

What do I
disclose?

SFI-Significant
Financial Interest

Covered Clinical
Study

Financial
Arrangement

Significant
Payment of
Other Sorts

Financial
disclosure

12/6/19

The Shades of Grey in Research Conflict of Interest

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*Executive Director of Research
Compliance*

Avera 

Conflict of Interest



"Are you ready for a conflict of interest?"

Disclosure Statement

- I have no relevant financial relationship(s) in connection with this educational activity.

Learning Objectives

- Recognize when a conflict of interest exists
- Identify federal criteria for financial disclosures in clinical research
- Explain Avera's requirements for financial disclosure and management of Conflicts of Interest

Agenda



Conflict of Interest Terms and Definitions

Case Examples

Avera's Requirements for Financial Disclosure

Small Group Activity – What would you do?

Polling

We want to hear from you!

- Let's do some polling!
- **Text AVERAHEALTH to 22333**
- Wait for response from PollEverywhere.



Remember

\$5,000

Conflict of Interest

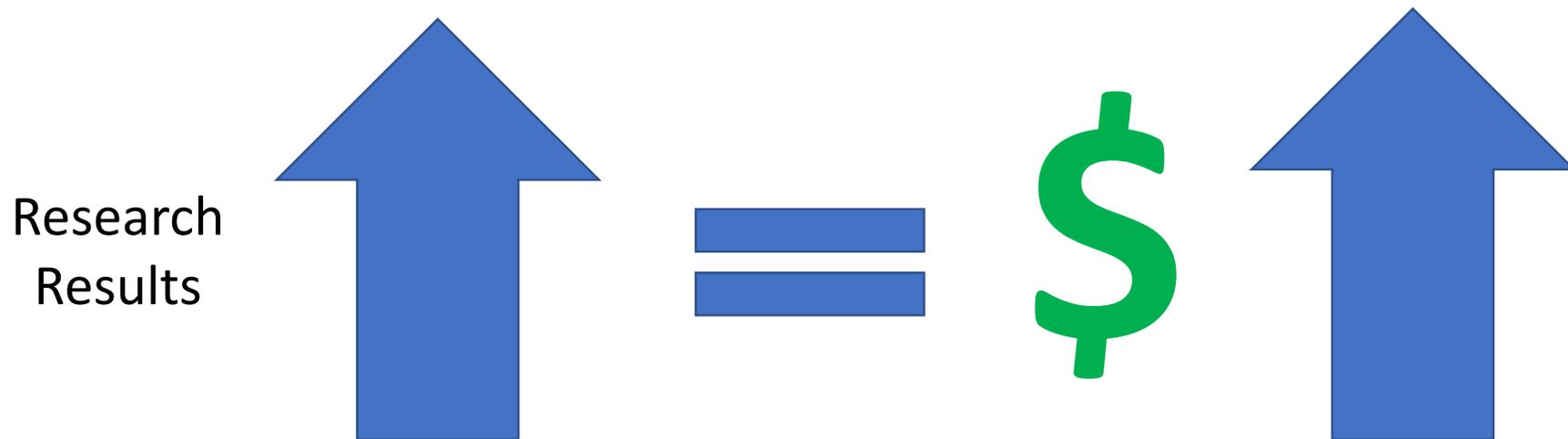


Conflict of Interest:

Terms, Definitions & Federal Regulations

Key Terms

- **Conflict of Interest** “*results when circumstances create a **reasonable possibility that professional judgments** or actions regarding a primary interest related to research will be **unduly influenced** by a secondary self-interest.*”*
 - Can be real or perceived
 - People often disagree over what might constitute “reasonable possibility..”



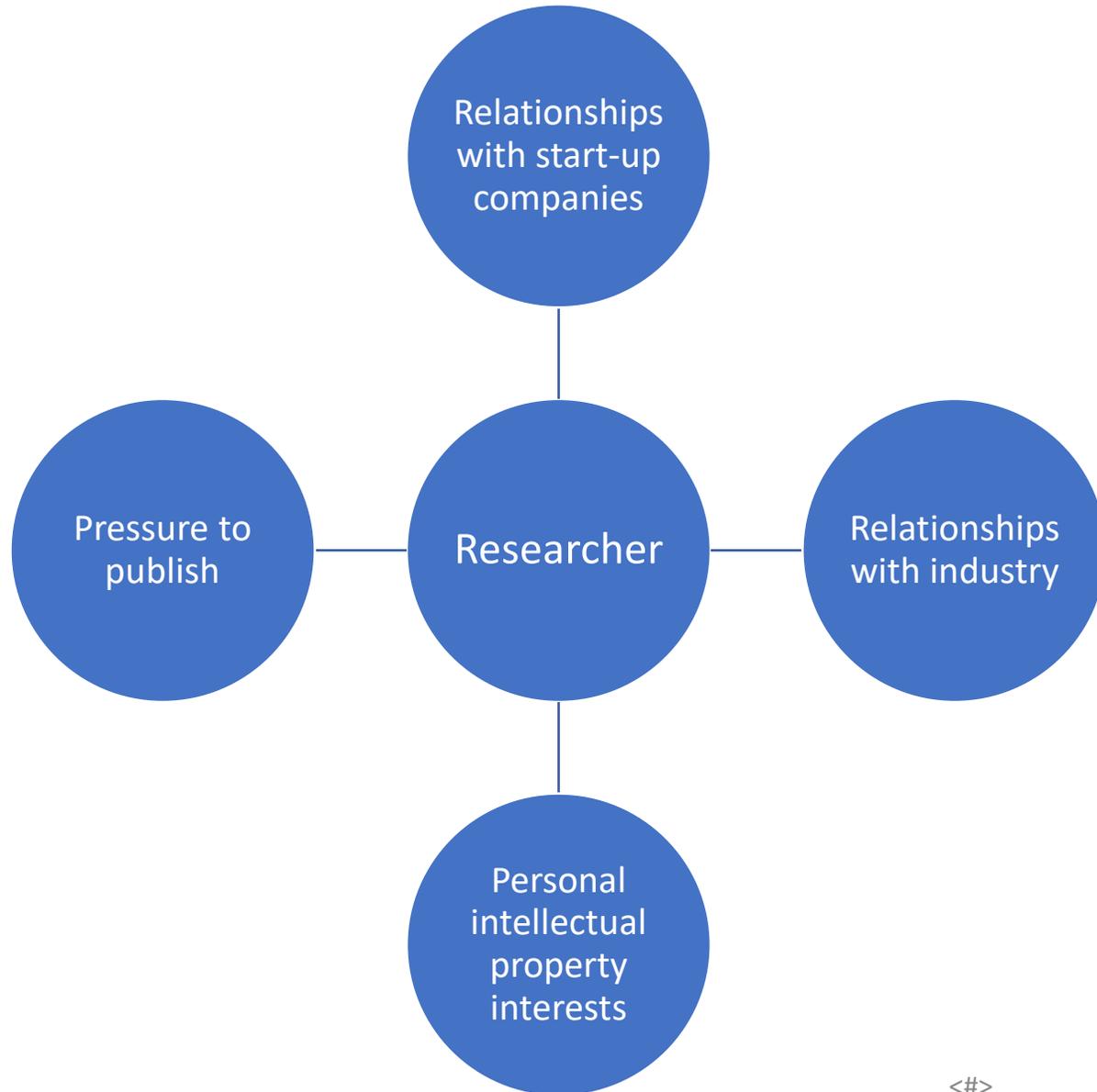
*Smith et al., Sept. 2010. *Meeting the Challenges of Identifying and managing Conflicts of Interest in Clinical Research*. ACRP The Monitor. P. 11-16

** - MSK Policy on Conflict of Interest and Commitment

Key Terms

- In clinical research, COIs become an issue when it affects the:
 - **Planning**
 - **Conduct**
 - **Reporting**
- COIs must be identified and either eliminated or managed to protect:
 - Researcher
 - Institution
 - Human subjects

Potential COIs for physician researcher



What are some scenarios that could create a potential COI?

Dr. A and Drug Company – Fun Pharma



- Dr. A is employed by a healthcare system and is an experienced site PI for FDA-regulated drug studies
- Dr. A participated in a phase III trial for drug X for Fun Pharma which was approved by the FDA last year
- Fun Pharma asked Dr. A to serve on their speaker's bureau on drug X and Dr. A agreed. She receives an \$2,000 honorarium each time she speaks.
- Recently, Fun Pharma has started a phase III trial for drug Z which includes 10,000 patients at 500 sites. Dr. A is agreed to be a site PI for this study.



Dr. A is compensated \$20,000 over a 10 month period for speaking. Does Dr. A have a conflict of interest?

Yes

No

I'm not sure.

Key Terms

- **Conflict of Commitment** exists when an individual's outside activities interfere with or detract from their job responsibilities.
 - Situations in which researcher is dedicating time to personal activities in excess of the time permitted by institutional policy.
- Examples
 - Physician researcher on speaker's bureau for drug company that takes place during a standard business day.
 - Researcher accepting an unpaid position of Scientific Advisory Board and having access to confidential information when the company is sponsoring the researcher's research.

Key Terms – What Financial Interest is

- **Financial Interest** includes the following from any single entity during a disclosure period for a researcher and their immediate family member:
 - Ownership/Equity Interests. Stock, stock options, and other ownership or equity interests in publicly and non-publicly traded entities, regardless of value.
 - Compensation. Any remuneration for services, such as consulting fees, advisory board compensation, honoraria, speaking fees, and paid authorship
 - Proprietary Interest. Property or other financial interest in the product including, but not limited to, a patent, trademark, copyright or licensing agreement. [21 CFR 54.2(c)]
 - Executive Officer Role. A role at an outside entity that carries with it a fiduciary duty to the entity and/or holds with it the responsibility to make business decisions on behalf of the entity (i.e. CEO, CSO, COO, CFO, etc.)



Key Terms – What FI is not

- Does not include:
 - Ownership or equity interests ***where the researcher does not control investment decisions*** (i.e. Personal retirement accounts, mutual funds)
 - Remuneration or travel paid by institution or federal, state or local government agency or institution of higher education

Key Terms

- **Immediate Family Member** – Spouse/partner, son, daughter, parent/legal guardian, grandparent, grandchild, sibling, cousin, niece, nephew, aunt, uncle, father-in-law, mother-in-law, sister-in-law, brother-in-law, son-in-law, daughter-in-law, step-parent, step-child, step-sibling
- **Financial Disclosure** – Mechanism to communicate specific information about Financial Interests



Federal Regulations

- Why?
 - Purpose is to promote objectivity in research
- How?
 - Standards that provide a reasonable expectation that the *design, conduct, and reporting* of research will be free from bias resulting from Investigator financial conflicts of interest

Free from:



Effect of Conflict of Interest in Clinical Research

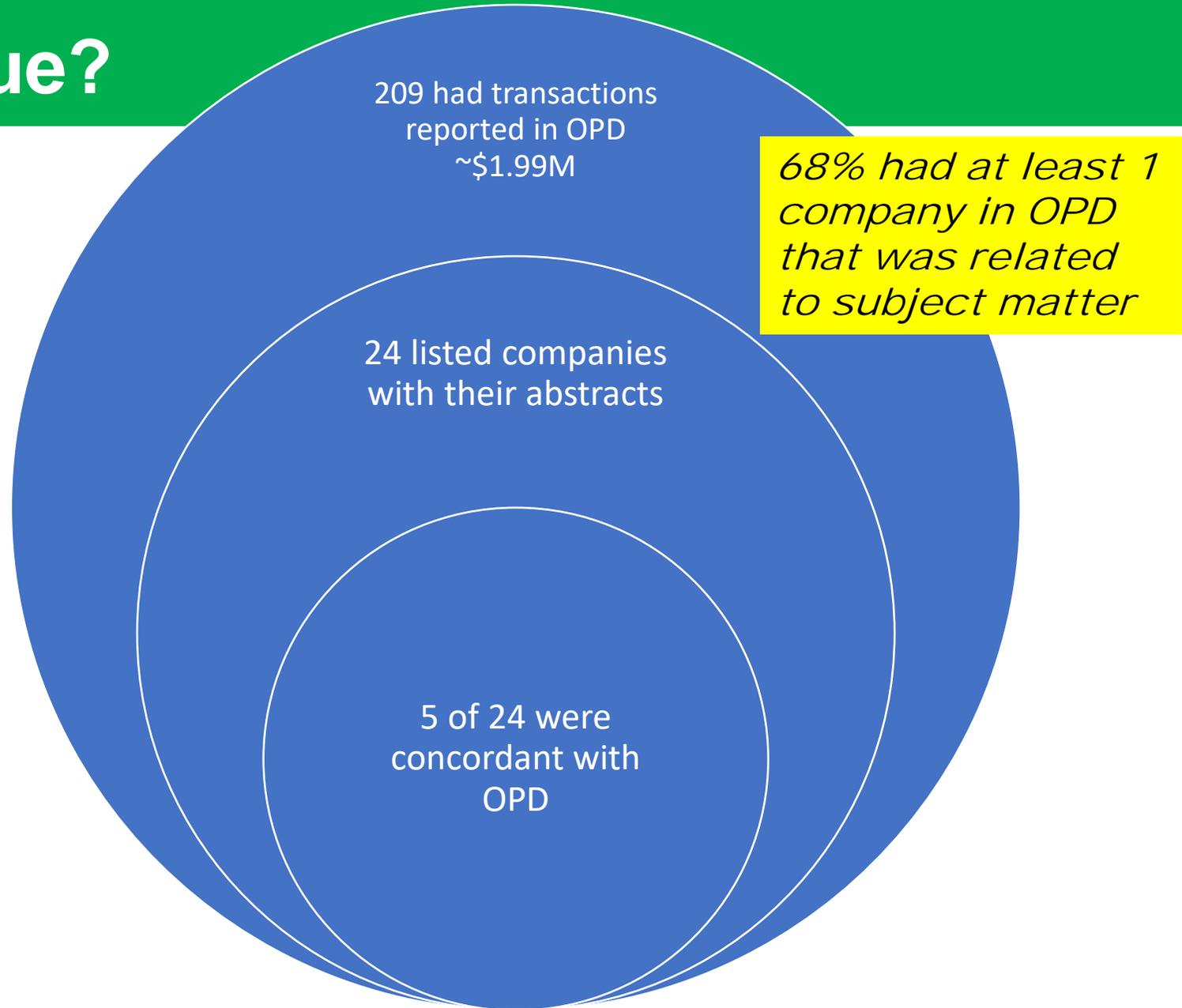
- American Journal of Psychiatry
 - 397 psychiatric clinical trials identified between 2001-2003
 - 239 (60%) reported receiving funding from a drug company
 - 187 (47%) included at least one author with a reported conflict of interest.
 - Researchers were 4.9 times more likely to report positive results¹
- Journal of General Internal Medicine - Relationship between COIs and research²
 - 38% of manuscripts about drug studies where authors had a COI
 - Strong association between COIs and positive results.

1 – Perlis RH, Perlis CS, Be M, Wu Y, Hwang C, Joseph M, Nierenberg AA. 2005. Industry sponsorship and financial conflict of interest in the reporting of clinical trials in psychiatry. *American Journal of Psychiatry* 162: 1957-60.

2 – Friedman Ls, Elihu Dr. 2004. Relationship between conflicts of interest and research. *Journal of General Internal Medicine* 19(1); 51-6.

Under-reporting issue?

- 41st Annual Scientific meeting of the Society of Gynecologic Surgeons
- *Included 335 physicians*
- Looked at concordance between physicians' financial disclosures reported to the CMMS Open Payments Database



PHS funded research such as NIH

PHS/NIH Disclosure requirements for Researchers

- **42 CFR Part 50, Subpart F** – Responsibility of Applicants for Promoting Objectivity in Research for which PHS funding is sought
- **45 CFR Part 94** – Responsible Prospective Contractors
- Who does this apply to?
 - Institutions that applies for or receives PHS/NIH grants or cooperative agreements for research
 - Any Investigator planning to participate or is participating in the research
 - Any individual applying for or receives PHS/NIH research funding
 - SBIR (Small Business Innovation Research)/ STTR (Small Business Technology Transfer) Phase II applicants/awardees

NIH Disclosure requirements for Researchers

- **Included Key Personnel** - the Project Director/PI and any other person identified as senior/key personal in the grant application or report submitted to the PHS
- **All researchers must disclose a financial conflict of interest to NIH**

Any person, regardless of title or position, who is responsible for the design, conduct, or reporting of research funded by PHS/NIH

Key Term for NIH-funded research



- **Significant Financial Interest (SFI)** include the following from any single entity during a 12-month period for a researcher and their immediate family member(s):
 - Remuneration exceeding **\$5,000** which includes: salary, any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship)
 - Ownership or equity interests in a publicly traded entity exceeding **\$5,000**
 - Any ownership or equity interests in a non-publicly traded entity, even if worth \$0 or value is unknown.
 - Intellectual property rights and interests exceeding **\$5,000**
 - Sponsored or reimbursed travel exceeding **\$5,000** (PHS-funded investigators)

Key Term – What an SFI is not

- Does not include:
 - Salary royalties, or other remuneration paid by the Institution to the Investigator if the Investigator is currently employed
 - Intellectual property rights assigned to the Institution
 - Income from investment vehicles ***where the researcher does not control investment decisions*** such as:
 - Personal retirement accounts
 - Mutual funds
 - Other diversified investment vehicle
 - Income or travel paid by institution or federal, state or local government agency or institution of higher education
 - Income from service on advisory committees or review panels for a federal, state or local government agency, or institution of higher education

PHS Disclosure requirements for Researchers

- **Financial Conflict of Interest (FCOI)**
- A significant financial interest (SFI) that could directly & significantly affect the design, conduct, or reporting of PHS-funded research
- **Includes any foreign component**



Anything > \$5,000

or any ownership interest in a non-publicly traded entity

Includes Key Personnel

Dr. A and Drug Company – Fun Pharma



- Dr. A is employed by a local hospital and is an experienced site PI for FDA-regulated drug studies
- Dr. A participated in a phase III trial for drug X for Fun Pharma which was approved by the FDA last year
- Fun Pharma asked Dr. A to serve on their speaker's bureau on drug X and Dr. A agreed. She receives an \$2,000 honorarium each time she speaks.
- Dr. A has received an NIH grant to study drug X and its' mechanism of action



Dr. A is compensated \$20,000 over a 10 month period for speaking. Is this considered a Significant Financial Interest?

Yes

No

FDA Disclosure requirement for Clinical Investigators



- **21 CFR 54 – Financial Disclosure by Clinical Investigators**
- **All Investigators must disclose using FDA Form 3455**

Key FDA terms

- **Covered Clinical Study** – Any study of a drug or device in humans submitted in a marketing application or any study in which a single investigator makes a significant contribution to the demonstration of safety. (excludes phase 1 tolerance studies, pharmacology studies, large open safety studies conducted at multiple sites, treatment protocols)
- **Financial Arrangement** – Compensation affected by the outcome of clinical studies.
 - Does investigator or key staff stand to financially gain or lose from the outcome?

FDA Level of disclosure for Investigators

Covered
Clinical
Study



- **Significantly different than PHS regulation**
- **Compensation affected by the outcome of clinical studies** – compensation could be higher for favorable outcome
 - **Ex. Equity interest to a study investigator**
- **Any financial arrangement** – where compensation to investigator could be influenced by outcome
- **Any Significant payments of other sorts** – equipment, retainer for consultation or honoraria
- **Any proprietary interest** in the product tested in the covered clinical study
- **Any significant equity interest** held by investigator in sponsor of covered study

FDA Disclosure requirement for Clinical Investigators

- **Significant payments of other sorts –**
 - **payments > \$25,000**
- **Proprietary Interest in tested product** – Property or other financial interest in the product including, but not limited to, a patent, trademark, copyright or licensing agreement
- **Significant equity interest in the study sponsor –**
 - **Any ownership interest > \$50,000**
 - Stock options, or other financial interest whose value cannot be readily determined or any equity interest in a publicly traded corporation during study execution and 1 year after study completion

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Form Approved: OMB No. 0910-0398
Expiration Date: April 30, 2022

DISCLOSURE: FINANCIAL INTERESTS AND ARRANGEMENTS OF CLINICAL INVESTIGATORS

TO BE COMPLETED BY APPLICANT

The following information concerning , who participated
Name of clinical investigator
as a clinical investigator in the submitted study
Name of

is submitted in accordance with 21 CFR part 54. The
clinical study
named individual has participated in financial arrangements or holds financial interests that are
required to be disclosed as follows:

Please mark the applicable check boxes.

- any financial arrangement entered into between the sponsor of the covered study and the clinical investigator involved in the conduct of the covered study, whereby the value of the compensation to the clinical investigator for conducting the study could be influenced by the outcome of the study;
- any significant payments of other sorts made on or after February 2, 1999, from the sponsor of the covered study, such as a grant to fund ongoing research, compensation in the form of equipment, retainer for ongoing consultation, or honoraria;
- any proprietary interest in the product tested in the covered study held by the clinical investigator;
- any significant equity interest, as defined in 21 CFR 54.2(b), held by the clinical investigator in the sponsor of the covered study.

Details of the individual's disclosable financial arrangements and interests are attached, along with a description of steps taken to minimize the potential bias of clinical study results by any of the disclosed arrangements or interests.

Details of disclosable
financial arrangement,
along with steps taken to
minimize the potential
bias of clinical study
results

FDA Disclosure requirement for Clinical Investigators

- **Examples to minimize potential bias or management plan**
 - Limit # of patients investigator can enroll
 - Have other staff responsible for data collection and/or analysis

Dr. A and Drug Company – Fun Pharma



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- Fun Pharma asked Dr. A to serve on their speaker's bureau on drug X and Dr. A agreed. She receives an \$2,000 honorarium each time she speaks.
- Recently, Fun Pharma has started a phase III trial for drug Z which includes 10,000 patients at 500 sites. Dr. A is agreed to be a site PI for this study.



Dr. A is compensated \$20,000 over a 10 month period for speaking. Must Dr. A disclose this as per FDA regulations?

Yes **A**

No because she has not received significant payments of other sorts (>\$25,000) **B**

Dr. A and Drug Company – Fun Pharma



- Dr. A is employed by a local hospital and is an experienced site PI for FDA-regulated drug studies
- Dr. A participated in a phase III trial for drug X for Fun Pharma which was approved by the FDA last year
- Dr. A purchases stock in Fun Pharma currently valued at \$60,000.
- Recently, Fun Pharma has started a phase III trial for drug Z which includes 10,000 patients at 500 sites. Dr. A is agreed to be a site PI for this study.



Dr. A has stock from Fun Pharma valued at \$60,000. Is this considered a financial conflict of interest per FDA regulations?

Yes

No

Not sure, more information is needed.

Potential Management Strategies

- Require that the researcher disclose:
 - His/her conflicting financial interests to all collaborators
 - His/her financial interest to subjects in the informed consent
 - Financial interests in any public release of study results (commonly required by journals)
- Require that the researcher revise aspects of project to mitigate any real or potential conflicts
- Prohibit researcher from participating in certain research activities such as data analysis
- Require that the researcher reduce or divest the significant financial interest

Dr. A and Drug Company – Fun Pharma



- Dr. A is employed by a local hospital and is an experienced site PI for FDA-regulated drug studies
- Dr. A participated in a phase III trial for drug X for Fun Pharma which was approved by the FDA last year
- Dr. A purchases stock in Fun Pharma currently valued at \$60,000.
- Recently, Fun Pharma has started a phase III trial for drug Z which includes 10,000 patients at 500 sites. Dr. A is agreed to be a site PI for this study.
- **Identified Financial COI –**
 - **Management plan – Fun Pharma limits # of patients site can enroll**

Financial Interest Case

A PI has equity interests in and received income from Company A, which is sponsoring her research trial involving their drug.

Safeguards to address potential risks of a COI:

- PI establishes an SOP that blinds the study, which includes:
 - Non-conflicted Researcher B codes the different compounds to be used in the study

Conflict of Interest:

Case Examples

Top Sloan Kettering Cancer Doctor Resigns After Failing to Disclose Industry Ties



Dr. José Baselga stepped down as the chief medical officer of Memorial Sloan Kettering Cancer Center. Thos Robinson/Pershing Square Sohn Cancer Research Alliance, via Getty Images

- Failed to disclose millions of dollars from companies in research articles to top medical journals
- 60% of the 180 papers published since 2013
- Served on several boards of drug companies
- MSK stated they had robust programs to manage relationships

- Investigation revealed repeated violations
 - Baselga received almost \$3.5 million in payments (listed in Open Payments), largest was \$3 million from ownership interest in Seragon Pharmaceuticals.
 - Not listed in Open Payments, \$250,000 in cash and stock options for serving on board of Infinity Pharmaceuticals
 - Officials frequently violated own policies
 - Hospital VP received \$1.4 million stake in newly public company
 - Hospital leaders' ties to companies dealt with on ad-hoc basis rather than vigorous vetting
 - Researchers unaware of senior executive's financial interest in the outcome of their studies

- Financial Interests
 - Not disclosed to journals
 - Not disclosed to MSK
- Core issue of self-disclosure



- MSK revamped program
 - Bars top leadership from serving on corporate boards of drug and healthcare companies.
 - CEO resigned from board of Merck & CRO
 - Revised Policies – Conflict of Interest and Commitment, Institutional Conflict of Interest, and Board of Managers Conflict of Interest
 - MSK staff prohibited from external activities:
 - Participation in speakers' bureaus sponsored by industry
 - Participation in activities where content is controlled by industry
 - Endorsement of products or commercial ventures
 - Interactions with industry



What is the FDA requirement for disclosure of significant payments of other sorts?

Payments more than \$5,000

Payments more than \$10,000

Payments more than \$25,000

Payments more than \$50,000

Conflict of Interest Example

- A researcher is doing NIH-funded research on a drug developed by Thrifty pharma, a non-publicly traded company. Which of the scenarios below meets the definition of a significant financial interest?
 - A. Thrifty pharma has paid researcher \$1,000/month for last 12 months
 - B. Researcher has received stock options from Thrifty pharma, value is unknown
 - C. Researcher has Intellectual Property rights from research of Thrifty pharma drug and is valued at \$10,000
 - D. All of the above scenarios are considered a significant financial interest.



Which of the scenarios below meets the definition of a significant financial interest?

Thrifty pharma is paying researcher \$1,000 a month over last 12 months.

Researcher has received stock options from Thrifty pharma, value is unknown.

Researcher has intellectual property rights from research on Thrifty pharma drug and is valued at \$10,000.

All of the above are considered a significant financial interest.

Conflict of Interest:

Avera's Requirements

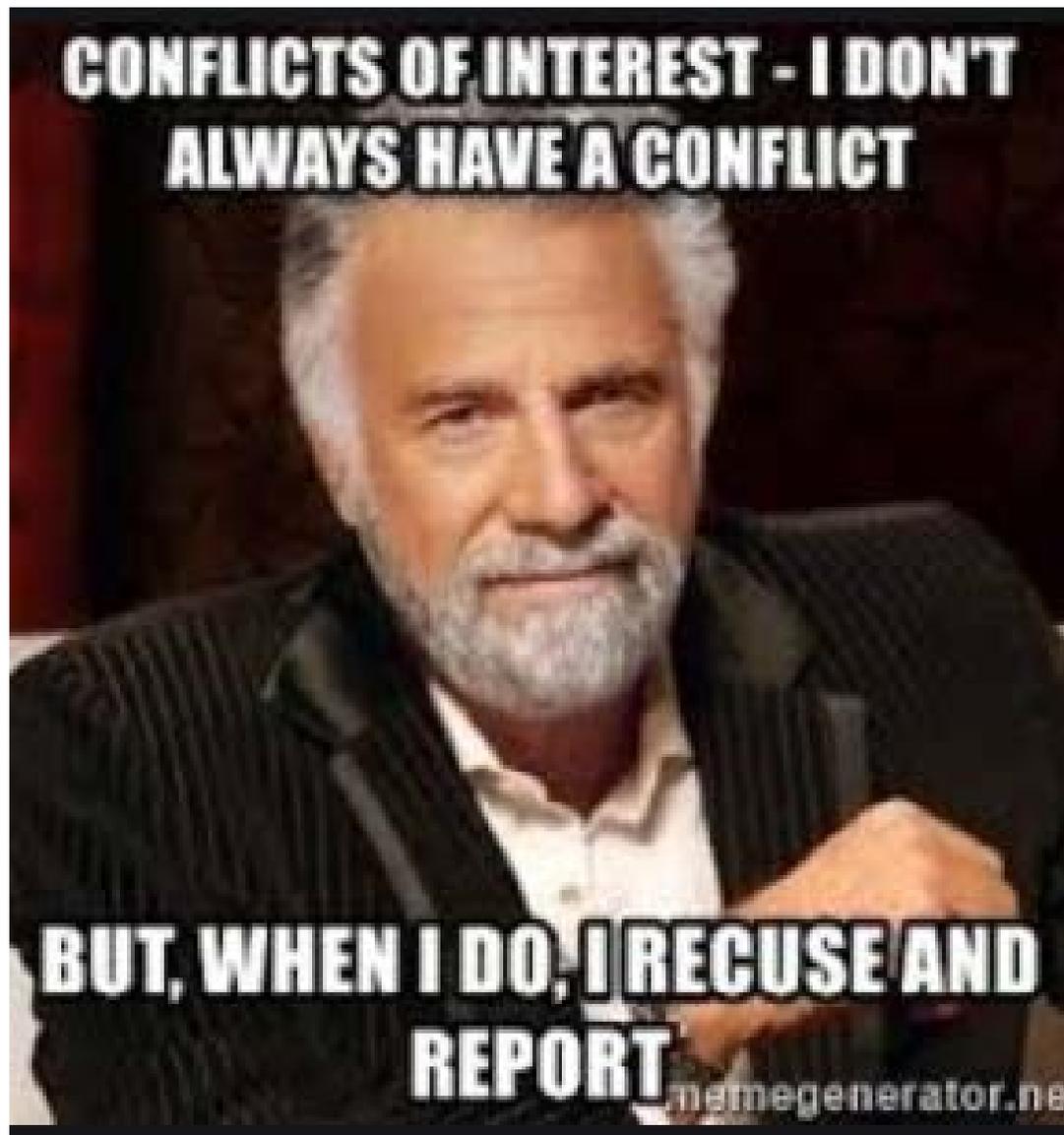
NIH requirements for Institutions

- Establish standards that provide a reasonable expectation that the design, conduct, and reporting of NIH-funded research will be free from bias resulting from Investigator financial conflicts of interest.
- Maintain policies that complies with regulations
- Maintain records of all disclosures of financial interests and the institution's review of, and response to, such disclosures
- Designate an Institutional Official to solicit & review disclosure statements from each investigator
- Develop management plans for any FCOI
- Inform Investigators of the regulation, institution's policy and investigator's responsibilities regarding disclosure

NIH requirements for Institutions

- Institutions must require Investigators complete FCOI training:
 - Prior to engaging in research related to any NIH-funded project
 - At least every four years
 - Immediately when any of the following circumstances apply:
 - Institution revises its policy that affect investigator
 - When an investigator is new to the institution
 - When institution finds an investigator is not in compliance with Institution's policy or management plan

Disclosure of Conflicts of Interest



- Could affect reputation and damage trust

Financial Disclosure and Management of Financial COI



- Required to complete annually and new form within 30 days of new financial arrangement.



Anything > \$5,000

or any ownership interest in a non-publicly traded entity including foreign

Includes Key Personnel

Annual COI Questions

12. Acknowledgement of Avera IRB Conflict of Interest Policy

I acknowledge and agree to abide by the [Avera IRB Conflict of Interest Policy](#) which required me to:

- Disclose any financial interest that the informed general public may reasonably perceive to bias the design, conduct, or reporting of research or other externally sponsored projects.
- Disclose any change in financial status as to create a new or potential conflict of interest.
- Promptly revise this disclosure within 30 days of the acquisition or the discovery that has the potential to create a conflict of interest.

13. Acknowledgement of Disclosing Protected Health Information (PHI) for Research and Limited Data Set

I acknowledge and agree to abide by Avera's Disclosing Protected Health Information for Research Policy ([#308](#)) which permits covered entities to use or disclose PHI for research provided this disclosure has been approved by an institutional review board (IRB). I also acknowledge and agree to abide by Avera's Limited Data Set Policy ([#312](#)) which permits covered entities of Avera to use or disclose a limited data set that meets certain specifications under the Privacy Rules.

Annual COI Questions

14. Research Payments

(There may be multiple disclosures for this question)

Do you, or an immediate family member, have a financial arrangement with any sponsor or vendor with whom you are currently doing research with, whereby compensation could be affected by the outcome of the Covered Clinical Study?

Please see the [Avera Institutional Review Board Conflict of Interest Policy](#).

FOR PHYSICIANS ONLY: Please remember to disclose sources of payments that are applicable and found on the Open Payments Database (OPD) maintained by the Centers for Medicare and Medicaid Services. As of the most recent data available, your OPD total amount is: [%USER_SSN%]. If there is no amount, this means your payments, if any, totaled less than \$5,000.

To access the OPD, please click here and search using your name: <https://openpaymentsdata.cms.gov/search/physicians/by-name-and-location>.

15. Research Payments

Have you, or an immediate family member, or any of you combined, received Remuneration from any entity (publicly or non-publicly traded) in the twelve months preceding this disclosure or an Equity Interest in the entity exceeding \$5,000?

Equity Interest:

Equity interest includes any stock, stock option, or otherwise ownership interest, as determined through reference to public prices or other reasonable measures of fair market value.

Remuneration:

Remuneration includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship)

Annual COI Questions

16. Research Payments

Do you, or an immediate family member, have a proprietary interest in any tested product which is the subject of any covered clinical study you are involved in?

proprietary interest:

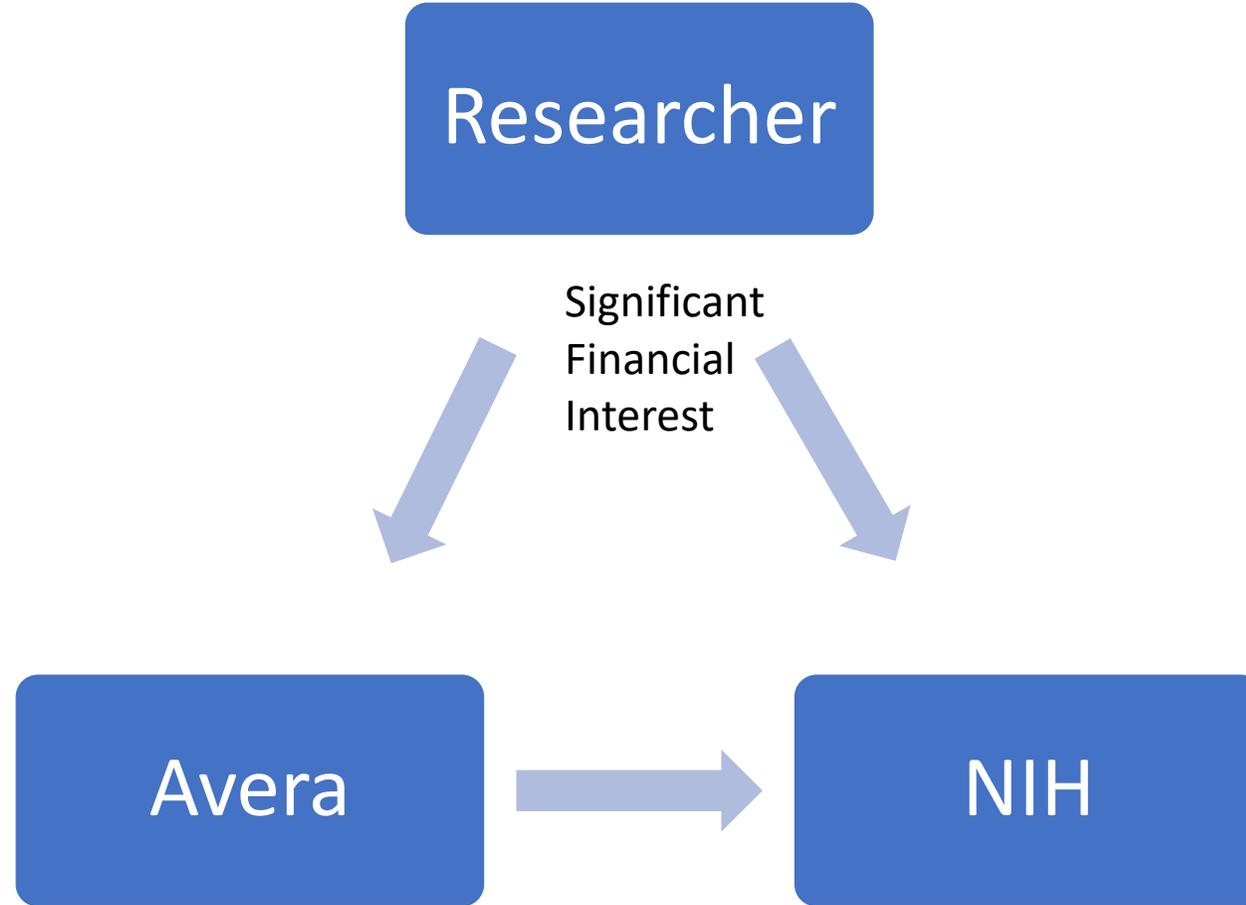
21 CFR 54.2 (c) defines this as: property or other financial interest in the product including, but not limited to, a patent, trademark, copyright or licensing agreement.

17. Research Payments

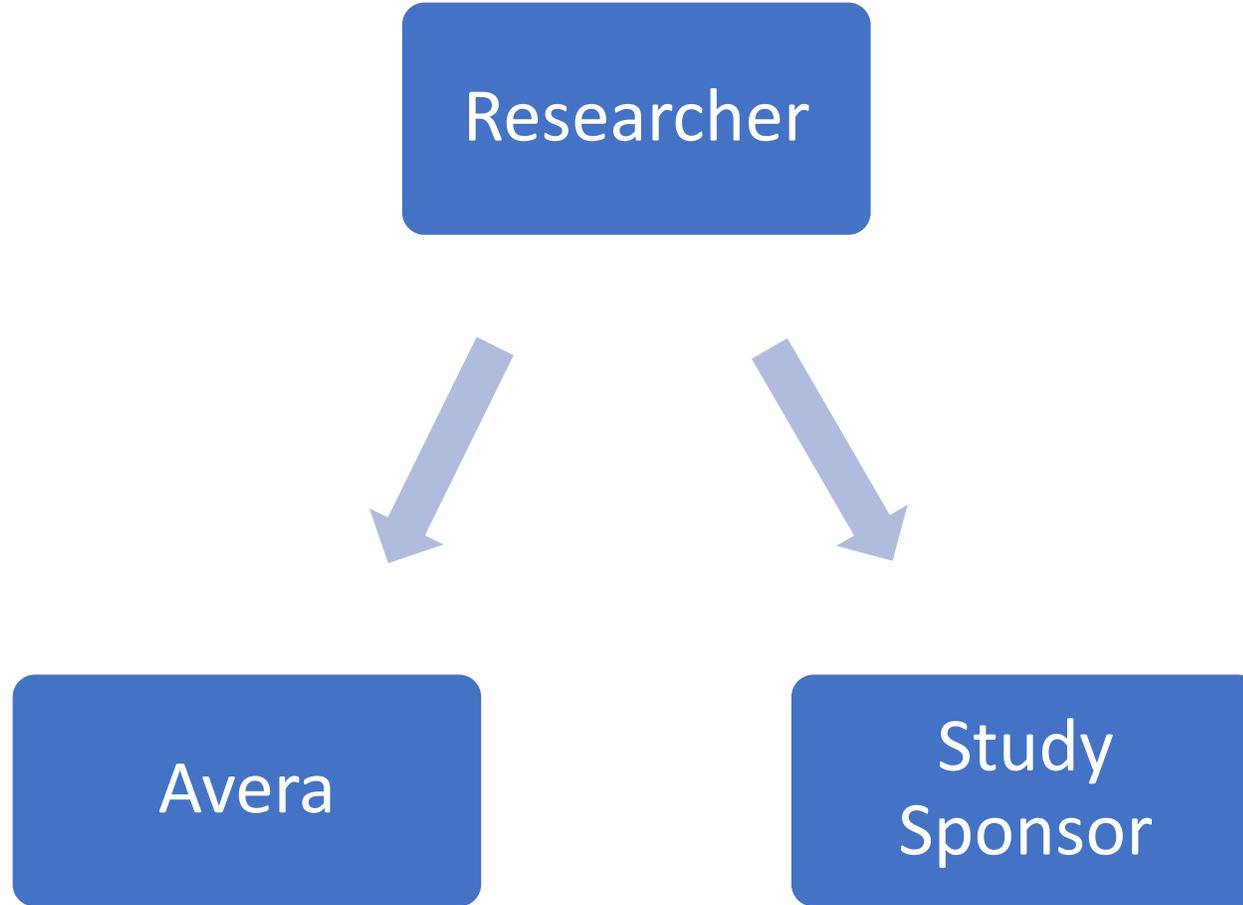
(There may be multiple disclosures for this question)

Have you, or an immediate family member, or any of you combined received payments by the sponsor of a covered study that has a monetary value of more than \$5,000, exclusive of the costs of conducting the covered clinical study? This includes the time you were carrying out the study and for 1 year following completion of the study.

Avera Researcher Disclosure Requirements -NIH funded



Avera Researcher Disclosure Requirements - FDA



In Summary

NIH and Avera

- Includes key personnel & foreign component
- FCOI (aka SFI) = Anything > \$5,000
- Ownership interest in a non-publicly traded entity



FDA

- Includes only covered clinical studies
- Significant payments of other sorts > \$25,000
- Significant equity interest > \$50,000
- Proprietary interest in tested product



What do you do if you become aware of a COI?

****Must be reported****

*If after this presentation, you need to disclose anything...
Research Compliance – 322-7836*

Compliance Hotline
1-888-881-8395

Investigator Disclosure

An Investigator received \$3,000 over the previous 12 months from ABC company for consulting services and, therefore, did not disclose this financial interest to the Institution at the time of annual disclosure.

Two months after the annual disclosure she receives another \$3,000 payment from same source.

Is the Investigator required to disclose the SFI to the institution that was acquired 2 months after the time of annual disclosure?



Is the Investigator required to disclose the SFI after the time of annual disclosure?

Yes

No



When should the SFI be disclosed to the Institution

Within 30 days of the payment

On annual disclosure form the following year

Any Questions?