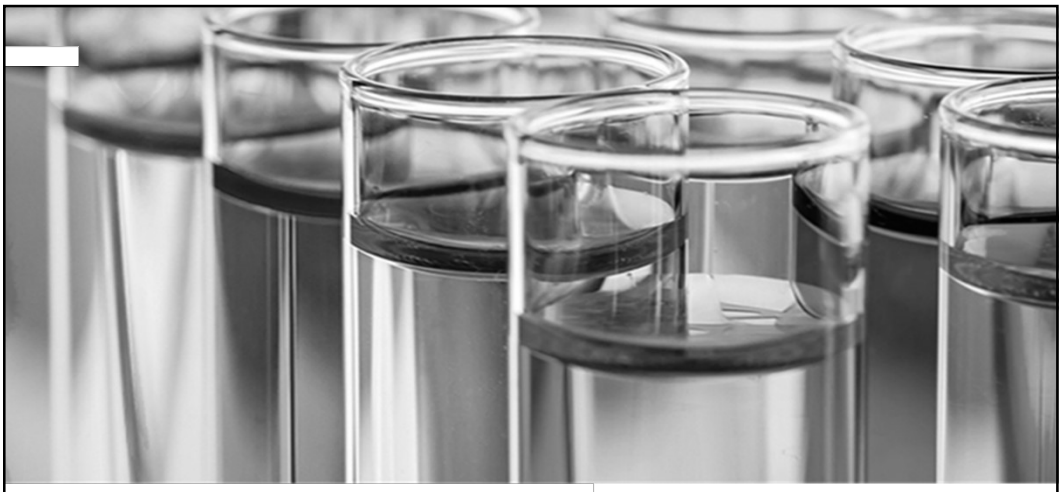

HCCA Pittsburgh Regional Conference

Conflicts of Interest in Clinical Research

October 4, 2019

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RESEARCH COMPLIANCE ROUND-UP

Slide Deck Prepared By Ankura Consultants

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RESEARCH CONSULTING, COMPLIANCE, INVESTIGATIONS & PROCESS IMPROVEMENT

- DPM, BS
- More than 29 years of combined experience as a podiatric physician/surgeon, clinical research investigator, institutional review board chair, human research protection program administrator, executive research administrator, and management consultant.
- Advises clients on matters related to good clinical practice noncompliance, human research protections, AAHRPP accreditation, conflict of interest, HIPAA, research billing compliance, and research program optimization.
- Conducted numerous research compliance program assessments at academic medical centers, universities, cancer centers, children's hospitals, hospitals, and health systems.

CLINICAL RESEARCH AND COMPLIANCE EXPERT

- MA, MS, BS
- Certifications: CRC
- Over 11 years of clinical research and compliance experience as a researcher, clinical coordinator, and consultant.
- Previously served as a clinical research program manager and clinical research coordinator at Boston Children's Hospital.
- Provide research consulting services to academic medical centers, community hospitals, independent research organization, and hospital/ health systems related to clinical research billing compliance, research operations, good clinical practice, and the protection of human subjects.

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COI Introduction

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ProPublica Electionland ProPublica Illinois Local Reporting Network Data Store Donate

PROPUBLICA TOPICS SERIES NEWS APPS GET INVOLVED IMPACT ABOUT SIGN UP

The Sarah Cannon Research Institute, based in Nashville, received nearly $8 million in payments from drug companies on behalf of its president operations, Dr. Howard Burris, largely for research work. Dozens of his articles published in prestigious medical journals did not include the requ those payments and relationships. (William DeShazer for The New York Times)

Prominent Doctors Aren't Disclosing Their Industry Ties in Medical Journal Studies. And Journals Are Doing Little to Enforce Their Rules

The New York Times

Memorial Sloan Kettering's Chief Executive Resigns From Merck's Board of Directors

Craig B. Thompson, chief executive of Memorial Sloan Kettering Cancer Center, will no longer serve on the board of drug maker Merck. Just last year, he received $300,000 in compensation for that position, in addition to an executive package of about $6.7 million at the hospital. Paul Zimmerman/Getty Images

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COLLABORATION DRIVES RESULTS

INSIGHTS

The Destructive Institutional Backlash When Faculty Fail to Disclose Financial Relationships with Industry to Medical Journals: What Compliance Officers Need to Consider

By Scott Lipkin, F. Lisa Murtha

October 23, 2018

A September 8, 2018, New York Times[1] article reported that Dr. Jose Baselga, Memorial Sloan Kettering Cancer Center's ("MSK") Chief Medical Officer, failed to disclose relevant

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U.S. Department of Health and Human Services
Office of Inspector General

February 2019 OIG Work Plan

"Recently, the Director of NIH issued a statement expressing concern about the increasing risks to the security of intellectual property in its biomedical research enterprise. NIH stated that it is addressing these concerns, in part, by taking steps to improve accurate reporting of all financial interests. Grantee institutions must submit sufficient information that would enable NIH to both:

(1) understand the nature and extent of a researcher's financial conflict of interest and;
(2) assess the appropriateness of the grantee institution's plan to manage this conflict.

OIG will examine NIH's oversight and monitoring of the financial conflicts of interest reported by grantee institutions.

NIH's Implementation of Financial Conflict of Interest Regulations

NIH Monitoring of Extramural Researchers' Financial Conflicts of Interest

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A conflict of interest *is a set of circumstances that creates a risk that professional judgment or actions regarding a primary interest will be unduly influenced by a secondary interest.*

Institute of Medicine (US) Committee on Conflict of Interest in Medical Research, Education, and Practice; Lo B, Field MJ, editors. Washington (DC): National Academies Press (US); 2009. 2, Principles for Identifying and Assessing Conflicts of Interest.

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Potential sources of conflict in AMCs, Hospitals, and Health Systems

Research

Clinical

Purchasing

Institutional

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Increased scrutiny for clinicians and investigators

- **Tougher rules for CME program accreditation**
- **Affordable Care Act reporting**
- **Disclosure requirements for journals**
- **Guidelines developed by professional associations**

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Conflicts of Interest in Clinical Research

Pillars of Ethical Research

- Scientific Integrity
- Patient Safety
- Investigator Objectivity

> In general terms, responsible conduct in research is simply good citizenship applied to professional life.

https://ori.hhs.gov/sites/default/files/rcrintro.pdf

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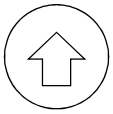
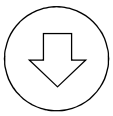
Evolving financial and political landscape driving change in the scope of conflicts in clinical research

Cost to bring new drugs to market



Federal research funding



Academic-Industry partnerships

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Regulatory Environment

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Regulations and Guidelines:

DHHS: 42 CFR Part 50, Subpart F (grants and cooperative agreements)

DHHS: 42 CFR Part 94 (contracts)

FDA: 21 CFR Part 54, Financial Disclosure by Clinical Investigators

NSF: Award and Administrative Guide IV.A

VA: VHA Handbook 1200.17

Reports:

The Association of American Medical Colleges ("AAMC")

The Association of American Universities ("AAU") Advisory Committee on Financial Conflicts of Interest in Human Subjects Research

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Who is Covered under *42 CFR Part 50, Subpart F* ?

- Each Institution that applies for or receives PHS/NIH grants or cooperative agreements for research.
  - Domestic, foreign, public, private (not Federal)
- Any Investigator, as defined by the regulation, planning to participate in or participating in the research.
- When an individual, rather than an Institution, is applying for or receives PHS/NIH research funding.

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§ 50.603 Definitions:

Financial interest means anything of monetary value, whether or not the value is readily ascertainable.

Financial conflict of interest (FCOI) means a significant financial interest that could directly and significantly affect the design, conduct, or reporting of PHS-funded research.

FCOI Management means taking action to address a financial conflict of interest, which can include reducing or eliminating the financial conflict of interest, to ensure, to the extent possible, that the design, conduct, and reporting of research will be free from bias.

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§ 50.603 Definitions:

Institution means any domestic or foreign, public or private, entity or organization (excluding a Federal agency) that is applying for, or that receives, PHS research funding.

Investigator means the project director or principal Investigator and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by the NIH, or proposed for such funding, which may include, for example, collaborators or consultants.

Investigator's Institutional Responsibilities means an Investigator's professional responsibilities on behalf of the Institution, and as defined by the Institution in its policy on financial conflicts of interest, which may include for example: activities such as research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data and Safety Monitoring Boards.

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Investigator Training

FCOI training required.

Each Investigator must complete training prior to engaging in research related to any NIH-funded grant and at least every four years, and immediately under the designated circumstances:

- Institutional FCOI policies change in a manner that affects Investigator requirements;
- An Investigator is new to an Institution;
- An Institution finds an Investigator noncompliant with Institution's FCOI policy or management plan.

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Travel Disclosure

All reimbursed or sponsored travel must be disclosed by the investigator within 30 days.

- Exceptions:
  - A federal, state and local governmental agency
  - A U.S. institution of higher education
  - A U.S. based academic teaching hospital
  - A U.S. based medical center
  - A research institute affiliated with a U.S. institution of higher education

Significant Financial Interest (SFI)

A financial interest consisting of one or more of the following interests of the Investigator (and those of the Investigator's spouse and dependent children) that reasonably appears to be related to the Investigator's institutional responsibilities:

- Remuneration from publicly traded entity in the 12 months preceding the disclosure that in aggregate exceeds $5,000.
  - Salary and consulting income, honoraria, paid authorship
  - Equity-stock, stock options or other ownership interest
- Remuneration from non-publicly traded entity in the 12 months preceding the disclosure that in aggregate exceeds $5,000 or any equity.
- Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.

Certain financial interest exclusions apply.

Public Accessibility

Make FCOI policy available via a publicly assessable web site. If the Institution does not have any current presence on a publicly accessible Web site (and only in those cases), the Institution shall make its written policy available to any requestor within five business days of a request.

Prior to the expenditure of funds, make certain information concerning FCOIs held by senior/key personnel via a publicly accessible, via a publicly accessible Web site or by a written response to any requestor within five business days of a request, and update such information as specified in the regulation.

Management of FCOI

For all identified FCOIs, Institutions must develop and implement a management plan (may include reduction or elimination of the SFI).

FCOI Reporting

Current requirements, plus annual updates on any previously-identified FCOI for the duration of the research project (including during an extension with or without funds).

Monitoring Management of FCOI

For disclosures that are reported as FCOI to the NIH, monitoring of the management plan will be required.

Whenever a management plan is implemented, the institution shall monitor investigator compliance with the management plan on an ongoing basis until completion of the PHS funded research project.

Subrecipient Disclosure and Monitoring

Subrecipient institutions or entities must certify whether they will follow their own COI policy or your institution's policy.

If subrecipients do not have an NIH compliant policy and elect to follow your institution's COI policy, you must:

- Collect disclosures from the subrecipient investigators;
- Ensure they have completed COI training; and
- Manage and monitor any positive financial disclosures.

Noncompliance

The Institution shall, within 120 days of the Institution's determination of non compliance, complete a retrospective review of the investigator's activities and the NIH-funded research project to determine if there was bias in the design, conduct, or reporting of such research.

Institution is required to document the retrospective review.

A Mitigation Report required if bias is found.

Financial Conflicts of Interest:
Programmatic Considerations

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Managing COI Disclosures

Prior to the Institution's expenditure of any funds under a PHS-funded research project, the designated official(s) of an Institution must:

1. Review investigator disclosures of SFIs
2. Determine whether each SFI is related to the PHS research
3. Determine whether each SFI is a FCOI
4. Develop and implement a management plan

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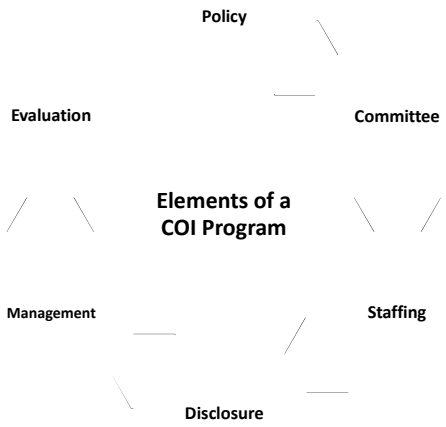
COI Program



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Operational Considerations

Policy

- Does the Institution apply all requirements of 42 CFR Part 50, Subpart F to ALL research or limit policy to PHS funded research only?

- If limited what requirements apply to non-PHS funded research?
  - Disclosure
  - Education
  - Reporting

Staffing

- Volume of disclosures/reviews
- Technology to support data collection
- Number of Offices and Committees supporting COI

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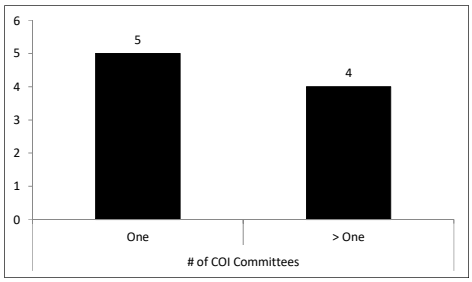
Operational Considerations

Disclosures

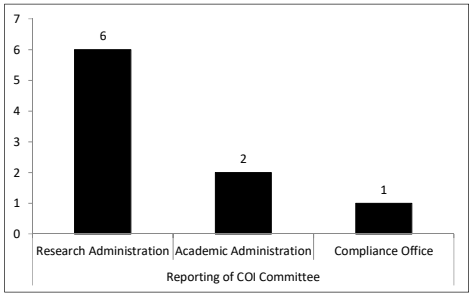
- How are disclosures submitted?
- Who receives disclosures?
- How is disclosure data managed?
- Who evaluates disclosures?
  - Committee
  - Sub-Committee
  - Individual

AMC Benchmarking (n= 9)

Number of COI Committees

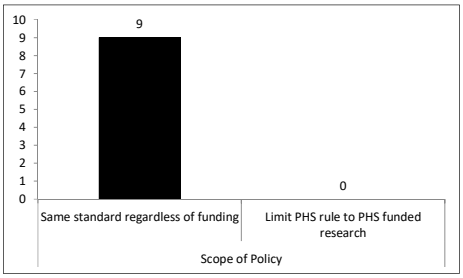


COI Committee reporting structure

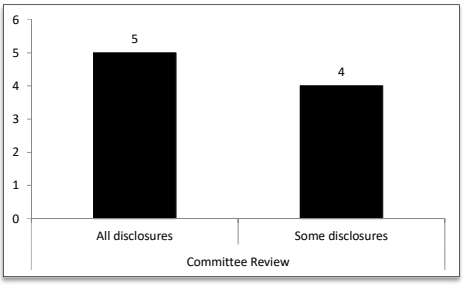


AMC Benchmarking (n= 9)

Scope of COI policy



COI Committee review responsibilities



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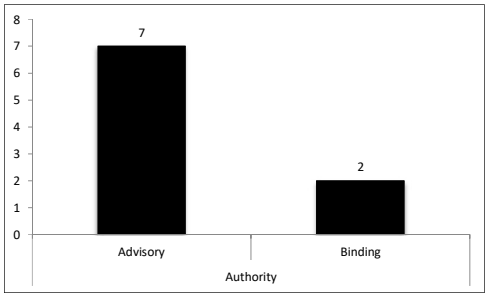
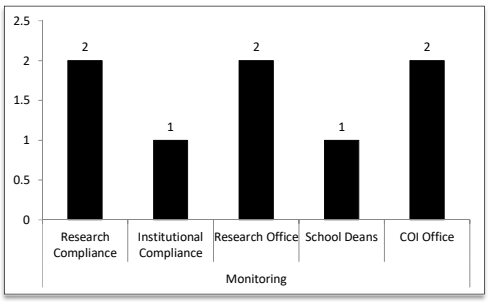
AMC Benchmarking (n= 9)

Committee Authority



Monitoring responsibilities



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Considerations and Elements of a Management Plan

- Identify the financially interested party
- Identify the nature of the SFI (e.g. equity, income)
- Describe the research project
- Describe the relationship between the financial interest and the research
- Describe the way in which the SFI could affect the design, conduct, and reporting of the research, or the way in which the interest could be affected by the research
- Describe the steps to protect interests of affected parties
- Describe the actions to monitor/ ensure compliance with the plan

Reporting & Transparency: Who will be informed of the FCOI and the management plan?

- PHS
- Research participants (informed consent document)
- Co-investigators and members of the study team
- Trainees (students, residents, fellows, post-docs)
- Collaborators at other sites
- Disclosure in publications

Management Examples

1. Public disclosure of financial conflicts of interest (e.g., when presenting or publishing the research)
2. For research projects involving human subjects research, disclosure of financial conflicts of interest directly to participants
3. Appointment of an independent monitor capable of taking measures to protect the design, conduct, and reporting of the research against bias resulting from the financial conflict of interest
4. Modification of the research plan
5. Change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research;
6. Reduction or elimination of the financial interest (e.g., sale of an equity interest
7. Severance of relationships that create financial conflicts

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Standard FCOI Management Options

- Disclose in publications and presentations
- Disclose to all individuals involved in the design, conduct, or reporting of the research
- Disclose to all research participants
- Disclose details of management plan to PI

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General Guidelines for CoIR Management

SFI related to research	Value of SFI	Elements of Management Plan					FCoI?
		Public Disclosure required?	Restricted role in Data Analysis?	Restricted Roles in Human Subjects Research			
				Eligibility determination	Consenting	UPs	
Compensation/earnings	≤5K	Not an SFI – does not require reporting in eCoI disclosure					No
Compensation/earnings	5-10K	Advised per journal policy	An SFI – requires reporting – but *typically* not considered a CoIR				No
Non-exclusive license received royalties	≤10K						No
Compensation/earnings (or received royalties)	10-50K	Yes	No	restricted	restricted	restricted	typically not
Exclusively licensed or optioned tech – used as a tool** (no start-up relationship)	potential license income, other unusual circumstances affect mgmt. & FCoI determination	Yes	typically not	restricted	restricted	restricted	typically not
Exclusively licensed or optioned tech – used as a tool** (start-up relationship)		Yes	case specific	restricted or not allowed	restricted or not allowed	restricted or not allowed	case specific
Exclusively licensed or optioned tech evaluated/enhanced (no start-up relationship)		Yes	case specific	not allowed	not allowed	not allowed	case specific
Stock or stock options	public: 10-50K; private: >0	Yes	case specific	not allowed	not allowed	not allowed	case specific
Compensation/earnings (including valuated stock/options or received royalties)	>50K	Yes	case specific	not allowed	not allowed	not allowed	case specific
Exclusively licensed or optioned tech evaluated/enhanced (start-up relationship)	any	Yes	Yes	not allowed	not allowed	not allowed	Yes
Start-up relationships: Multiple interests such as founder/fiduciary role and/or stock/options and/or licensed tech	any	Yes	Yes	not allowed	not allowed	not allowed	Yes

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http://www.ohsu.edu/xd/research/about/integrity/coi/upload/CoIR-Management-General-Guidelines.pdf

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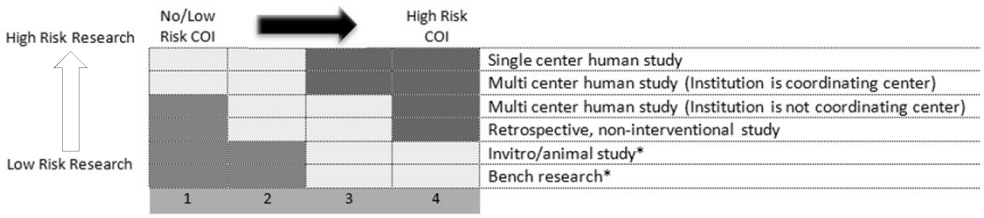
Typical Risk Model Related to Royalties and Licensing



1. Research using licensed IP
2. Research using licensed IP & company funded
3. Research evaluating or enhancing licensed IP
4. Research evaluating or enhancing licensed IP and company funded

Typically no COI or minimal management
Typically a COI with minimal or moderate management
Typically a COI with moderate or aggressive management

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Institutional Conflicts of Interest

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Institutional COI

"Institutional conflicts of interest (ICOIs) occur when the institution or leaders with authority to act on behalf of the institution have conflicts of interest (COIs) that may threaten the objectivity, integrity, or trustworthiness of research because they could impact institutional decision making."

Resnik, D. B., Ariansen, J. L., Jamal, J., & Kissling, G. E. (2016). Institutional Conflict of Interest Policies at U.S. Academic Research Institutions. Academic medicine : journal of the Association of American Medical Colleges, 91(2), 242–246.

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Identifying Institutional COI

1. When the institution or institutional officials are entitled to receive royalties from the sale of the investigational product that is the subject of the research.
2. When the institution or institution officials have technology licensing and equity interest in a non-publicly traded sponsor of human subjects research at the institution.
3. When the institution or institution officials have technology licensing and equity interest of greater than $100,000 in value in a publicly traded sponsor of human subjects research at the institution.
4. When the institution has received substantial gifts (including gifts in kind) from a potential commercial sponsor of human subjects research.

Resnik, D. B., Ariansen, J. L., Jamal, J., & Kissling, G. E. (2016). Institutional Conflict of Interest Policies at U.S. Academic Research Institutions. Academic medicine : journal of the Association of American Medical Colleges, 91(2), 242–246.

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Failure to Disclose COI to Journals

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INSIGHTS

The Destructive Institutional Backlash When Faculty Fail to Disclose Financial Relationships with Industry to Medical Journals: What Compliance Officers Need to Consider

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Failure to Disclosure Financial Relationships with Industry to Medical Journals

Failure to disclose industry relationships calls into the question the objectivity and validity of the research results.

- Disparate COI disclosure requirements that are set forth by medical journals and professional societies.
- General lack of COI disclosure "fact checking" and enforcement by medical journals.

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Journal Disclosure Policies and Code of Conduct

International Committee of Medical Journal Editors (ICMJE): Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals

- The submitted work:
  - Timeframe of disclosure – initial conception to the present
  - Disclose if author or author's institution received funds from a 3rd party to support the work
- Relevant financial activities outside the submitted work:
  - Financial relationships that could be perceived to influence, or that gives the appearance of potentially influencing the written material
  - Intellectual Property
- Disclose any patent, copyrights, whether pending, issues, licensed and/or receiving royalties.

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What Can Be Done at Your Institution?

- Review current COI policies and procedures.
- Review compliance of internal COI disclosure, review, management, and reporting.
- Include Institutional COI policies as part of the assessment. If your institution has not yet implemented an ICOCI policy, consideration should be given to establishing one.
- Provide training and education to staff and faculty. Physicians should be encouraged to review and if necessary, dispute their financial data that is posted on open payments website.
- Review disclosures made by staff to medical journals. This assessment should include reconciliation of institution-based disclosures with those made to journals as evidenced by review of the publications. The review sample should include faculty or staff with large numbers of publications and those with multiple COI disclosures.

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Questions?
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