National Institutes of Health
NIH Ethics Program

ETHICS MATTERS WHAT, WHEN, & WHY

January 19, 2023

Tonia Awoniyi
Director, NIH Ethics Office

Deputy Ethics Counselor (DEC) responsibility is to ensure no conflicts for NIH Federal employees serving on protocols.

Ethics review is required for covered protocols.

Conflicts of Interest

18 USC § 208 – Conflict of Interest:

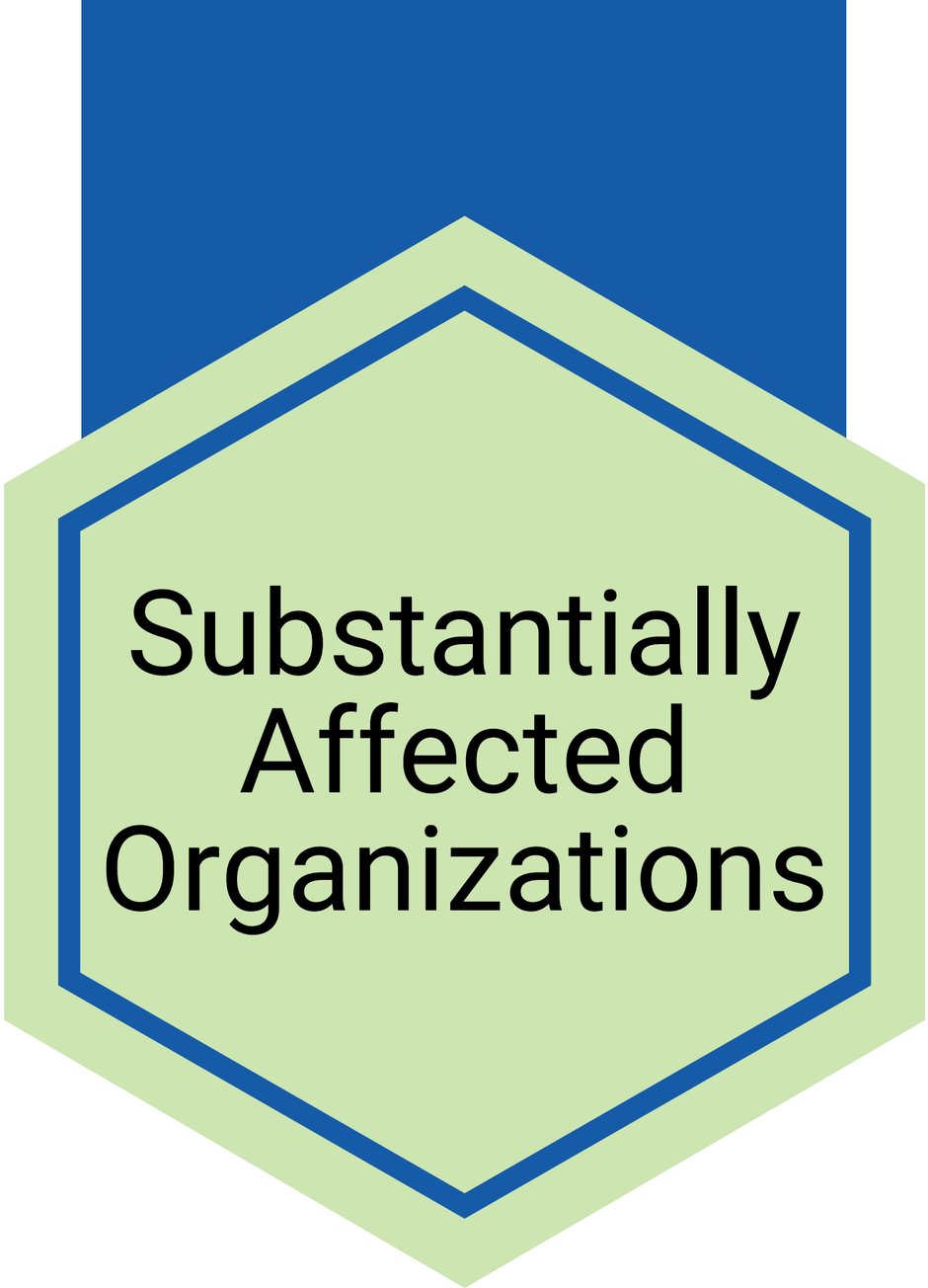
Prohibits a Federal employee from participating personally and substantially in an official capacity in any particular matter if that matter will affect the employee's personal or imputed financial interests.

Imputed Financial Interests:

- Spouse
- Minor children
- Employee's general partner
- Organization or entity which the employee serves as officer, director, trustee, general partner, or employee
- Person with whom the employee is negotiating for, or has an arrangement concerning, prospective employment

HHS Regulations

- Prohibit or limit ownership and other financial interests in Substantially Affected Organizations (SAOs)
- Require certain categories of employees to report their holdings in SAOs



Financial Disclosure Reports

NIH Federal staff serving as covered individuals must:

- Report SAO holdings on *Confidential Report of Financial Interests in SAOs for Employees of the NIH* (HHS-717-1)
- Provide an update that is within six months of the ethics clearance date of a protocol

Other Examples of Real or Apparent Conflicts:

- Royalty sharing agreements for patented technology
- Employee’s spouse, parent, or dependent child serves as officer, director, trustee, general partner, agent, attorney, consultant, contractor, or employee
- Organization in which the employee has an outside activity

PI Responsibility

- PI reviews list of SAOs from Ethics Office (no owner or values listed)
- PI determines whether the SAOs are **directly affected**, **indirectly affected**, or **not related** to the protocol
- If PI identifies any affected organizations (directly or indirectly), Ethics Office must resolve the conflict(s) before protocol may be cleared by the DEC

Thank You

For questions or assistance, contact your ICO Ethics Office:

https://ethics.od.nih.gov/contacts

CONFLICT OF INTEREST TOOLS FOR STUDY TEAMS

Heather Bridge

Office of Human Subjects Research Protections (OHSRP)

AGENDA

- Single COI Certification
- Manual Chapter 3014-102 updates
- OHSRP DEC Ancillary Review webpage
- Who to contact for what

SINGLE COI CERTIFICATION

- There is now only one Conflict of Interest (COI) Certification to be signed by any NIH investigator or statistician working on a Covered Research Protocol (CRP) who is not an NIH ethics filer
- In August 2022, the single COI Certification came into effect
- The single COI Certification is located on the DEC ancillary review page

POLICY 3014-102 INVESTIGATOR COI AND GOVERNMENT ROYALTIES UPDATE

Policy revised to address

- Single COI Cert
- Implementation of Huron PROTECT system
- Published 1/11/2023

DEC ANCILLARY REVIEW WEBPAGE

https://irbo.nih.gov/confluence/pages/viewpage.action?pageId=74613147

INFORMATION FOR STUDY TEAMS

- Definitions
- IC DEC Submission Checklist
- Frequently Asked Questions (FAQs)

IMPORTANT COI DOCUMENTS

- COI Guide
- COI Certification

LINKS

- Link to Policy 3014-102

WHO TO CONTACT FOR WHAT:

Contact your Institute/Center (IC) **Ethics Office** for questions about:

- Conflicts of interest (COI)
- Personal or imputed interests
- Financial interests in Substantially Affected Organizations (SAOs)
- Financial Disclosure Reports
- Protocol Ethics Clearances

Contact your IC **Technology Transfer Office** for questions about:

- Inventions and Royalties
- Agreements

Contact **IRBO/OHSRP** for questions about:

- The definition of a Covered Research Protocol
- Manual Chapter 3014-102 Investigator COI and Government Royalties
- COI FAQs
- COI Guide or COI Certification
- Conflict of Interest Committee (COIC)
- Huron PROTECT Trainers or PROTECT technical assistance

THANK YOU

Points of Contact for Questions or assistance:

IRBO: IRB@od.nih.gov

OHSRP: Heather Bridge – bridgeh@od.nih.gov

COIC Committee:

- Chris Witwer – chris.witwer@nih.gov
- Jonathan Green – Jonathan.green3@nih.gov

Government Royalty Payments to NIH Investigators and COI Review

JONATHAN M GREEN, MD MBA

DIRECTOR, OHSRP

Definitions and a distinction

NIH policy definition of a COI

- When a government matter, including clinical research, will have a direct and predictable effect on the financial interests of an individual or the individual's spouse, minor children, general partner(s), or certain other organizations in which the individual serves as an officer, director, trustee, general partner or employee, and any entities with which the individual is negotiating for, or has an agreement regarding, prospective employment. (18 U.S.C. § 208)

Some other definitions

- Conflicts of interest are "situations in which financial or other personal considerations may compromise, or have the appearance of compromising, an investigator's judgement in conducting or reporting research." AAMC, 1990

  "A conflict of interest in research exists when the individual has interests in the outcome of the research that may lead to a personal advantage and that might therefore, in actuality or appearance compromise the integrity of the research." NAS, Integrity in Scientific Research

Different than a "Disqualifying Financial Interest (DFI)".

- A type of COI that NIH prohibits investigators from having (w/o a waiver).

Government Royalties

NIH investigator invents something

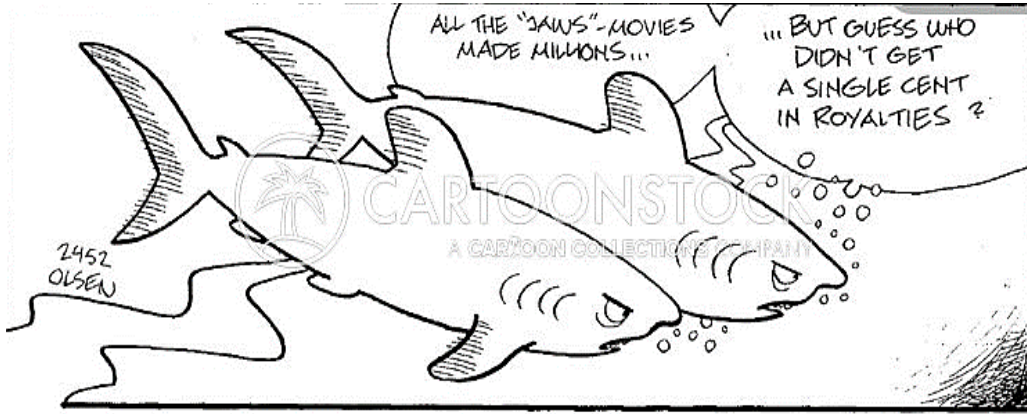
Invention statement filed with Tech Transfer Office (TTO)

TTO files patent application/pursues license agreements

Licensee pays money to NIH

NIH shares some of that money with inventors

- Important: NIH inventor is required to accept the payment



Royalties as an apparent COI

Royalty payments to NIH investigators can present an “apparent” COI, even if not a DFI if:

- Investigator is an inventor of IP
- The IP is the object of the investigation
- The IP is licensed
- Value of royalty payments can be influenced by outcome of the research

Why is the IRB involved?

Potential to introduce bias that impacts:

- Scientific Integrity
  - The collection, analysis and reporting of data.
- Human Subjects Protections.
  - During the process of obtaining informed consent
  - Adjudication and attribution of adverse events

IRB Criteria for Approval of Research (45 CFR 46.111)

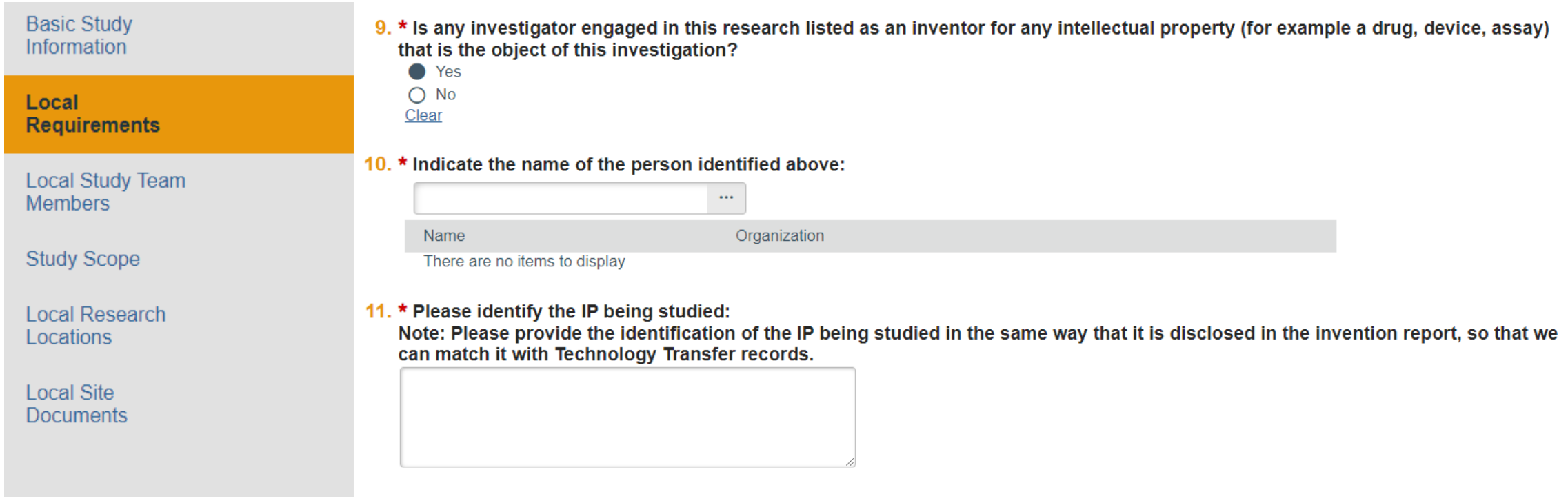
- Minimization of risks
- Informed consent
- Adequate data and safety monitoring

Expectations of HHS Office of Human Research Protections

Expectations of Association for the Accreditation of Human Research Protection Programs (AAHRPP)

Review Process

Inventor/investigator must notify the IRB that they are identified as an inventor of IP that is being studied in a clinical protocol.



Review Process (step 2)

Is the IP licensed?

- Discussion with relevant IC Tech Transfer Office

Does the outcome of the research have the potential to impact the value of the royalty payments?

- Discussion with TTO and PI/inventor if necessary

If above are yes, then meet with PI/inventor

- Discuss study design and risks
- Role of conflicted investigator in study
  - Consent
  - AEs
  - Data/safety monitoring

Administrative review or Committee review

Outcome

Unlicensed invention

- No conflict. No management (admin review)

Licensed invention

- Not the object of the investigation – no conflict. Standard disclosure language in consent. (admin review)
- Object of the investigation, but outcome of research has no influence on value of royalty payments to investigator – standard disclosure language in the consent (admin review)
- Object of the investigation and outcome of research has the potential to influence the value of royalty payments – standard disclosure language in the consent and management. (admin or committee review)

Review

Admin review: Myself and staff (Chris Witwer)

COIC review

- High risk research
- Above financial threshold of $5000 in prior 12 months (based on extramural thresholds)

COIC composition

- OHSRP Director
- OHSRP Assoc Director
- IRBO Director
- DDIR representative
- Tech Transfer representative
- NIH Ethics Office representative
- NIH Ethics Advisory Committee representative
- Clinical Directors (2)

Management plans for human subjects protections

Conflicted investigator should not get informed consent

Process for Adjudication/attribution of AEs to include non-conflicted investigators

Data and safety monitoring plan independent of conflicted investigator, when appropriate based on risk level of study

"What conflict of interest?!
I work here in my spare time."


Questions
?
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Answers
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