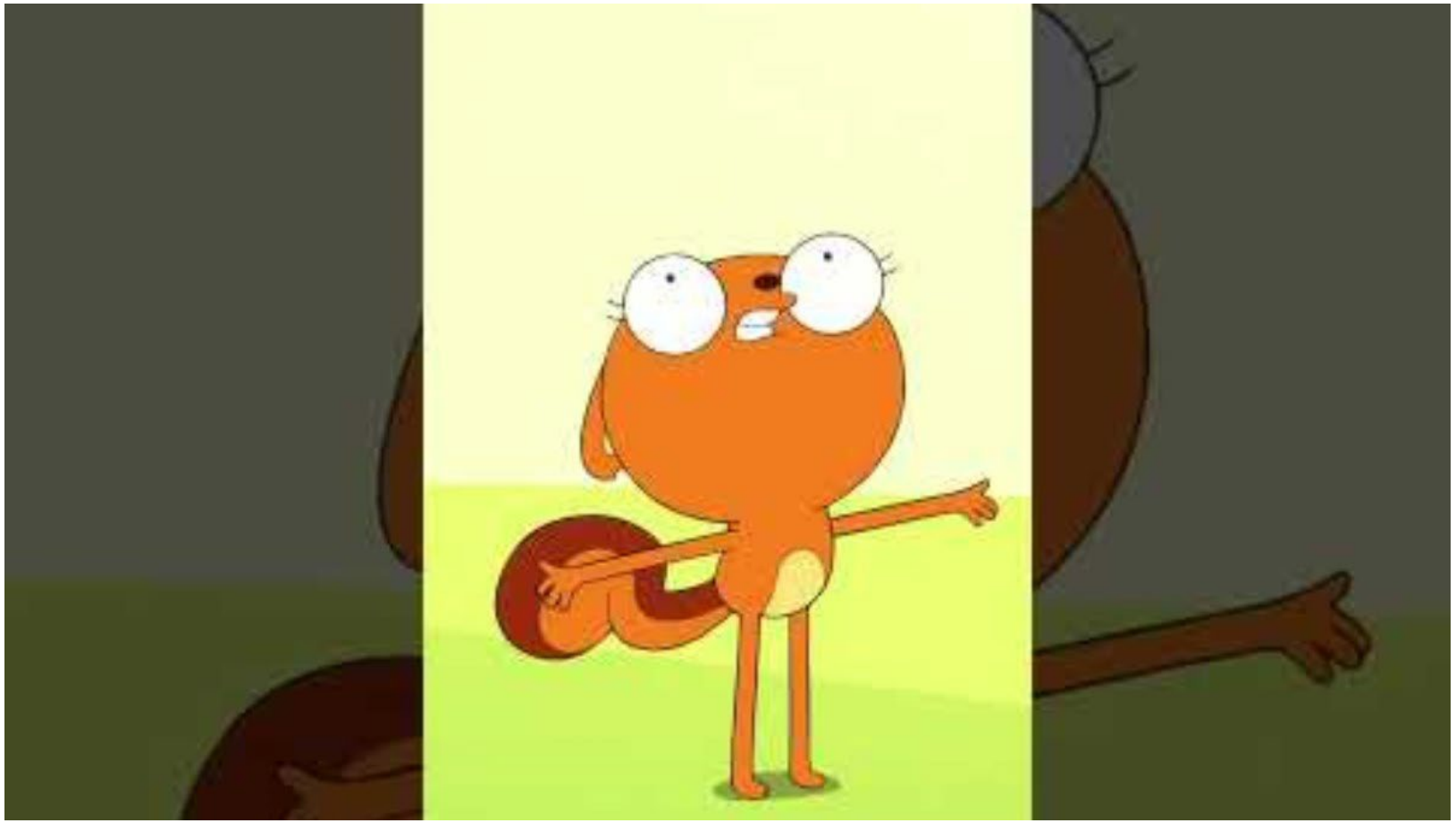
Data Warehouses

Related databases

3rd party data entry systems

Paper

Secure Streamlined Systems



A musical theme of data harmonization:

- **Visually and audibly represent the interconnectedness and coherence of data**
- **Data Integrity refers to the ability to maintain and validate data throughout its lifecycle.**

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CURATING CONNECTION
Innovations Interlude

Data Validation Techniques

Data Validation

Eliminating errors & discrepancies

Accuracy & Quality of Data

Trustworthy & usable data

A musical theme of data validation:

- **Highlight the importance of maintaining data accuracy, completeness, and consistency**
- **Evoke the sense of a well-structured, reliable, and trustworthy data ecosystem**

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CURATING CONNECTION
2025
IRB Member
Retreat
Innovations Interlude

The Perfect Harmony...

By combining these elements, we can create synchronization that is not only pleasing to the ear, but also effectively communicates the intention of data integrity and its significance.

Thank You!

Kanchan Sakhrani
Supervisor, Business Systems Analyst
k.sakhrani@miami.edu

Best Practices for Data Handling

Joey Casanova, BBA, CIP, CHRC, CIPT
Data Broker Manager

Relevant Conflicts

- I DO NOT have an actual or potential conflict of interest in relation to this program/presentation.

Learning Objectives

By the end of this session, the attendee should be able to:

- List different practices that should be followed depending on the location to be used for data storage.
- Describe requirements for secure access to identifiable data from locations and/or devices not located on-site at the University of Miami
- Describe required practices for sharing identifiable data with other study team members, sites and other 3rd parties

De-identification of Data

Importance of De-identification

- Retain only de-identified data if specified
- Remove identifiers as soon as feasible
- Best practice when de-identifying data is to use the safe harbor method

Sensitive Identifiers

- Social Security numbers (SSN)
- Medical Record Numbers (MRN)
- Health Insurance Policy Numbers
- Email Addresses
- Telephone Numbers

Secure Storage and Access Restrictions

- Restrict access to appropriate members of the research team
- Use UM-provided/controlled secure location(s) for identifiable data
  - Current UM Cloud resources – preferred and specific for study
  - Encrypted devices
  - University-supplied laptops
  - On-premises Workstations
  - PHI should not be stored on mobile phones or tablets
    - Use approved apps for mobile devices (e.g. EPIC Haiku and Canto)
  - All devices must have University-IT approved full disk encryption
- Access control
  - One group access identifiable data
  - Another group accesses de-identified or coded data set

Physical records management

- Physical Controls
  - Locked file cabinet
  - Card key restricted office area
- Disposal of Sensitive Information
  - Refrain from printing sensitive or identifiable documents
  - Avoid Use of Sensitive Documents at Home
  - Destroy all identifiable information areas
  - Do not dispose of such information in regular trash
    - Use approved Shred-It bins for identifiable or sensitive information

Cloud Storage

University-Managed Cloud Accounts

- Use Box or OneDrive accounts provided by the university
- Access via UM email address/SSO
- Avoid personal cloud accounts

Share Data Selectively

- Only share with those involved in the project
- Limit sharing to the necessary time period
- Grant only the necessary access (view only, noshare/print/download)

Jackson HEALTH SYSTEM

- Store Jackson related data on Jackson IT approved storage
- Use Jackson IT managed Sharepoint
- Consult Jackson IT/Compliance for appropriate practices

Remote Access

- Approved Methods
  - Only use methods approved by UM IT
  - Applicable to non-UM networks (wired and wireless)
- Telecommuting and Remote Operations
  - Access UM's Network via UMIT's Approved Remote Access Tools
  - Follow Data Broker Telecommuting Guidelines
  - UM Remote Work Policy
- Avoid Using Public, Insecure Wireless Networks
  - Examples include coffee shops, airports, bookstores, hotels
  - Connect to UM Provided VPN Resources
    - Accessible from anywhere through public networks
    - Protects sensitive information
    - Required for accessing certain University applications

Data Sharing/Data Transfer

- Encrypting Emails
  - Type [secure] in the subject line
- Recommended solutions
  - Authorizing external access (i.e. UM REDCap, UM Box)
  - VPN Tunnels
  - SFTP methods
- Restrictions
  - Do not send PHI or sensitive data to unauthorized individuals
  - Ensure recipients have a business or clinical reason
  - Use only miami.edu or jhsmiami.org email addresses
  - Do not share identifiable or sensitive information externally without proper agreements

Caution with Online Meetings

Sharing Links and Data

Caution sharing links and data

Only share with authorized individuals

Exercise care for meetings involving non-UM individuals

Screen Sharing

Remind attendees not to share sensitive information inadvertently

Be careful when sharing screens

Software Updates

Consistently update videoconferencing software

Thank You!

Joey Casanova, BBA, CIP, CHRC, CIPT
Data Broker Manager
jcasanova@miami.edu

Non-Committee Space

Meghan Stein, B.A.
Sr. Regulatory Analyst
Human Subjects Research Office

Relevant Conflicts

- I DO NOT have an actual or potential conflict of interest in relation to this program/presentation.

Non-Committee Space

Areas to Cover

- Operating in the Non-Committee Space
- Bottlenecks / Stop-gaps
- Quality Assurance / Quality Improvement

Operating in the Non-Committee Space

- **Not Human Subjects Research (NHSR) Reviews**
- **Screening Reviews**
- **Exempt/Expedited Reviews**
- **Withdrawal Process**

Not Human Subjects Research (NHSR)

Definition of a Human Subject:

A human subject is a living individual about whom research data or information is gathered through interaction, intervention, or observation. This includes obtaining information or biospecimens directly from the person, or accessing identifiable private information or biospecimens. (According to 45 CFR 46)

Definition of Research:

A systematic investigation designed to develop or contribute to generalizable knowledge. (According to 45 CFR 164.501)

NOT Human Subjects Research does not fit above as "human subject" and/or "research" – for example:

1) **Research that does not intervene or interact with individuals or analyze private identifiable information (secondary data analysis from public site)**

2) **Interactions with individuals and analyzing private identifiable information that does not meet the definition of Research (case studies, QI projects)**

Not Human Subjects Research (NHSR) Reviews

Requests

Streamlined the workflow, where previously they may have been lost

Triage

Inbox is monitored daily and requests are triaged to an appropriate staff member.

Determination

A confirmation of NHSR is made and a determination letter is sent OR instructions are given on how to submit a protocol.

One Dedicated Email Address

Most requests come to one email address specifically for NHSR letters HSROletterrequest@miami.edu

Feedback

Initial feedback within 48 hours – typically a request for additional information, clarification of the online form responses

Turnaround Time

With this improved process flow, we have drastically cut turnaround times to an average of under 5 business days.

Screening Reviews (All IBIS Submissions)

Real-Time

Submissions are reviewed in real-time as they come in daily M-F.

Initial Review

Screening team scans submission for administrative issues – pending Ancillary Committee Approvals, COI Disclosures, incomplete forms

Full Board, Non-Committee (Exempt/Expedited)

Screening team assigns the submission to the appropriate queue.

Administrative

Modification and the changes are administrative, such as change in study personnel, typo on a study form, the change is approved and letter sent within 24-48 hours.

Exempt/Expedited Reviews

Note: Exempt and Expedited Reviews are processed in the exact same way. The determination and requirements after approval are different.

Queue

Queue monitored in real-time daily, allowing for swift distribution and action. All submissions are assigned to a specific team member.

Pre-Review

In depth review of COI Disclosures, Ancillary Approvals, IBIS form submission, protocol, consent and study documents. Completed within 24-48 of receipt.

Clarifications Requested

Communication is sent in the system with step-by-step instructions as to what changes are needed and what items are still pending. We give a 7-day turnaround time.

Completed Submission

Once submitted back, we re-review within 24-48 hours and if complete, we forward to a Designated Reviewer for approval.

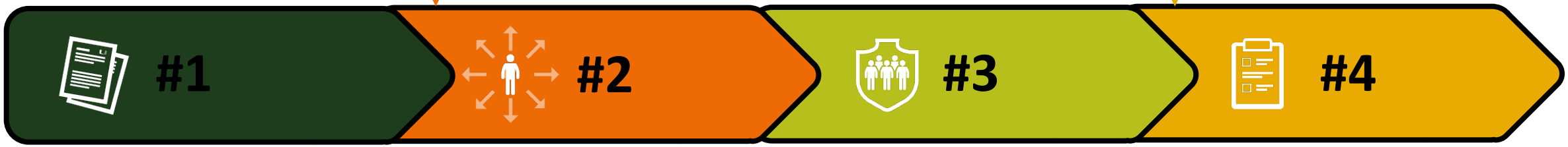
Withdrawals

No Penalties

The Withdrawal process does not have penalties, and the submission comes right back to the HSRO staff who initially reviewed it. They do not need to start over in the system

No Response or Not Approvable

If there is no response or the submission is not approvable within 7 days, we Withdraw the study.



Clarifications Requested

A 7-calendar day turnaround once clarifications are requested.

Withdraw (Pre-Submission)

The Withdraw action in the system sets the study back to Pre-Submission where study teams can work offline with us until the protocol is ready to re-submit.

Bottlenecks/Stop Gaps

Common areas holding up reviews

- Most Common - Incomplete IBIS Submissions
  - No documents uploaded, not in protocol template form (incomplete sections), incorrect answers on the IBIS form, wrong consent form, uploading documents in the wrong section
- Department Reviews
  - Pending Department Review or Department has requested clarifications
- Ancillary Reviews: PRMC, DSAC, EHS, Radiation
  - Pending Ancillary Review or never submitted documentation
- COI Disclosures
  - Awaiting Profile Update or DSAM status is Under Review

Actively developing strategies to further streamline these common issues through education and consistent communication

Quality Assurance/Quality Improvement

- Pioneered a quality assurance and improvement initiative with two main goals:

1. **Improve Turn Around Times**

2. **Improve Quality of Reviews**

Improve Turn Around Times (TATs)

Quarterly Reviews

Conduct a quarterly review of all submissions

Outliers

Review the outliers

10 submissions that took the longest in each group – FB, Exempt/Expedited, Modifications

Communication

Inform Team managers of any overarching themes affecting these TAT

TATs

TAT numbers have improved for Exempt from 12 to 7 days and Expedited from 24 to 9 days in the past year

Improve Quality of Reviews

Monthly Reviews

Conduct monthly reviews on a random set of studies, primarily federally funded, FDA, special population studies

Checklists

A QA Checklist is completed on each study to determine any deficiencies

Identification

Any errors, issues for clarification, points of concern are identified to make immediate fixes, reach out to the reviewer or send back to board

Improvement

There are significantly less issues and errors than when we initially began this process over a year ago.

In Summary ~

- **Through our efforts we have drastically improved the way we operate in the Non-Committee Space. Better submissions, improved turnaround times, great relationships with community.**
- **We will always continue to look for more ways to improve our process and help the community have a great experience from start to finish!**

Thank You!

Contact Information

- m.stein@miami.edu

I NEED AN ADULT!

Knowing When An LAR Is Appropriate In Research

Presented by: Stephanie Venero, Manager, HSRO

In Collaboration with: Cristy de la Portilla, Sr. Regulatory Analyst, HSRO

Relevant Conflicts

- I DO NOT have an actual or potential conflict of interest in relation to this program/presentation.

What is a legally authorized representative (LAR)?

According to OHRP, “Legally authorized representative (LAR) means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research”

- **When is it appropriate to obtain consent from LARs?**
- **When is it NOT appropriate to obtain consent from LARs?**

Research Involving Children – Parents as LARs

PARENTAL CONSENT – ONE SIGNATURE

Signature of one parent required for studies that are no more than minimal risk OR more than minimal risk and hold prospect of direct benefit

PARENTAL CONSENT – TWO SIGNATURES

Signature of two parents required for studies that more than minimal risk and do not hold prospect of direct benefit

CHILD ASSENT – IF CAPABLE

Typically required for ages 7-17; if capacity allows for it (depends on condition being studied)

RECONSENT AT AGE OF MAJORITY

If a child reaches the age of majority while on the study, the PI is required to reconsent them with the main consent form in order for participation to continue

Research Involving Children

IRB submission checklist for including children in research

Submit Parental Consent and Assent documents

Complete relevant questions in HRP-503(a)- Local Addendum and upload to IBIS application

Research Involving Cognitively Impaired Subjects

PROTOCOL CONSIDERATIONS

Who will determine if the subject is able to provide informed consent?

How will capacity to provide consent be determined?

Are subjects likely to regain capacity during the study, and if so, what will be the process to obtain consent?

IRB REQUIREMENTS

- Complete relevant section in HRP-503(a)- Local Addendum
- Submit Proxy consent form
- HIPAA authorization should include LAR

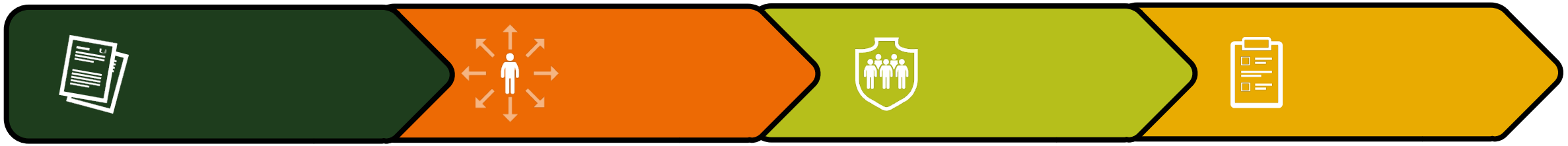
DURING THE STUDY

Assessing capacity should be an ongoing process as well as ensuring that participants are not unduly distressed by the research

An LAR is NOT appropriate...

When a minor has reached the age of majority (this varies by state, in FL it is 18 years old)

When a participant does not speak English, or does not read or write English



An emancipated minor

When a participant has a physical disability that makes it difficult for them to sign a consent form, but they are NOT cognitively impaired

Thank You!

CONTACT INFORMATION

- Stephanie Venero – sdv19@miami.edu
- Cristy de la Portilla – c.delaportilla@miami.edu

Networking Lunch

Ethical Ensemble: Perspectives from other IRB

- Review and discuss contemporary issues related to human subjects protections that are commonly faced by IRBs, and that may not have clear guidance in the federal regulations.
- Share best practices, policies and procedures, forms, and methods that aid in resolving difficult issues presented by investigators and research study staff.
- Evaluate different perspectives, interpretations, and decision making when approaching similar human research oversight topics.

Ethical Ensemble: Perspectives from other IRBs

Vivienne Carrasco, MPH, CIP
IRB Associate Director; IRB Member & SBS IRB Administrator
University of Miami- HSRO

R. Peter Iafrate, Pharm.D.
IRB-01 Chair and Assistant Director Research Programs & Services
University of Florida College of Research

Megan Kasimatis Singleton, JD, MBE, CIP
Associate Dean, Human Research Protections & Director of the Human Research Protections Program
Johns Hopkins University School of Medicine

Learning Objectives

- Review and discuss contemporary issues related to human subjects protections that are commonly faced by IRBs, and that may not have clear guidance in the federal regulations
- Share best practices, policies and procedures, forms, and methods that aid in resolving difficult issues presented by investigators and research study staff
- Evaluate different perspectives, interpretations, and decision making when approaching similar human research oversight topics.

The Cases

- Research Involving AI
- Pragmatic Clinical Trials
- Physically Disabled Participants
- Considerations for Data Sharing
- Research involving children/What is a minor increase over minimal risk?
- Open Discussion!

Data Sharing: The Rare Disease Repository

The Case

- The Study: An investigator-initiated clinical trial evaluating a new investigational treatment for a rare genetic disorder
  - The genetic disorder primarily impacts children and enrolled individuals aged 12-22
- The study has been closed to enrollment for 5 years and is in the data analysis stage
- The investigator contacts the IRB to inquire about a new plan for data sharing

The "Ask"

- Data from this study will be combined with data for other clinical trials of the same disorder in an open- access repository managed by a third party advocacy group
- The repository is designed to increase learning about the disorder and help inform future interventions

Data to be shared:

- Genomic data
- Key clinical variables collected over the course of the trial (dates may be date-shifted)
- Demographic information

More Complexity!

Consent/Assent

- Neither the consent nor assent discussed sharing data via a repository
- The consent/assent forms did include language that stated "data may be shared with future research collaborators with appropriate protections"

Possible Funding

- The investigator indicates she plans to apply for federal funding to support data preparation for this and other similar studies to enable its use via the repository
- The funding would include a requirement for a data management and sharing plan

IRB Discussion

- How might the IRB advise the investigator?
- Does the consent permit the sharing?
- Are risks to participants sufficiently minimized with the current plan? Why or Why not?
- Is the data to be shared identifiable?

Pragmatic Clinical Trials (PCT)

Designed to answer questions about how well a treatment works in real-world settings, rather than under highly controlled conditions.

Example: Evaluation of a Stop Smoking Program (loosely based on an actual protocol)

- A randomized, single blinded study
- A comparative effectiveness clinical trial (2 SOC)
- Randomized to one of two Stop Smoking Programs:
  1. Educational material, letter to your private doc, vs.
  2. Educational material, a central group calling you to set up a clinic visit with a psychiatric professional
- Study subjects are just told they are enrolling in a Stop Smoking Program, don't know they are being randomized

The complaint!

IRB’s are too strict on how they interpret the Common Rule as it relates to consenting subjects into a Pragmatic Clinical Trial.

How “pragmatic” is it??

PRECIS - Pragmatic Explanatory Continuum Indicator Summary

The definition can vary: How different is the study design vs. normal patient care? (ie: Explanatory\Pragmatic Continuum)

1. The recruitment of investigators and participants
2. The intervention and its delivery within the trial
3. The nature of the follow-up
4. The nature, determination, and analysis of outcomes as relatable to everyday patient care

Waiver or Alteration of consent
(45 CFR 46.116(d))

1. The research involves no more than minimal risk to subjects;
   - Is it relative risk, or absolute risk?? Does it occur as part of "daily life"? Federal regulations don't help with either decision.
2. The waiver or alteration will not adversely affect the rights and welfare of subjects;
   - Rights - An individual's right to decide about their care is absolute, and if patients are unaware of a choice to be made or that a choice has already been made for them, their rights have been adversely affected by the waiver or alteration of consent.
   - Welfare – if everything is "a" standard of care and minimal risk, no welfare issue?

Waiver of consent or altered form of informed consent (45 CFR 46.116(d))

3. The research could not practicably be carried out without the waiver or alteration;
   - How much is concealed to the subject? Can they still make an informed decision?

4. When appropriate, the subjects will be provided with additional pertinent information after participation.
   - Subjects be provided with additional pertinent information after participation
   - Disclose for deception or incomplete disclosure
   - Appropriate for a PCT?


Dry Falls, N.C.

Research Physically Disabled Adults

The Case
* loosely based

This study will evaluate the effect of a family-based intervention study for spinal cord injury (SCI) patient's and their caregivers.

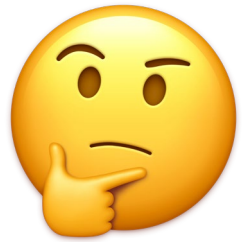
Eligibility:

Adult aged 18-70 who are living with spinal cord injury (C5 to the T10 levels and self-reported impairment levels (AIS) A-D)) and identified adult caregiver.

Outcomes: Physiological biomarkers of stress (blood pressure, heart rate, metabolic rate); Quality of Life and Sleep Index

Procedures: Pre/ Post baseline, 3-, 6- and 12-months interventional psychotherapy; blood tests, questionnaires, and standard metabolic tests.

What's the catch?

- Minimal risk procedures… CHECK
- Adults… CHECK
- Cognitively capable… CHECK
- Approvable under Sections 111… CHECK
- Sign your consent 

Key Questions

- What is a proper consent process for SCI participants?
- If the SCI participant is cognitively capable but cannot physically sign; who signs? Does the SCI participant need to sign?
- Can the SCI participant make a mark? Predetermined manner like blinking?
- Impartial vs Unbiased Witness (UM states Impartial). Is the caregiver impartial?

Key Regulatory Determinations

- Ensuring Truly Informed Consent
- Respectful and Inclusive Language and Practices
- Respecting Autonomy

The General Requirement for Informed Consent (45 CFR § 46.116(a)):
The Common Rule states that no investigator may involve a human being as a subject in research covered by this policy unless the **investigator has obtained the legally effective informed consent** of the subject or the subject's legally authorized representative. This general requirement underscores the fundamental ethical principle of **respect for persons** and the need for individuals to **voluntarily agree** to participate in research after understanding what it entails.

(a) Except as provided in paragraph (c) of this section, informed consent shall be **documented by the use of a written informed** consent form **approved by the IRB and signed** (including in an electronic format) by the subject or the subject's legally authorized representative. A written copy shall be given to the person signing the informed consent form.

Minor Increase Over Minimal Risk

Research Involving Children That Does Not Have A Prospect Of Direct Benefit

Example: Natural History Of Duchene's Muscular Dystrophy (DMD)

- Study mostly involves collecting clinical data on patients with DMD
- Subjects are kids >4 years old
- No prospect of direct benefit
- Involves a muscle biopsy

*Does this qualify as a minor increase over minimal risk?

Minor Increase Over Minimal Risk (45 CFR 46.406)

- the risk of the research represents a minor increase over minimal risk;
- the intervention or procedure presents experiences to the child subjects that are reasonably commensurate with those inherent in their actual, or expected medical, dental, psychological, social, or educational situations;
- the intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the disorder or condition; ***and***
- adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians, as set forth in HHS regulations at 45 CFR 46.408.

Also…..

- The procedure does not meet minimal risk criteria
- The investigator has presented sufficient evidence about the procedures, population, and the qualifications of research personnel to assure the IRB that:
  - The increase in the probability and magnitude of harm is only slightly more than minimal risk.
  - Any potential harms associated with the procedure will be transient and reversible in consideration of the nature of the harm (restricted to time of procedure or short post-experimental period).
  - There is no or an extremely small probability that participants will experience severe pain, discomfort, stress, or harm associated with the procedure.

Q5: What is a risk assessment guideline for some common research procedures? ***(NOTE: The IRB reserves the right to vary from this guideline on a case-by case basis given the circumstances of an individual study)*:**

PROCEDURE	CATEGORY OF RISK			Comment
	Minimal	Minor Increase Over Minimal	Greater-Than-Minimal Risk	
Routine History Taking	X			
Routine Physical Exam	X			
Hearing Testing	X			
Complete Neurological Exam	X			
Collection of Saliva	X			
Collection of Small Sample of Hair	X			
Breath Collection	X			
Fasting <12 Hours, Health Child	X			
Oral Glucose Tolerance Test	X			
Venipuncture / finger stick / heel stick within specified blood volume guidelines	X			The amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.
Intravenous line or heparin lock	X	X	X	Risk depends on age of the child, duration, number and volume of samples, and setting of the research.
Single IM or SC Injection	X	X	X	Risk depends on the substance injected.

PROCEDURE	CATEGORY OF RISK			Comment
	Minimal	Minor Increase Over Minimal	Greater-Than-Minimal Risk	
Urine Collection via bag	X			
Urine Collection via Catheter		X		
Urine Collection via Suprapubic Tap			X	
Chest X-Ray	X			
Bone Density Test (DEXA)	X			
Wrist X-Ray for Bone Age	X			
Lumbar Puncture			X	
Bone Marrow Aspirate			X	
Vision Testing	X			
Fundoscopic Eye Exam with Sedation		X	X	If procedural sedation – generally minor increase over minimal, although risk depends on sedation medications and monitoring plan.
Topical Pain Relief	X	X		Risk depends on age, weight, and history of child.
Skin Punch Biopsy w / Topical Pain Relief		X		
Muscle Biopsy		X	X	Risk depends on number of biopsies, location of test, adequacy of resources and experience of staff, ability to assent subject, importance of knowledge gained.

Research Involving AI

The Case

A study is evaluating the use of a new AI tool to better detect potential lesions of concern in follow-up CT scans of the lung for individuals being monitored for potential metastases after treatment for a primary breast cancer. As the algorithm is still being developed, the study proposes to route CT scans for their standard clinical read and simultaneously for a read by the AI tool. The AI read will not be shared with patients or clinicians, even if different than the clinical read as it is not yet known whether the AI tool is effective at reading the scans. The research team plans to compare the AI output to the clinical read to assess the tool's effectiveness. The comparison data will be recorded and the reads from the AI tool will be destroyed.

Key Questions

- What questions might the IRB ask?
- What might the IRB want to know about the tool?
- What level of review might the study qualify for (e.g. exempt, expedited, convened)
- Is the approach to sharing of the output of the AI tool appropriate?

Key Regulatory Determinations

- Is the study FDA-regulated? If yes, how so?
  - Non-significant or significant risk device?
- Does the study qualify for a waiver of consent?

Requirements for waiver and alteration. *In order for an IRB to waive or alter consent the IRB must find and document that:*
(i) The research involves no more than minimal risk to the subjects;
(ii) The research could not practicably be carried out without the requested waiver or alteration;
(iii) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
(iv) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
(v) Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

IRB Discussion

- A radiologist on the IRB expresses concerns as to whether the images should be retained as often multiple scans are required to adequately assess potential metastases, suggesting the single read is a flawed design and won't be able to assess the accuracy of the tool. **How might you address this concern?**

- Another member of the IRB raises the question as to whether there is any risk to not sharing the results of the AI read if they are different than the clinical read and may warrant a re-read of the clinical scan. **How might you address this concern?**

QUESTIONS???

Regulatory Acapella: ICH GCP E6 R3

- Explain the FDA's recommendations regarding the roles of sponsors and IRBs in identifying and responding to protocol deviations.
- Discuss the IRB's responsibilities related to compliance with 21 CFR Part 11, as outlined in the FDA's recent final guidance.
- Identify common challenges associated with decentralized clinical trials and discuss practical strategies for addressing them.
- Explore the key revisions introduced in the updated ICH E6 Good Clinical Practice guidance.

REGULATORY UPDATE

2025 IRB Retreat University of Miami
Cindy Gates, J.D., R.N.

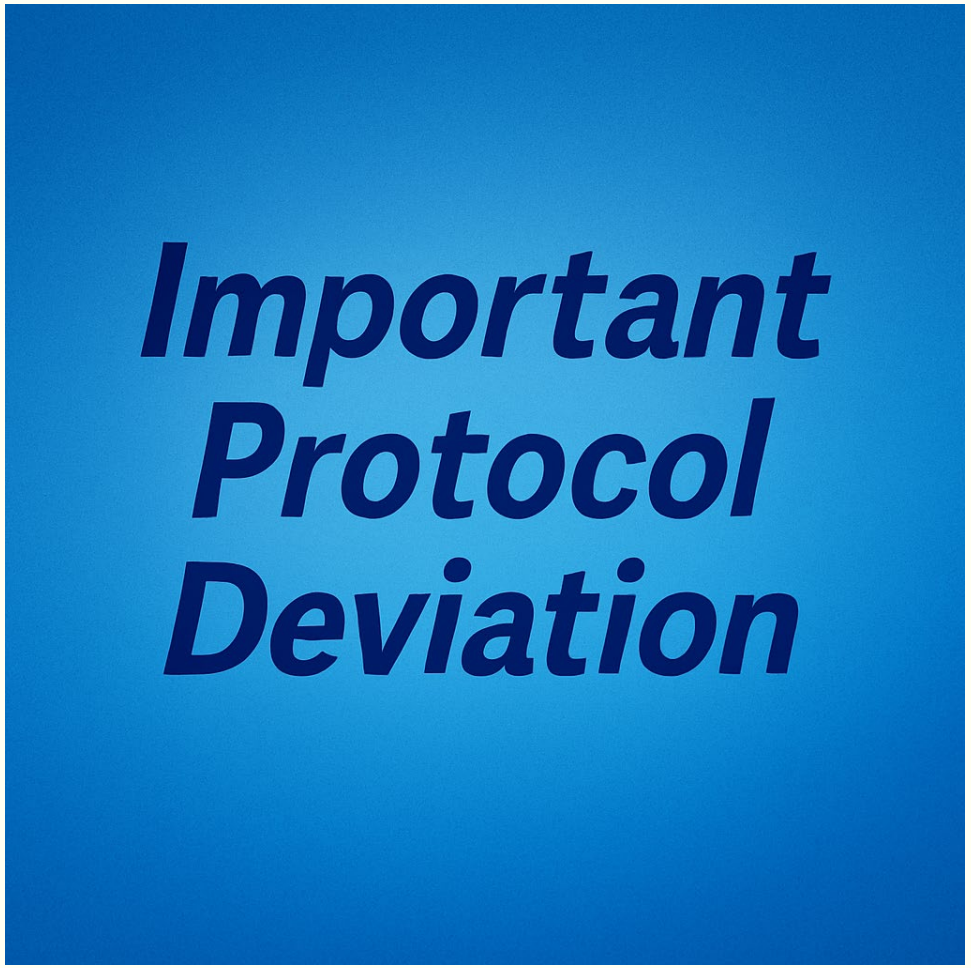
Goals of this presentation:

- Provide an overview of recent regulatory guidance affecting human subject research.
- Provide clarity on FDA expectations for protocol deviations.
- Discuss the responsibilities of IRBs and investigators for reviewing and responding to protocol deviations.
- Explain the ethical considerations for biopsies in clinical trials.
- Discuss important revisions to ICH E6.

PROTOCOL DEVIATIONS

FDA Draft Guidance:
Protocol Deviations for Clinical Investigations of Drugs, Biological Products, and Devices
December 2024

Understanding Protocol Deviations



- A protocol deviation is any change or departure from the IRB-approved protocol, no matter how minor.
- New category of deviations: Deviations that can impact patient rights and safety or data reliability
- Investigators should have procedures in place (routine monitoring) to identify unplanned deviations.
- Pre-approval is still required for planned deviations is required unless the deviation is necessary to protect participants from imminent harm.

Examples of possible Important Protocol Deviations

- Failure to obtain informed consent
- Enrollment of an ineligible participant
- Incorrect administration of the IP
- Failure to perform required safety test
- Administration of a prohibited concomitant medication
- Failure to withdraw a participant when withdrawal criteria are met
- Premature unblinding of treatment assignment not specified in the protocol
- Breach of confidentiality or mishandling of protected health information

Examples of Deviations not considered important

- One page of informed consent missing initials but full signature and date present
- Minor timing deviation for a non-safety-related procedure
- Re-consenting a participant outside of a window when no procedural changes occurred
- Protocol-required questionnaire administered by alternate site staff not impacting data quality
- GCP documentation issue (e.g., delegation log not initialed) if not explicitly required in the protocol

Understanding Roles in Addressing Protocol Deviations

PI's Role:

- Track, document, and assess all deviations
- Report "Important Deviations" to the sponsor and IRB
- Assess root cause for deviation
- Develop corrective and preventive action plan based on root cause analysis

IRB's Role

- Evaluate the risk to participant safety and data integrity
- Identify trends (continuing non-compliance)
- Determine if corrective and preventive actions are adequate
- Report to regulatory authorities, as applicable

DECENTRALIZED TRIALS

FDA Guidance
Conducting Clinical Trials With Decentralized Elements Guidance for Industry
September 2024

Decentralized Clinical Trials: Transforming Research

- DCTs enable flexible trial activities beyond traditional settings.
- Key components include remote consent wearables, and telehealth services.
- Digital health technologies enhance participant engagement.
- The aim is to improve access and reduce participant burden.
- DCTs can contribute to a more diverse participant pool.

Understanding Digital Health Technologies

- Wearable devices enhance real-time data collection.
- Electronic diaries provide valuable patient-reported outcomes.
- Mobile health apps increase participant engagement in trials.
- Environmental sensors can monitor external factors affecting health.
- Data security is critical for compliance and trust.

IRB Responsibilities in Decentralized Clinical Trials

- Evaluate the added risks associated with remote data collection and procedures (privacy, data accuracy, adequate training to participants and research staff).
- Ensure local telehealth laws and licensure requirements are addressed.
- Confirm that informed consent processes meet federal standards—even when remote.
- Scrutinize how data will be stored, transmitted, and secured.

Investigator Responsibilities in Decentralized Clinical Trials

- The Principal Investigator (PI) holds **ultimate responsibility** for trial integrity.
- Local providers and vendors must be thoroughly vetted for qualifications and training must be documented.
- Investigational Product (IP) tracking is crucial from shipment to return.
- Centralized digital platforms can facilitate coordination and monitoring effectively.

Ensuring Safe IP Delivery in DCTs

- FDA permits direct shipment of study drugs or devices to participants.
- Sponsors must monitor temperature and delivery conditions.
- Participants must receive training on proper storage and administration, when applicable.
- PI must ensure IP accountability logs are maintained.

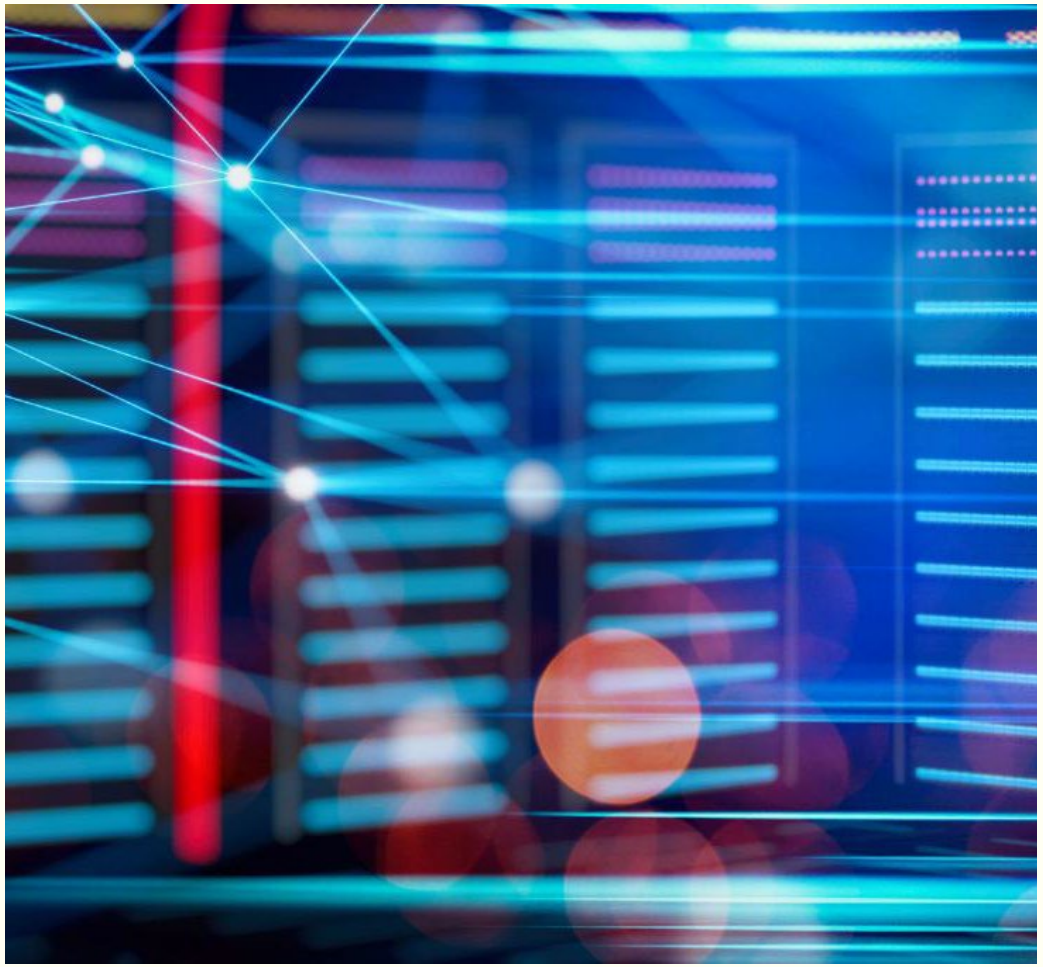
Ensuring Participant Safety in DCTs

- Quality by design
- Safety monitoring plans (site & sponsor)
- Develop clear communication channels for urgent issues.
- Educate staff (including remote staff)
- Train participant or caregiver
- Document activities

ELECTRONIC SYSTEMS AND SIGNATURES IN CLINICAL TRIALS

FDA Guidance:
Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations Questions and Answers
October 2024

Importance of Electronic Systems in Clinical Trials



- Electronic systems streamline data collection and management processes.
- Compliance with FDA regulations ensures system reliability and data integrity.
- Validation processes mitigate risks associated with data inaccuracies.
- Audit trails provide transparency and accountability in data handling.

Understanding Certified Copies in FDA Guidance

- Certified copies are validated electronic records replacing originals.
- Certified copies must include associated metadata (e.g., the date and time stamp, user identity).
- Audit trails ensure traceability of electronic records.
- Original documents can be discarded

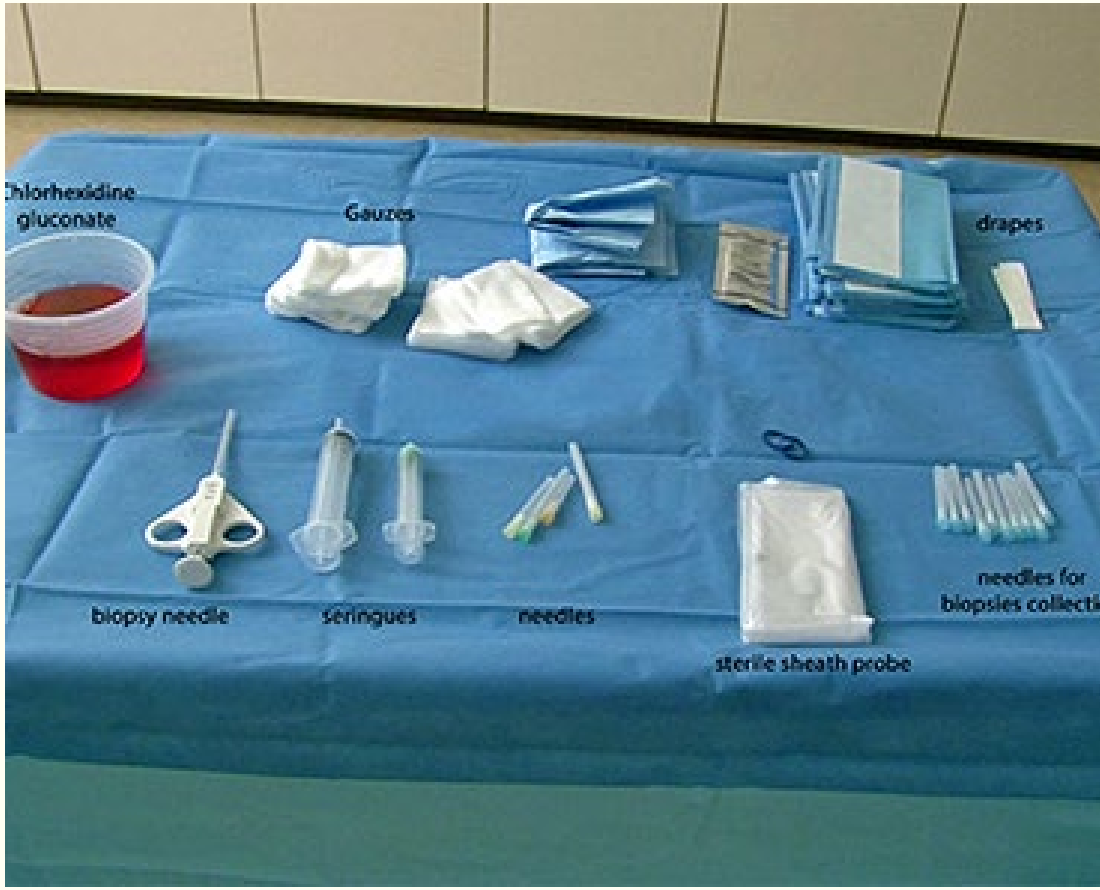
Regulated entities should have written standard operating procedures (SOPs) to ensure consistency in the certification process.

Ensuring Compliance with Electronic Systems

- eConsent platforms must comply with federal regulations.
- Documentation is crucial for validation processes.
- Regular training ensures users understand the system.
- IRB workflows should integrate compliance checks.
- Monitoring is essential for ongoing system effectiveness.

CONSIDERATIONS FOR INCLUDING TISSUE BIOPSIES IN CLINICAL TRIALS

FDA Draft Guidance
Considerations for Including Tissue Biopsies in Clinical Trials
January 2025



Considerations for Required Biopsies

Required biopsies must be essential to trial objectives; optional biopsies should not impact participation.

Protocol Should:

- Include rationale and justification for each biopsy.
- Specify how biopsy results will be analyzed in endpoint analyses.

Risk Minimization:

- Exclude participants for whom biopsies pose unacceptable risks.
- Use the least invasive approach when possible.

Considerations for Required Biopsies

In general, biopsies conducted for the evaluation of non-key secondary endpoints, exploratory endpoints, or for unspecified future research uses should be optional.

- **Purpose:**
  - Evaluate non-key secondary or exploratory endpoints.
  - Obtain specimens for unspecified future research (e.g., biobank contributions).
- **Participant Rights:**
  - Participants should be able to decline optional biopsies without impacting their ability to take part in the trial.

Informed Consent for Biopsy

Search the protocol to see if it includes a biopsy procedure – Check the consent document to ensure it includes a description of the biopsy procedure and the risks of the biopsy (including anesthetic)

Key Elements:

- Clearly state whether biopsies are required or optional.
- Include foreseeable risks (physical and informational) and discomforts.
- Ensure participants retain the right to withdraw consent at any time.

Minimize Coercion:

- Avoid undue influence during consent.
- Ensure participants understand their rights.

Reviewing biopsies from children

- Assess the prospect of direct benefit to the child
- If there is a potential benefit, the benefit to risk should be at least as favorable as that presented by available alternative approaches.
- If there is no direct benefit
  - The risk must not exceed a minor increase over minimal risk.
  - The biopsy must be intended to create important biomedical knowledge about the child's condition
- Review parental permission and child assent processes.

ICH E6 (R3)

Understanding ICH E6(R3)

"ICH E6(R3) provides a unified standard to facilitate the mutual acceptance of clinical trial data for ICH member countries and regions by applicable regulatory authorities.... The Guideline comprises of Principles and Annexes that expand on the principles, with specific details for different types of clinical trials. The principles outlined in this guideline may be satisfied using differing approaches and should be applied to fit the intended purpose of the clinical trial. Annex 1, including its Appendices, is intended to provide information on how the Principles can be appropriately applied to clinical trials."

- ICH E6(R3) updates GCP standards for modern trials.
- Focuses on risk-based approaches for compliance.
- Strengthens protections for human subjects in research.
- Encourages more flexible IRB review processes.

Key Themes of ICH E6(R3)

ICH E6(R3)

Quality by design

Proportionality

Participant safety

Data reliability

- Clarifies roles and responsibilities in clinical trials.
- Promotes risk-based monitoring to improve outcomes.
- Promotes proportionate oversite and training.
- Emphasizes quality-by-design for reliable data.
- Encourages technology integration in trial processes.
- Supports decentralized approaches for wider participation.

Key Concepts Of ICH E6(R3)

- New section on data governance – similar to 21 CFR Part 11
- Encourages use of technology
- Essential records – PIs determine which records are essential
- Defines "important protocol deviations" and provides guidance for addressing these deviations
- Encourages direct communication between sponsor and IRB
- Emphasizes the need to supervise vendors who perform research procedures

ICH E6(R3)

Data Governance
Essential Records
Important Deviations
Vendor Supervision

ICH E6 (R3) and Informed Consent

Encourages use of varying formats, videos,, images & interactive methods to enhance understanding

Allows for remote and electronic consent when IRB approved

Explains purpose of The signature of the person conducting the consent process is an attestation:

- Consent was freely given
- Information was accurately explained
- Participant understood

Emphasizes the need to ensure the identity of the individual providing consent

ICH E6(R3) and participants who lack capacity to consent

Adults

- No longer requires IRB to specifically approve the inclusion of adults who lack consent capacity in non-therapeutic trials
- Discusses the need for assent from adults who are capable

Children

- Discusses age-appropriate assent from children
- Reminds Pis to obtain consent from children who reach the age of majority

Questions?