Reportable Events in Research

Karina Avila, MPH
Clinical Research Manager, Medicine

K. Zoe Tsagaris, MS, OTR/L, CCRP
Director, Clinical Research Resources

EINSTEIN
Albert Einstein College of Medicine

Montefiore

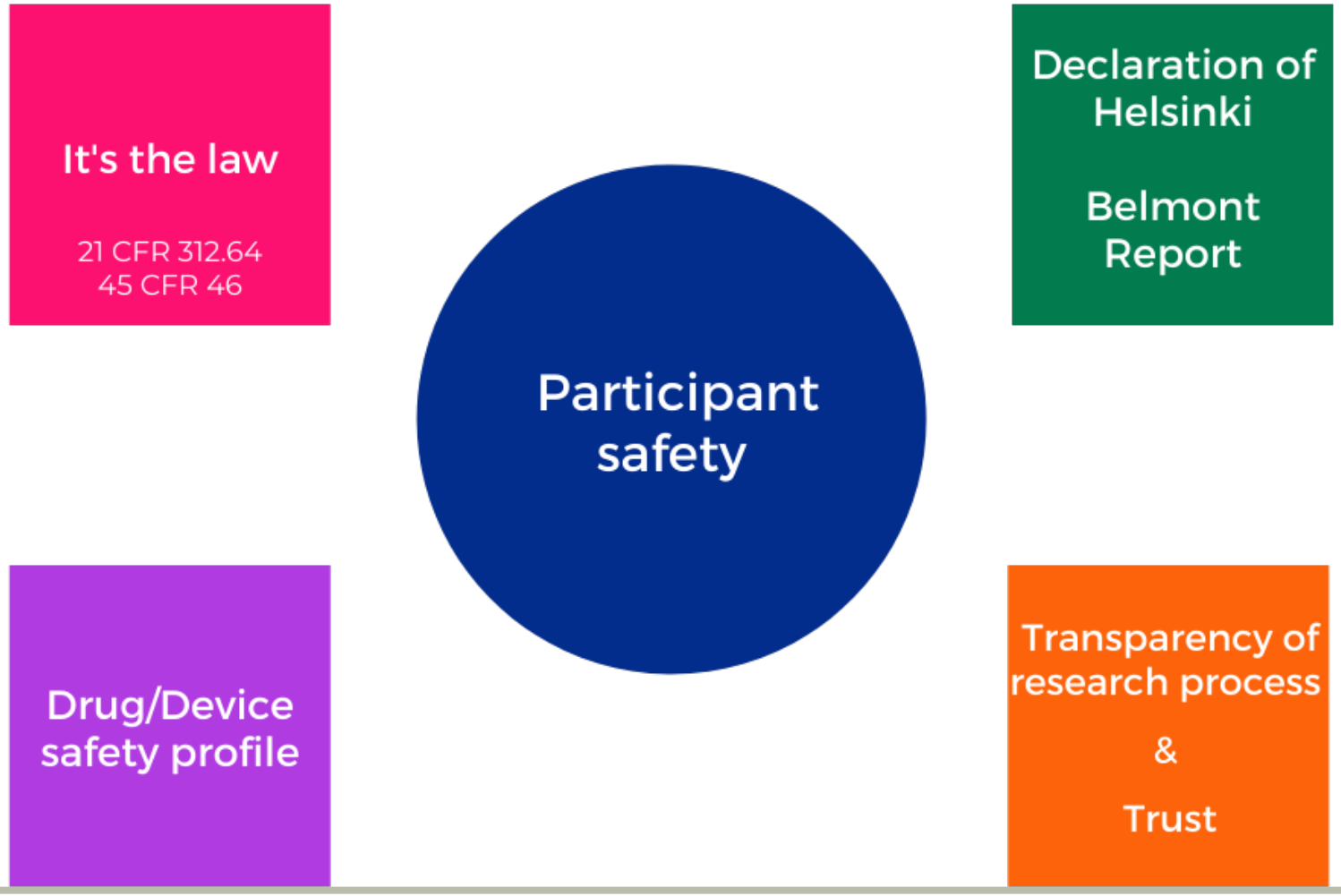
Agenda

- Introduction/Overview
- Key definitions
- Identification of event
- Assessment of event
- Preparing submission & informing others

EINSTEIN
Albert Einstein College of Medicine

Montefiore

Why does reporting matter?



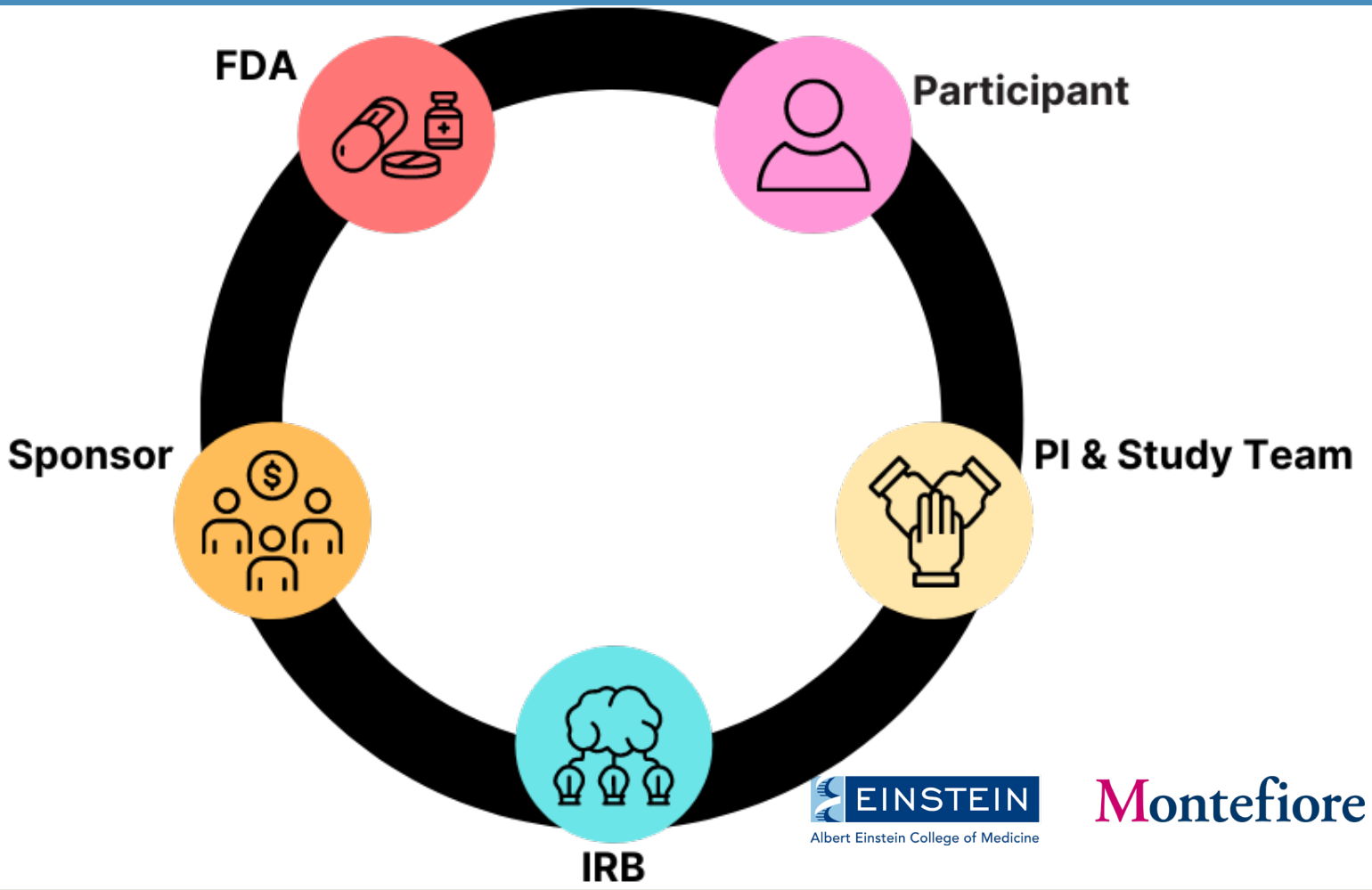
Stakeholders

- Participants
- Principal Investigator & Study team
- Overseeing IRB
  - Einstein IRB & Office of Human Research Affairs
  - BRANY IRB – Biomedical Research Alliance of New York
  - Other external IRBs
- Sponsor
  - Sponsor-Investigator if PI holds IND/IDE
- FDA – U.S. Food and Drug Administration
- DSMB/DMC

EINSTEIN
Albert Einstein College of Medicine

Montefiore

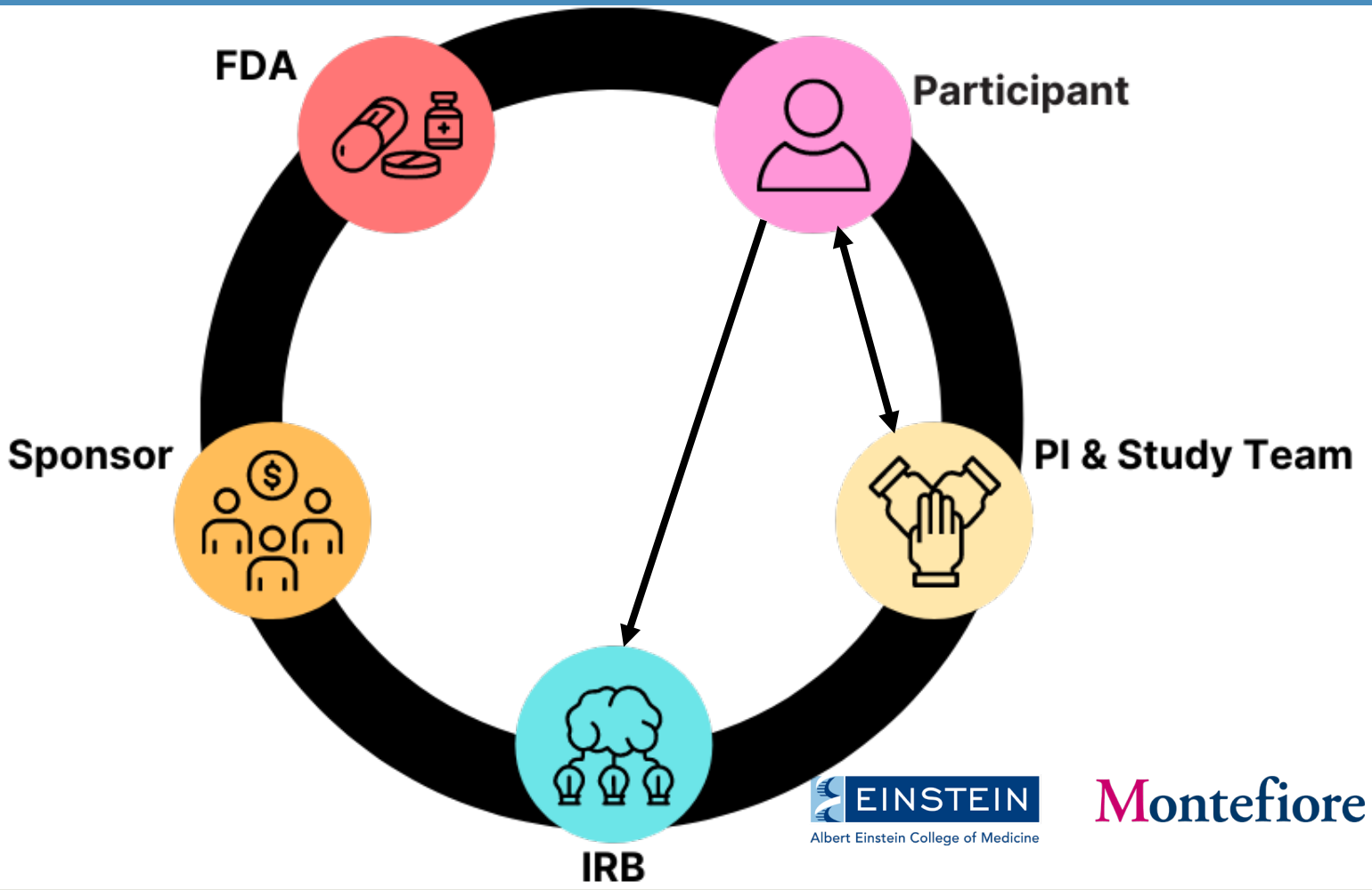
Stakeholders



EINSTEIN
Albert Einstein College of Medicine

Montefiore

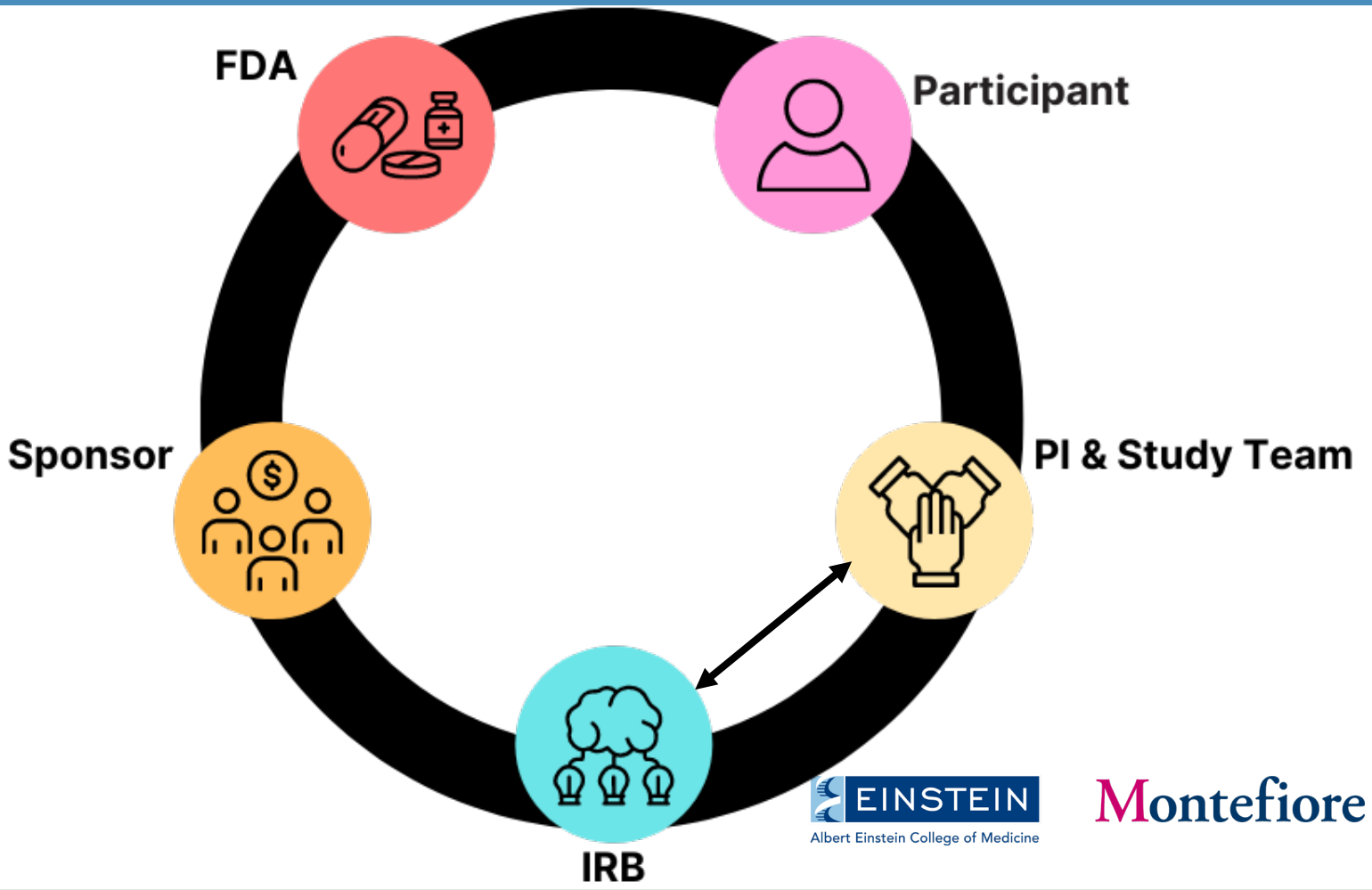
Stakeholders



EINSTEIN
Albert Einstein College of Medicine

Montefiore

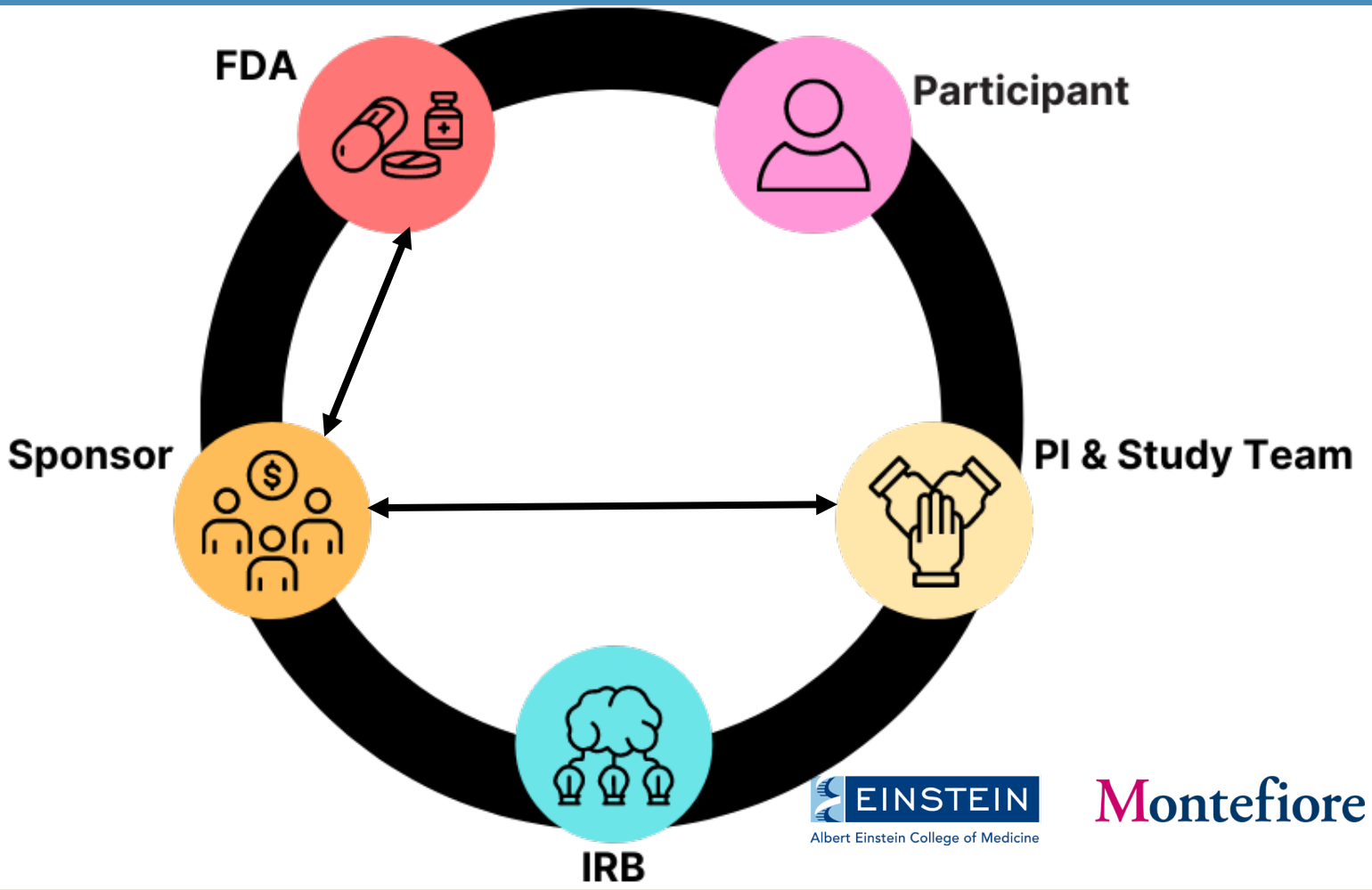
Stakeholders



EINSTEIN
Albert Einstein College of Medicine

Montefiore

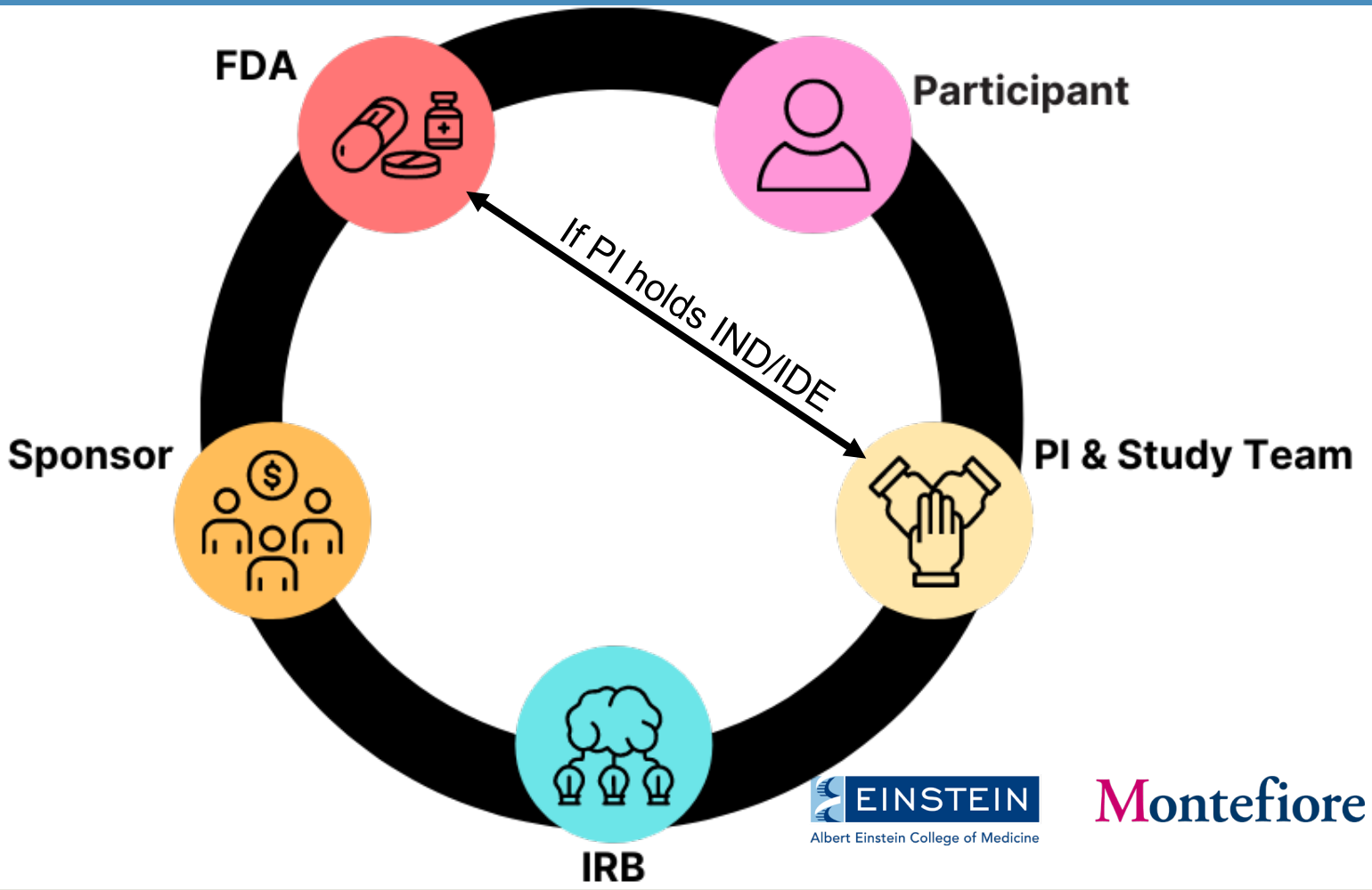
Stakeholders



EINSTEIN
Albert Einstein College of Medicine

Montefiore

Stakeholders



EINSTEIN
Albert Einstein College of Medicine

Montefiore

Key Terms

Reportable Events

- **Protocol Deviation**
  - Minor vs Major
- **Adverse Event**
  - Serious Adverse Events
- **Unanticipated Problem**

EINSTEIN
Albert Einstein College of Medicine

Montefiore

Definitions

- **Protocol Deviation:** Any **alteration or deviation** from the IRB-approved research plan as **defined in the study protocol**.
  - Minor Protocol Deviation: A deviation that **does not affect** participant safety, rights, welfare, or data integrity.
  - Major Protocol Deviation: A deviation that **affects** participant safety, rights, welfare, or data integrity.

EINSTEIN
Albert Einstein College of Medicine
Montefiore

Definitions

- **Adverse Event (AE):** Any untoward or unfavorable medical occurrence in a human subject, including **abnormal signs, symptoms, or disease, temporally associated** with, but not necessarily considered related to, the subject's participation in the research study.

Expected AEs:

> Outlined in protocol and ICF
> Described in Investigator's Brochure (IB)
> Described in Package insert

EINSTEIN Albert Einstein College of Medicine Montefiore

Definitions

- **Serious Adverse Event (SAE):** An adverse event that results in:
  - Death
  - A life-threatening event
  - Inpatient hospitalization or prolongation of existing hospitalization
  - Persistent or significant incapacity or substantial disruption of ability to conduct activities of daily living
  - A congenital anomaly/birth defect
  - Other serious important medical events

21 CFR 312.32

EINSTEIN
Albert Einstein College of Medicine

Montefiore

Definitions

Unanticipated Problem: any incident, experience, or outcome that meets ALL of the following criteria:

1. **unexpected (in terms of nature, severity or frequency)** given (a) the research procedures that are described in the protocol-related documents; and (b) the characteristics of the subject population being studied;

2. **related or possibly related to participation in the research;** and

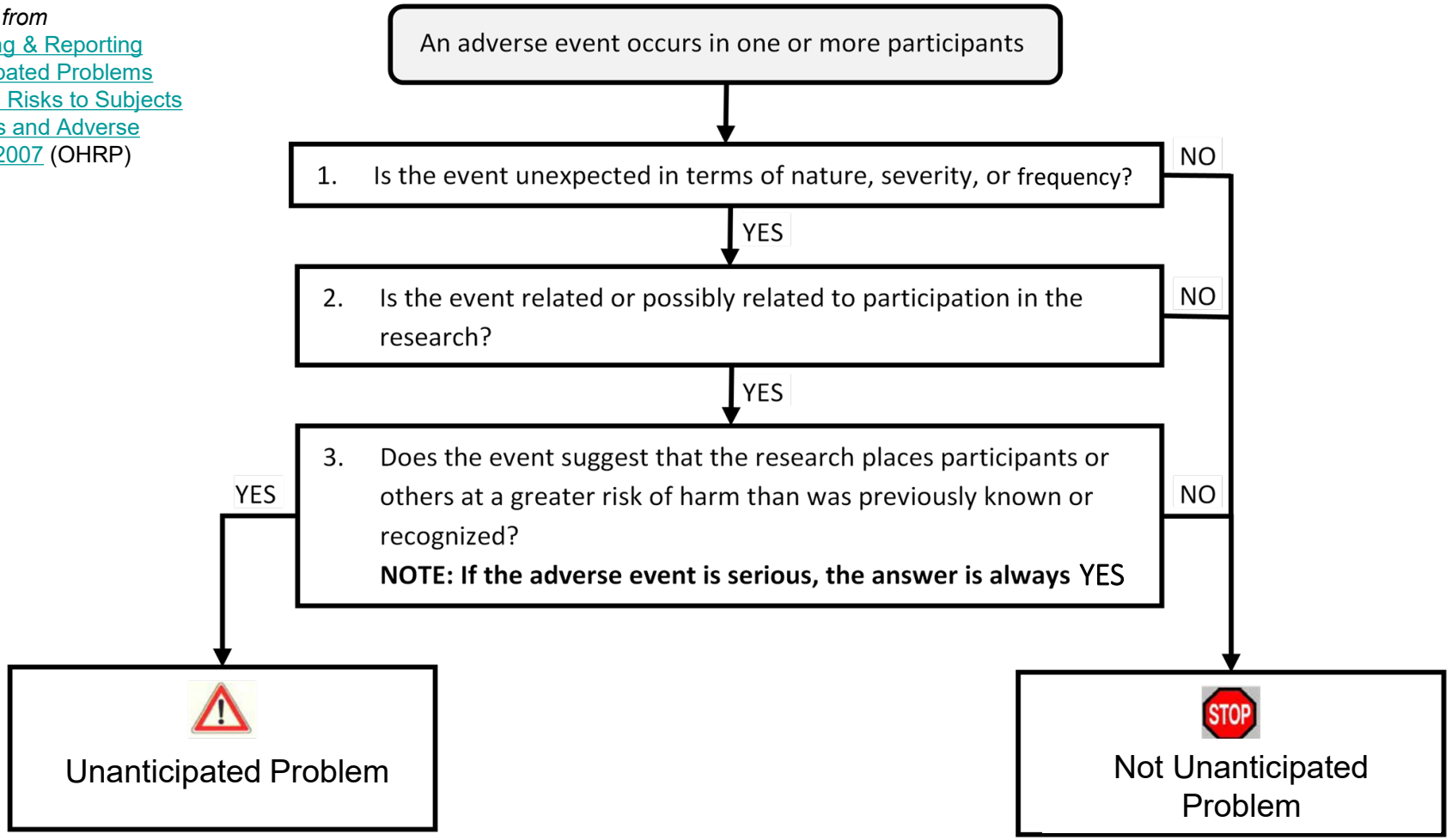
3. suggests that the research **places subjects or others at a greater risk of harm** (including physical, psychological, economic or social harm) than was previously known or recognized.

EINSTEIN
Albert Einstein College of Medicine

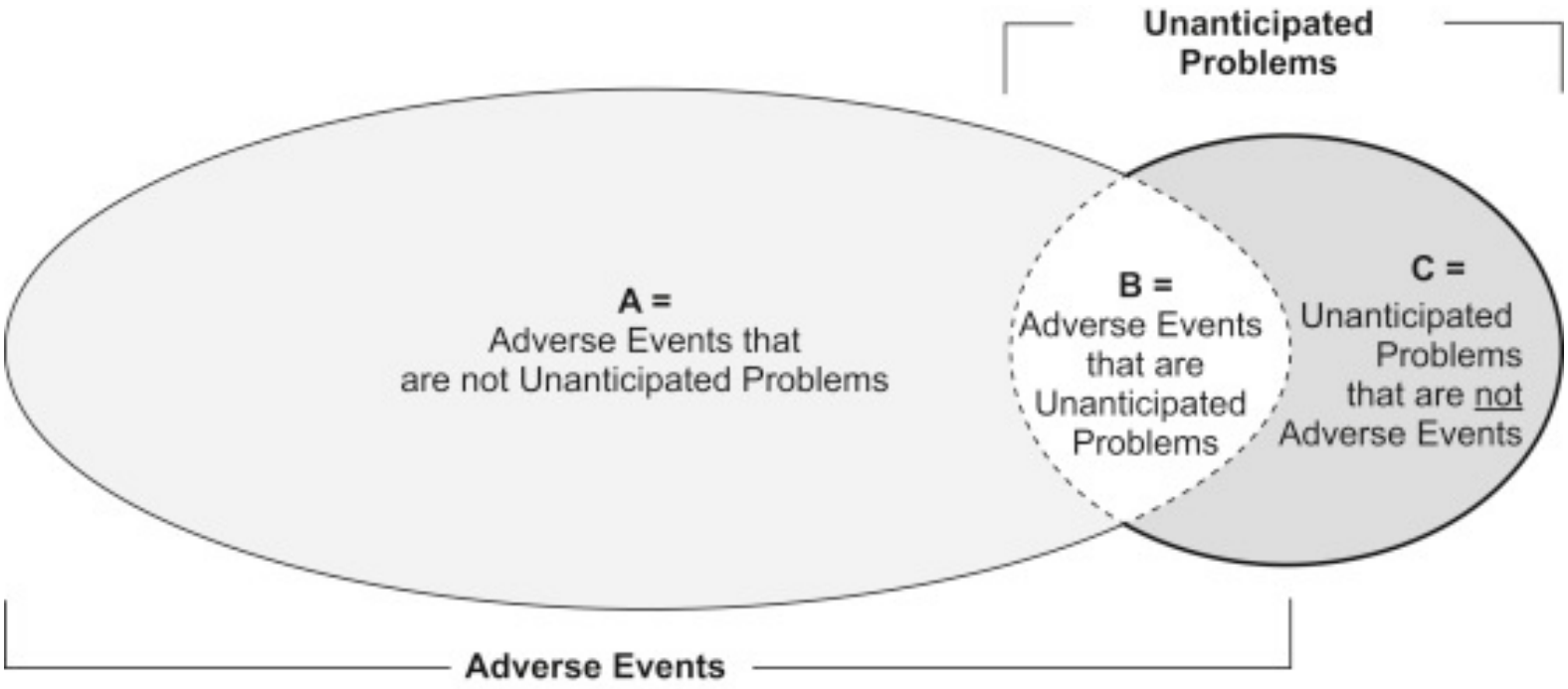
Montefiore

Decision Tool:
How do you determine which AEs are unanticipated problems?

Adapted from Reviewing & Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, 2007 (OHRP)



How do you determine which AEs are unanticipated problems?



Under 45 CFR part 46: Do not report A, Do report (B+C)

EINSTEIN
Albert Einstein College of Medicine

Montefiore

IRB Reporting

Event Identification

via participant interaction

- Self-report via open-ended questions
- Medical Records
- EPIC Alerts
- Diaries/questionnaires

Assessment

Principal Investigator or medically qualified person identified on DoA Log

Prepare Report

- Understand IRB and/or Sponsor documentation requirements
- Timelines may differ
- Include supporting documentation

Submission

PI and/or study team to IRB and sponsor, if applicable*

EINSTEIN
Albert Einstein College of Medicine

Montefiore

Safety Monitoring

- Data Safety Monitoring Plan
  - Detailed in protocol
- Data and Safety Monitoring Board (DSMB)
  - If your study has a DSMB, may require additional reporting

EINSTEIN
Albert Einstein College of Medicine
Montefiore

What information will I need?

Protocol Deviations	Adverse Events
Participant ID	Participant ID
Date of deviation	Onset date/time
Description of deviation	End date/time
Corrective action	Adverse event term
Date reported to sponsor (if applicable)	Severity • mild/moderate/severe/life threatening
	Related to drug/device/trial • Not related/unlikely related/possibly related/probably related/definitely related
	Outcome of event • recovered or resolved/recovering/recovered with sequelae/not recovered/fatal
	Action taken with study treatment • Dose not changed/ increased/ reduced/ interrupted/ withdrawn/ N/A

IRB Reporting Timelines

	Einstein IRB	BRANY IRB
Unanticipated Problems & Unanticipated Serious Adverse Events (AEs)	Within 5 days	Within 5 days
Anticipated Adverse Events & Anticipated SAEs	Report in aggregate with continuing review	Report in aggregate with continuing review
Unanticipated Adverse Device Effects	Within 5 days	Within 10 days
Major Deviations	Within 5 days	Within 10 days
Minor Deviations	Report in aggregate with continuing review	Report in aggregate with continuing review
Unresolved Complaints	Within 5 days	Within 5 days

What happens after a report is submitted?

If no further action needed: your report will be acknowledged

If action needed: IRB will work collaboratively with study team to determine next steps

EINSTEIN
Albert Einstein College of Medicine

Montefiore

Keep in mind…

- Known risks are described in the ICF
- Consider study population
  - AEs can be expected
- People make mistakes
- Audits (routine internal and external)
- Monitoring visits (sponsor)
- Research non-compliance
  - Local
  - State
  - Federal

EINSTEIN
Albert Einstein College of Medicine

Montefiore

Best Practices & Tips

- **Know your sponsor, IRB, and institutional reporting reqs**
- **Know your role in the research team**
  - Delegation of Authority Log
- **Communication is key**
  - Ask questions, talk to your PI
- **Develop processes to help identify and document events**
  - Checklists, SOPs, Note to File templates, etc.
- **Be mindful of frequently occurring deviations & their implications**

Best Practices & Tips, Cont.

When in doubt – ASK!

Your PI

Einstein IRB:

irb@einsteinmed.edu

718-430-2237

BRANY IRB:

Svetlana Abramova, Sr Adverse Event Specialist

sabram@brany.com

516-470-6929

EINSTEIN
Albert Einstein College of Medicine

Montefiore

In summary…

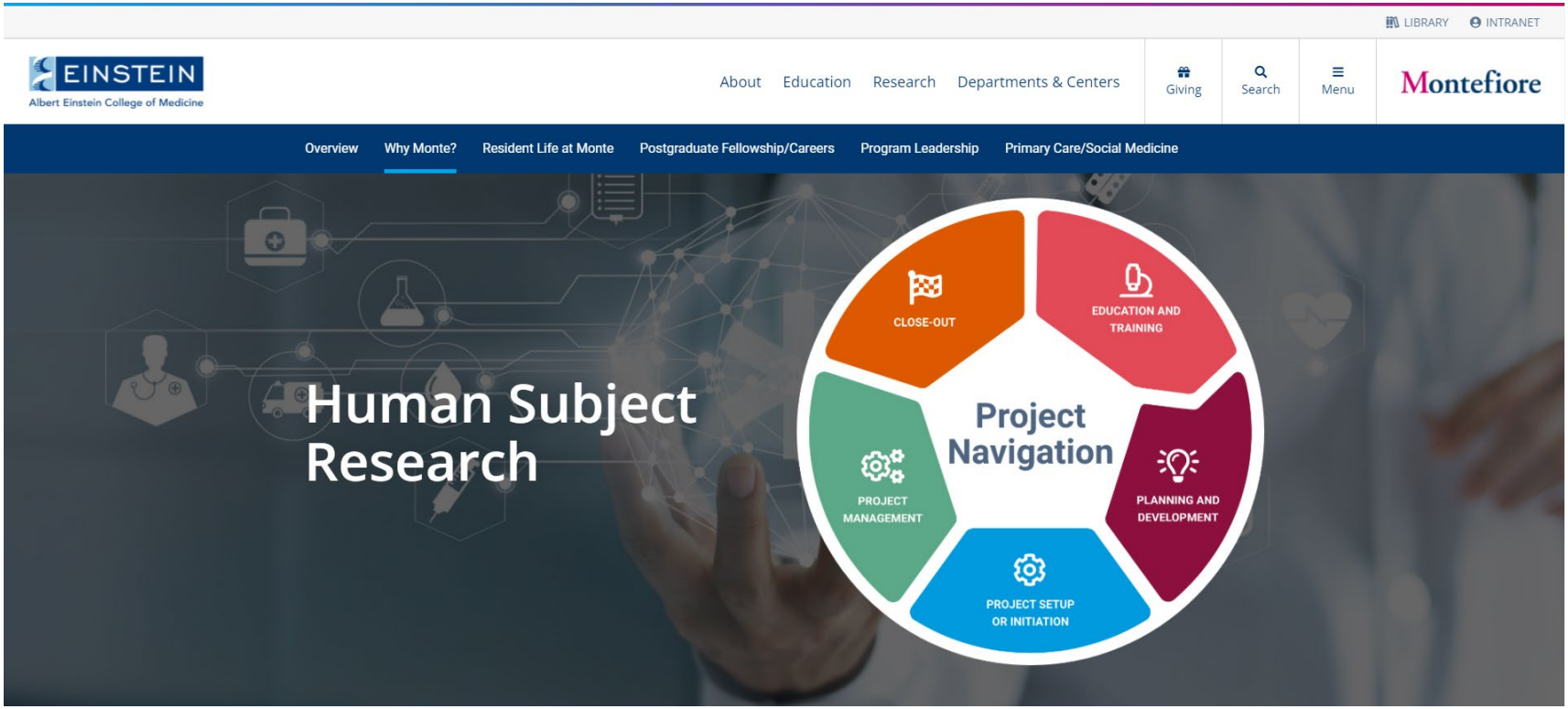
- Deviations, AEs and SAEs, and Unanticipated Problems are reportable events
- Reportable events will always be submitted to the IRB and Sponsor
  - PI/study team will submit reportable events to FDA *only if PI holds IND/IDE*
- Be aware of IRB, Sponsor, institutional reporting requirements and timelines
  - > Expedited reporting timelines apply to certain events
- Unsure if an event classifies as a reportable event?
  - > Reach out to the IRB!

EINSTEIN
Albert Einstein College of Medicine

Montefiore

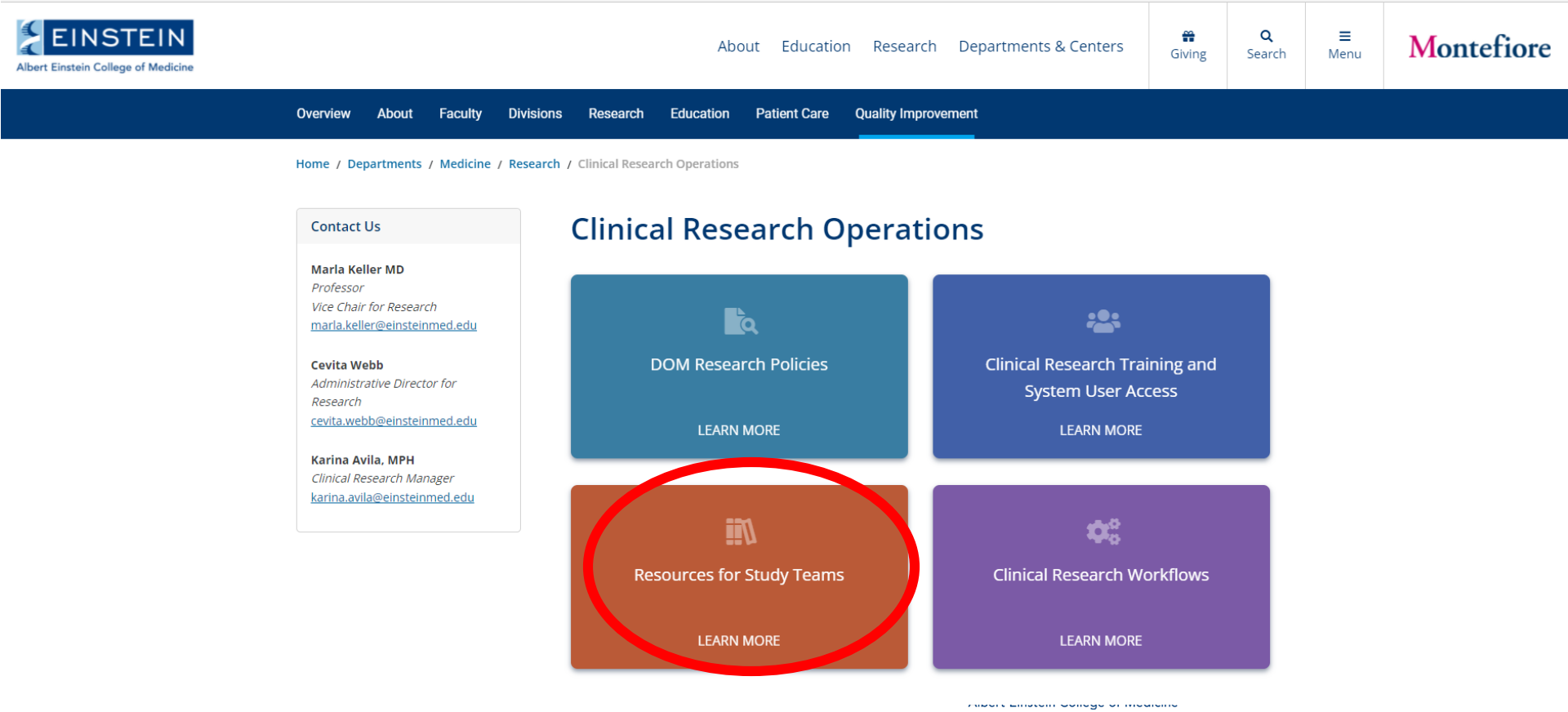
New Resource Alert

Human Subject Research Project Navigation Tool



Department of Medicine Website

https://einsteinmed.edu/departments/medicine/research/clinical-research-operations/



Thank You!

Karina Avila, MPH
Clinical Research Manager
Department of Medicine

karina.avila@einsteinmed.edu
718-430-2003

https://einsteinmed.edu/departments/medicine

K. Zoe Tsagaris, MS, OTR/L, CCRP
Clinical Trials Network Manager
Institute for Clinical & Translational Research

zoe.tsagaris@einsteinmed.edu
718-430-8804

https://einsteinmed.edu/centers/ictr/

Suggestions for webinar topics?
Let Karina know!

EINSTEIN
Albert Einstein College of Medicine

Montefiore

References

- **Einstein IRB Policies:**
  - Unanticipated Problems Procedure
  - Other Reportable Events Procedure
  - All other Policies & Procedures
- **BRANY IRB Policies**
  - Reporting Timelines, Forms, and Procedure Downloads
- **OHRP Guidance** Reviewing & Reporting Unanticipated Problems Involving Risks to Subjects or Others and Adverse Events, 2007
- **Code of Federal Regulations**
  - CFR 21 – Food and Drugs
  - 45 CFR 46– Protection of Human Subjects
- **Declaration of Helsinki**
- **Belmont Report**

EINSTEIN
Albert Einstein College of Medicine

Montefiore