UNIVERSITY
OF MIAMI

Conflicts of Interest in Research and Scholarly Activities:

Review of investigator interests at the University of Miami

May 2014

Office of Research Compliance (ORC)

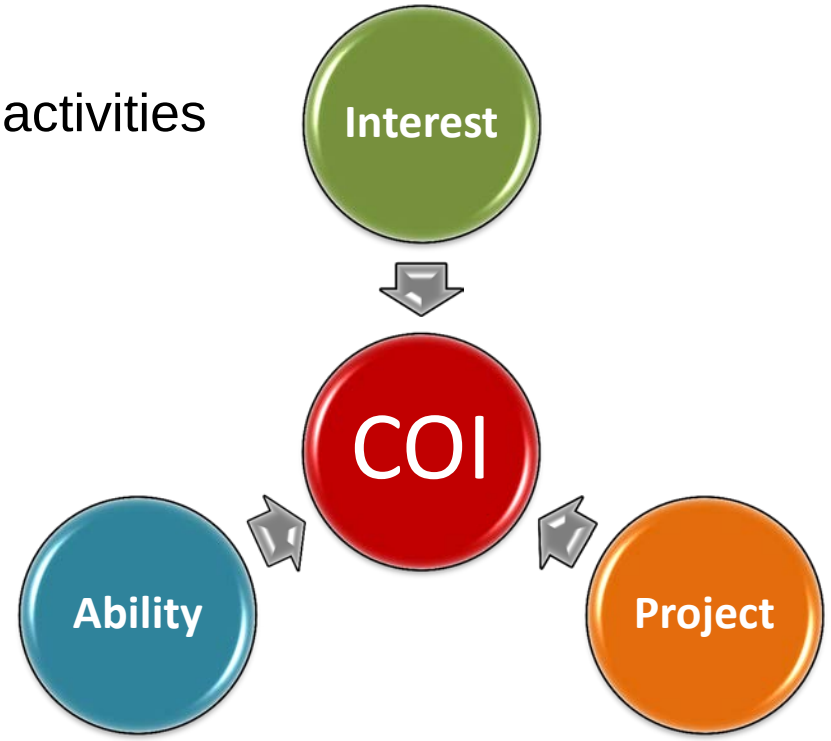
- **Leadership:** John L. Bixby, PhD, *Vice Provost for Research*
- **Staff:** Lory A. Hayes, PhD, *Associate Director*
  Jerry Engel, Esq., *Research Compliance Officer*
  Jenisse Madera, *Compliance Specialist*
  Heather Osorio, *Compliance Specialist*
  Sana Syed, *Compliance Specialist*
- **Phone:** 305-243-4054
- **Email:** researchcompliance@med.miami.edu
- **Websites:** **ORC website:** http://uresearch.miami.edu/compliance
  - **Disclosure Profile System (DPS):** http://uresearch.miami.edu/DPS
  - **Research Reporting System (RRS):** https://research.miami.edu
  - **'Cane Watch Compliance:** www.canewatch.ethicspoint.com
- **DPS helpline:** 305-243-0877

Conflict of interest (COI), Regulations and Disclosures at UM

- Definitions, regulations, policies
- Disclosure Profile System (DPS), Research Reporting System (RRS), and Compliance Assessment and Management System (CAMS)
- Interest review process for potential conflicts
- COI Committee guidelines for relatedness
- COI Committee management of conflicts

Conflict of interest (COI)

1. Financial or obligatory interest
2. that could directly and substantially affect, or be affected by,
3. the outcome of:
   - research, or
   - funded scholarly/educational activities

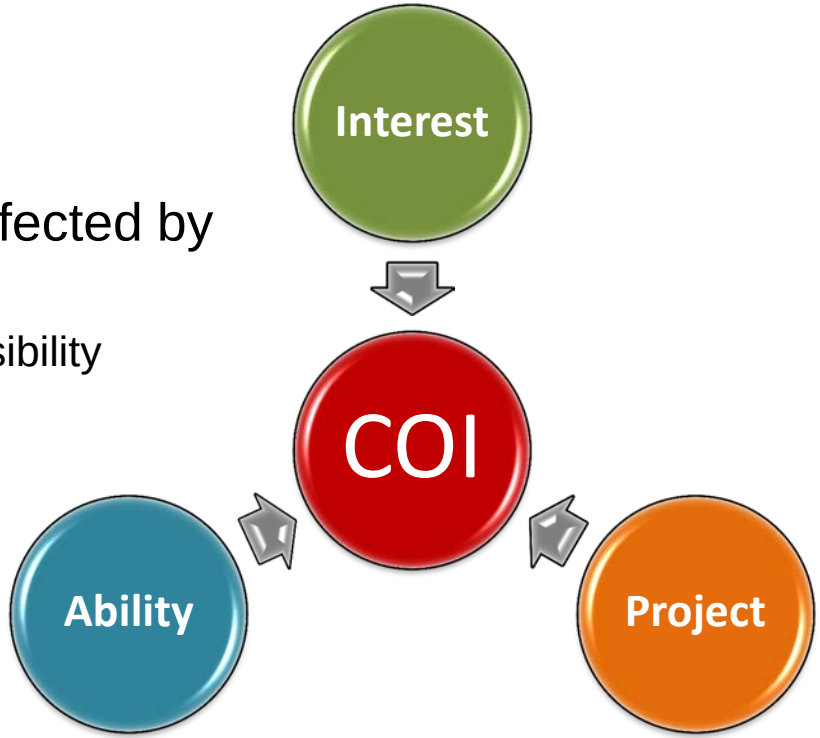


COI

COIs cannot (and probably should not) be avoided.

How can they be managed?

- alter the interest/relationship
- alter the project
- alter the ability to affect, or be affected by
  - alter investigator's role
  - add a "supervisory" layer of responsibility



Types of Interests

- **Individual Interests:**
  - **Financial**
    - income, gifts, loans – salary, consulting fees, honoraria, travel expenses, gifts-in-kind and equity interests (e.g., stocks, stock options, warrants).
  - **Proprietary**
    - intellectual property rights (e.g., patents, copyrights, royalties)
  - **Obligations**
    - consultant, lecturer, speaker's bureau, trustee, employee, advisory board
- **Institutional Interests**

COI in Research: UM Policies

Faculty Manual

- "University faculty members undertaking or engaging in sponsored work, who have a
  - **significant financial interest** in, or a
  - **consulting arrangement** with a private business concern,

  must avoid conflicts of interest between their sponsored University research obligations and their outside interests and other obligations."

University of Miami Medical Group (UMMG) Policy

- Interaction with Health Industry Entities

Sponsored Programs Policies

- **Updated June 2012**
- Office of Research Administration (ORA)
- C: Non-financial Compliance Issues Policy
  - C8: Conflict of Interest
  - mandates disclosure of interests to the Vice Provost for Research

Federal Regulations: sponsored research

Food and Drug Administration (FDA)

- 21 CFR 54
  - "Financial Disclosure by Clinical Investigators" (FDA 2000; **new guidelines published in February 2013**)

National Science Foundation (NSF)

- 510 Conflicts of Interest Policies (NSF 05-131 July 2005)

Public Health Service (PHS)

- 42 CFR Part 50, Subpart F & 45 CFR 94
  - "Responsibility of Applicants for Promoting *Objectivity in Research* for which PHS Funding is Sought" (PHS 1995; **PHS 2011**)
  - "Responsible Prospective Contractors" (PHS 2004; **PHS 2011**)

Major Changes to the PHS Regulations

1. investigator training required
2. PHS Significant Financial Interest (SFI) threshold decreased
3. investigators must disclose all SFIs related to institutional responsibilities (exceptions for academic, gov't);

   institution determines relatedness to project

Philosophical shift – institution bears responsibility to connect SFIs with proposed work

4. additional details required when reporting financial conflicts of interest (FCOIs) to PHS
5. public accessibility to policy/FCOIs required
6. retrospective reviews required

PHS regulations

Timing of disclosures hasn't changed

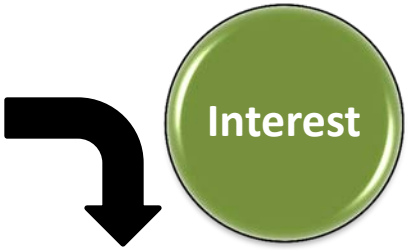
- **At the time of application:**
  - The Institution must be aware of interests that pose potential COIs (Investigator disclosures).

- **Prior to the expenditure of funds:** (NoGA)
  - The Institution must report an identified significant COI to the PHS and assure that it has been managed.

- **FCOI identified after the initial report:**
  - The Institution must report to the PHS within **60** days of acquisition and assure that it has been managed.

Review Process for potential COIs

Investigators disclose in DPS



Disclosure Profile System (DPS)

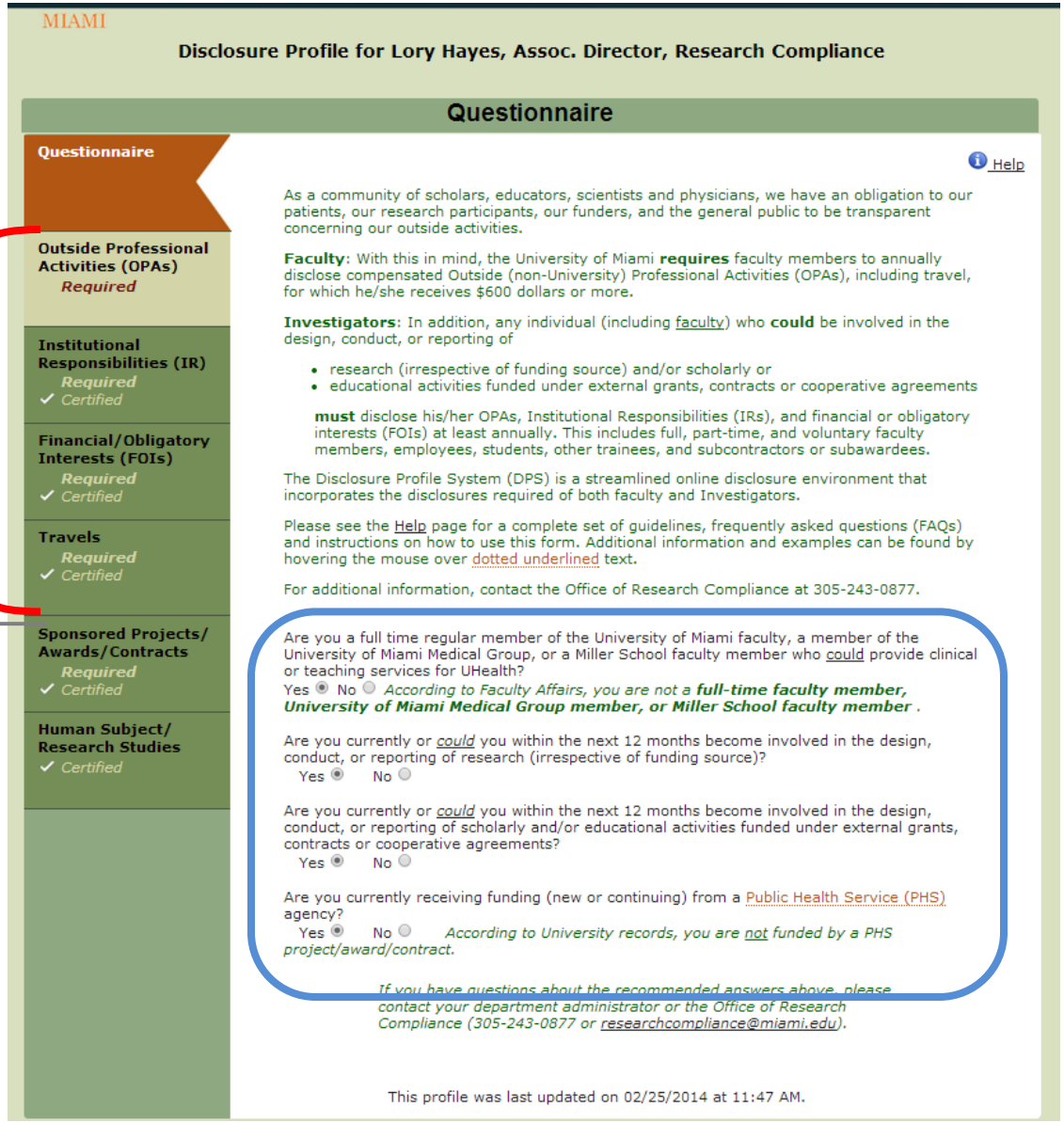
- disclosure section
  - information repository, compliant with federal regulations
  - combines
    - Faculty Disclosure Forms (FDF),
    - Financial Interest Declaration (FID)/Individual Interest Disclosure (IID)
    - Human Subject Research (HSR) disclosures
- projects section
  - Project/Award/Contract: designate team members
  - HSR: team members make project specific disclosures
- pending upgrades
  - improved workflow
  - administrative access
  - linking InfoEd numbers into projects

DPS:

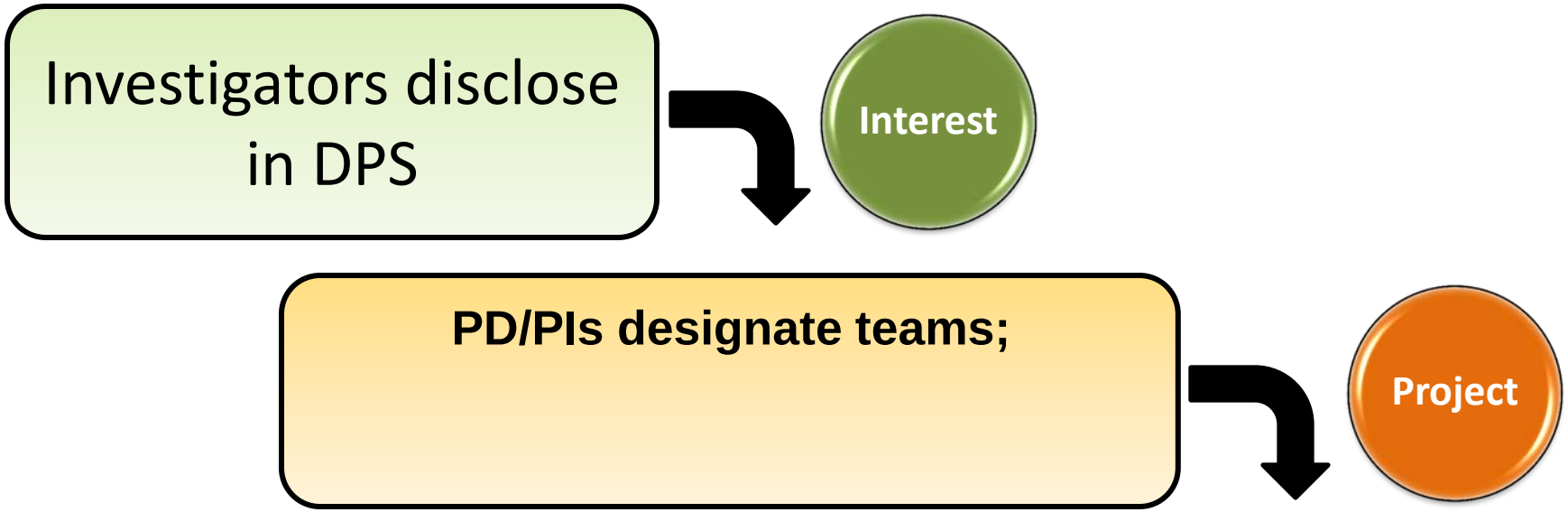
Internet Explorer v8+ or Google *Chrome*

Interests:

- Disclosed immediately
- If new, w/in 30 days
- Updated annually



Review Process for potential COIs



DPS (cont)

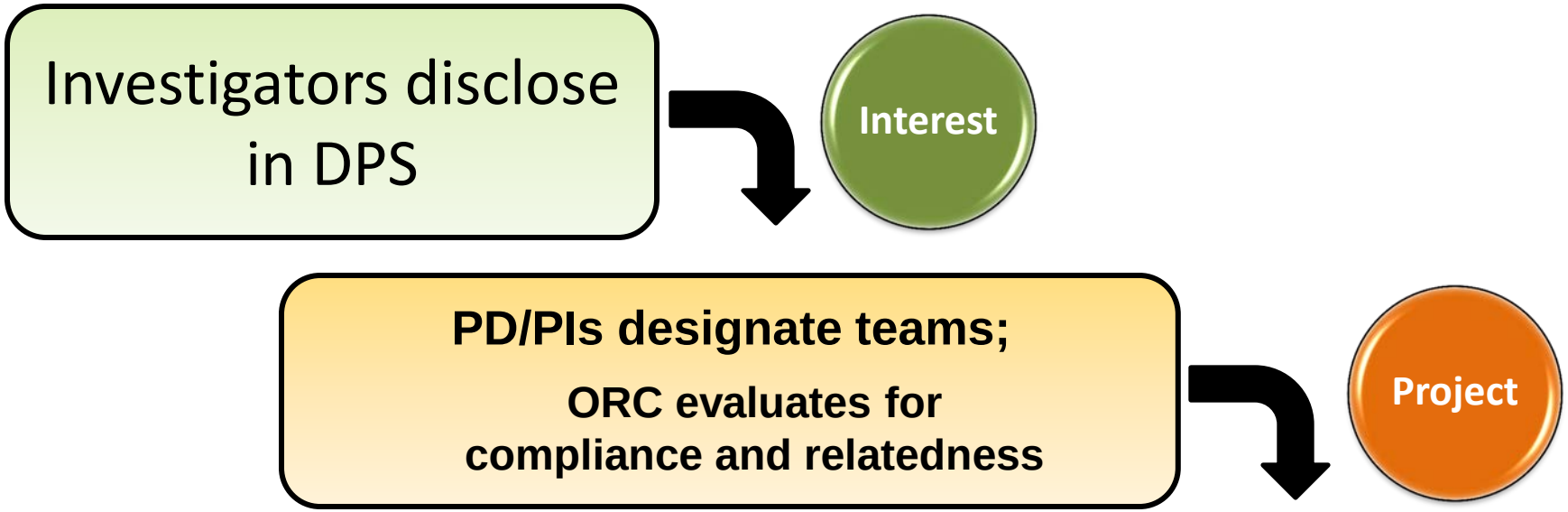
Projects:

- PD/PI enter as directed
- Designate teams
- Update when necessary

Research Reporting System (RRS) Compliance tools

- www.research.miami.edu
- Individual Compliance Report:
  - C Numbers for all UM personnel and all DPS Investigators
  - whether he/she has completed
    - COI training through the CITI system and/or
    - the disclosure process in the DPS.
- Project Compliance Report:
  - InfoEd numbers entered into the DPS by the PI, or ORA has notice of grant award (NoGA).
  - displays the status of a project and its team members.
  - ascertain whether an account on hold due to COI concerns
- Research Information Technology (RIT): 305-243-2314

Review Process for potential COIs



Compliance Assessment & Management System (CAMS)

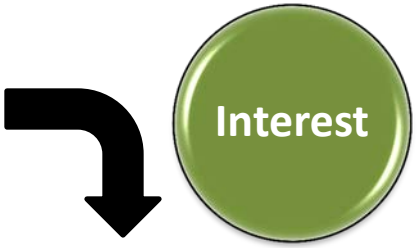
- prior to expenditure of funds
  - confirm compliance status of team members and alert the ORA/ORC of non-compliant individuals
  - alert the ORC of SFIs that may be related to the proposed work
- ORC contacts individual
- ORC determines relatedness
  - If none, result registered in CAMS
    - ✓ ORA releases funding
    - ✓ 2,600 InfoEd numbers through system
  - If related, send to Vice Provost for Research and the COI Committee (COIC)

What is “related”?

- investigator has financial or obligatory interest in
  - project sponsor
  - entity with the same/similar focus as project
  - entity that might be expected to benefit from project
  - entity that might be expected to compete with the work product
  - parties to MTAs or CDAs
  - intellectual property (IP) related to the project
- investigator is/was/will be
  - IND/IDE holder (sponsor)
  - directly involved in project design with the IND/IDE holder
  - directly involved in bringing work product to market

Review Process for potential COIs

Investigators disclose in DPS



PD/PIs designate teams;

ORC evaluates for compliance and relatedness

COIC confirms and manages COIs

Identification of a COI by the COI Committee

1. Might the interest affect, or be affected by, the results of the study?

2. Does the conflicted individual have the ability to influence the results of the study?

UM Conflict of Interest Committee

- **John Bixby, Molecular & Cellular Pharmacology, VP Research (Chair)**
- **David Birnbach, Anesthesiology, VP Faculty Affairs**
- **Richard Thurer, Cardiothoracic Surgery**
- **Michael Kolber, Infectious Diseases (Medicine)**
- **James Grichnik, Dermatology**
- **Keith Candiotti, Anesthesiology**
- **Eden Martin, Human Genetics**
- **Gerhard Dahl, Physiology & Biophysics**
- Charles Carver, Psychology
- Lynne Fieber, RSMAS
- Rene Sacasas, Business Law
- Ken Goodman, Medicine, Ethics Programs (non-voting)
- Cynthia Augustyn, General Counsel (non-voting)
- James O'Connell, Office of Technology Transfer (consultant)

Committee Management of COIs

- financial COI management
  - removal of conflicted personnel
  - reduction/elimination of financial interest
  - severance of relevant financial relationships
- disclosure (inform the relevant groups)
  - proposal reviewers
  - publication reviewers/readers
  - presentation attendees
  - collaborators, students

Committee Management of COIs (con't)

- data collection/interpretation
  - removal of conflicted person from involvement in data collection/entry/analysis.
  - oversight by an independent researcher/statistician.
  - de-identification and/or limitation of data set (if analysis of existing human subjects data)

Committee Management of COIs (con't)

- for human subjects research:
  - study design
    - non-conflicted persons involved in study development
    - add study sites with non-conflicted personnel
    - use blinded designs
    - reduce %age of study population enrolled at UM
  - revise protocol to be no more than minimal risk

Committee Management of COIs (con't)

- for human subjects research (con't):
  - disclosure of the conflict to the IRB (investigator follows IRB management recommendations).
  - increased frequency of continued review and/or monitoring by the IRB.
  - disclosure of the conflict to research participants in informed consent forms.
  - disclosure to external study site PIs (who follow their institutional policies on notification)

Committee Management of COIs (con't)

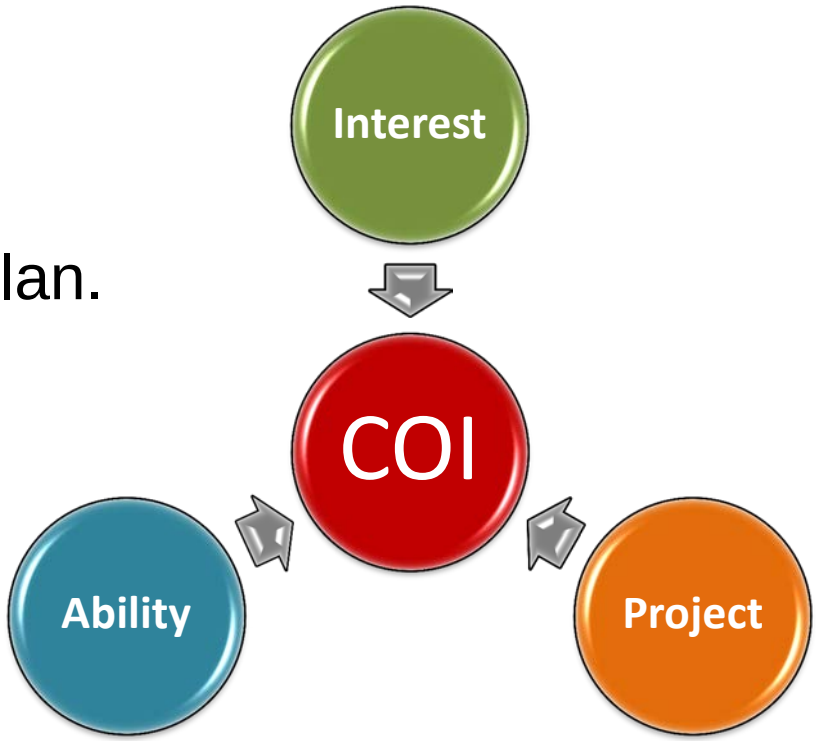
- for human subjects research (con't):
  - investigator will not consent subjects.
  - use clinical research organization/associate (CRO/CRA) or non-conflicted individual to monitor research.
  - Data Safety Monitoring Board (DSMB)
    - rather than an Investigator or Sponsor
    - can be external to institution
    - has *a priori* rules (e.g., safety and efficacy) for stopping study.
  - non-conflicted individual as research subject advocate or ombudsperson.

Committee Management of COIs (con't)

- additional management mechanisms:
  - external entity involved in conflict will not have access to private information
  - no University resources will be utilized for the benefit of the external entity involved in conflict

COI Management

- Management plan draft sent to Investigator.
- Executed by the COIC Chair.
- ORC notifies awarding entity (if necessary)
- Investigator complies with the plan.
- ORC monitors compliance with the plan.



What should you do?

1. Disclose interests in the **Disclosure Profile System** (DPS) www.miami.edu/dps using *Internet Explorer 8+* or *Chrome* ahead of time.

2. Complete training entitled **"Conflict of Interest Course"** in the CITI system www.citiprogram.org once every four years.

3. Use the **Research Reporting System** (RRS) www.research.miami.edu to determine compliance status of team members and/or projects.

4. Call the **DPS help line** for assistance 305-243-0877

Office of Research Compliance (ORC)

- **Leadership:** John L. Bixby, PhD, *Vice Provost for Research*
- **Staff:** Lory A. Hayes, PhD, *Associate Director*
  Jerry Engel, Esq., *Research Compliance Officer*
  Jenisse Madera, *Compliance Specialist*
  Heather Osorio, *Compliance Specialist*
  Sana Syed, *Compliance Specialist*
- **Phone:** 305-243-4054
- **Email:** researchcompliance@med.miami.edu
- **Websites:** **ORC website:** http://uresearch.miami.edu/compliance
  - **Disclosure Profile System (DPS):** http://uresearch.miami.edu/DPS
  - **Research Reporting System (RRS):** https://research.miami.edu
  - **'Cane Watch Compliance:** www.canewatch.ethicspoint.com
- **DPS helpline:** 305-243-0877

Case Study: Several compensated relationships; no COI

- Interests: Compensated consultant for five pharma companies, receiving $60,000 in past 12 months
- Project: federally funded “bench” research on rodent models
- Potential COI: Pharma companies could benefit from knowing the results of the research; Investigator could perform additional consulting/receive additional compensation if research is successful
- Related factors:
  - Exacerbating: Investigator will supervise the project, design the experiments and analyze the data.
  - Mitigating: Early stage, exploratory research; Pharma companies are not developing drugs that target the cell-surface molecule central to the research.
- Outcome: COIC Issued COI determination letter requesting disclosures in publications/presentations

Case Study: Compensated interest/Equity with COI

- Interests: Consultant for outside entity and owner of private practice; receiving $25,000 in past 12 months; delivering same therapy as that performed and evaluated in the funded studies
- Project: perform and evaluate efficacy of therapy on patients for federally funded awards
- Potential COI: Investigator could receive additional compensation/garner additional clients if treatment proven effective
- Related factors:
  - Exacerbating: Investigator will perform clinical interventions and will participate in all aspects of the trials.
  - Mitigating: Investigator not involved in data analysis or interpretation.
- Outcome: COIC executed COI management plan that included: disclosure in informed consent forms (ICF)/publications/presentations, limit to $10,000 per related interest.

Case Study: Several compensated interests with COI

- Interests: Consultant for 7 pharma companies, receiving $90,000 in past 12 months
- Projects: Multiple clinical studies, usually multi-center, randomized, open-label or double-blind design, some funded by same pharma companies.
- Potential COI: Outcome of research could be modified for positive affect on pharma companies; Investigator could receive additional compensation if treatment proven effective
- Related factors:
  - Exacerbating: Investigator will oversee all aspects of the study.
  - Mitigating: Study design; low participant enrollment at UM; Investigator is world-renowned scientist and clinical expert.
- Outcome: COIC executed COI management plan that included: disclosure in informed consent forms (ICF)/publications/presentations, limit to $10,000 per related interest.

Case Study: Equity and IP; no compensation or royalties

- Interests: equity in, and IP licensed to, private company; UM has no interest in the IP.
- Projects: federally funded blinded “bench” analysis of de-identified patient samples
- Potential COI: Company could benefit if IP proven effective
- Related factors:
  - Exacerbating:
  - Mitigating: early phase of IP development; Investigator not PI on clinical studies; study design; data to be confirmed at other sites; non-UM co-investigators analyzing data and preparing manuscripts and presentations; results of lab analysis will not affect patient treatments
- Outcome: COIC executed COI management plan that included disclosure in ICF/publications/presentations and reporting to the NIH.

Case Study: Equity/board membership/IP

- Interests:
  - UM released IP to Investigator but retains 1/6 rights to future royalties
  - Foundation:
    - Investigator is founding member and secretary
    - Investigator assigned IP to Foundation which licensed to company “P”
    - Has not received any compensation, stocks, stock options or gifts in the past 12 months.
  - Company “P”:
    - Investigator is Chief Scientific Officer, Director, Consultant
    - company interested in therapies for same diseases and with same treatment as research.
    - consulting on research development of products which UM does was not developing.
    - Investigator had not received compensation for his activities in the past 12 months.
    - Investigator owns 78,000 common shares, greater than $10,000.
  - Company “TB”:
    - Subsidiary of Company “P” responsible for developing and marketing the IP technology
    - Investigator on the Board of Directors, though had not received any compensation, stocks, stock options or gifts in the past 12 months.
- Project: Funded by Company “P,” patients treated with IP followed by “bench” analysis of cells; no subsequent effect on patient treatment.

Case Study: Equity/board membership/IP (con't)

- Potential COI: Outcome of research could be modified for positive affect on IP; Foundation/companies could benefit if IP proven effective
- Related factors:
  - Exacerbating: Investigator not forthcoming with disclosure information; Investigator only person performing "bench" experiments with no oversight; monitoring of clinical study by Company "P" only
  - Mitigating: Investigator participation considered essential to project as specialist in techniques used in the laboratory.
- Outcome: COIC executed COI management plan that included requirement for inclusion of negative controls and blinding of samples; oversight of lab data by non-conflicted clinical PI; disclosure in ICF/publications/presentations; limitation on compensation received from Company "P" to $10,000 in any 12-month period.
- Outcome: Institutional plan executed to address IP interest