

# Office of the Vice Provost for Research

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## Procedures for Identifying, Reviewing and Managing Institutional Financial Conflict of Interest Related to Human Subjects Research<sup>1</sup>

### Potential Sources of Institutional Conflict of Interest (ICOI) Resulting from Financial Payments or Other Considerations

Gifts or other significant funds not directed to fund identified research. An ICOI may arise when the University has received a gift of any value (including monetary gifts, gifts of equity in a private company, or gifts in kind) from a potential commercial sponsor of research, from a company that owns or controls products being studied or tested, or from any individual (including a potential research subject), and the funds are intended to directly support the conduct of human subject research.

Payments related to Licensing, Technology Transfer, and Patents. An ICOI may arise when the University owns and/or has licensed or optioned intellectual property<sup>2</sup> that is being tested, evaluated, or developed through research involving human subjects, inclusive of clinical trials,<sup>3</sup> and one or more Penn Investigators are participating in that research.<sup>4</sup>

Financial Interests of Institutional Leaders. An ICOI may arise when the financial interests of an institutional official who has authority to act on behalf of the University, might affect—or reasonably appear to affect—institutional processes for the design, conduct, reporting, review, or oversight of human subjects research. Institutional leaders include the Board of Trustees, the President and other senior officers, the Provost and the Vice Provost for Research (VPR), Deans of Schools, the CEO of the Health System, as well as all other individuals with authority to approve and oversee the approval or conduct of human subject research, such as submission of protocols to the IRB or review of the conduct of such research.

The following financial interests do not give rise to an ICOI:

- University equity positions (e.g., endowments, retirement funds) in publicly held companies do not give rise to an ICOI because the University Investment Board's decision-making related to Penn's assets is independent of that related to the conduct and oversight of research.
- The Investment Board is not permitted to communicate with institutional leaders and

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<sup>1</sup>For purposes of these Procedures, human subjects research is defined as any research that requires review and approval by Penn's IRBs, whether full or expedited.

<sup>2</sup>It is understood that the license may entitle Penn to various forms of financial consideration, including but not limited to milestone payments, royalties or commercial collaboration support.

<sup>3</sup>For purposes of these Procedures, a clinical trial is defined in accordance with *University of Pennsylvania Policy on Conflicts of Interest Related to Research*, effective August 24, 2012.

<sup>4</sup>Participation in a trial includes, but is not limited to, serving as a Principal Investigator, Co-Investigator, regulatory sponsor/IND holder or in any other role responsible for the design, conduct, or reporting of the trial (including reporting results to the FDA), performing any other subject-related activity specific to the trial, such as the recruitment, selection, or enrollment of subjects, obtaining informed consent, providing subject treatment and care specific to the trial, or performing study procedures, or collecting, analyzing, or interpreting data.

investigators concerning the conduct of research performed at the University. This firewall is an important separation between the academic functions and the investment functions of the University.

- Any equity<sup>5</sup> received by the University under a license agreement with any company, whether publicly or privately held, will be held by the Office of the Treasurer until such time that the University Investment Board decides to liquidate such equity.
- As the same internal controls described above apply to equity received pursuant to a license, private equity will generally not be considered as giving rise to an ICOI.

### **Process by which Potential ICOIs Related to Human Subjects Research are Identified**

Gifts. The Principal Investigator is responsible for identifying any known gifts that will be used to support the research in the initial IRB application, or upon receipt of a gift, for each research protocol or request for approval of an investigational treatment opportunity. The Principal Investigator must also specify whether those gifts are known to be from a potential participant in the research or another family member. In the instance of a gift provided to support human subject research, University Policy requires that each gift agreement signed by a donor includes a certification that an individual gift may not be conditioned upon the donor or donor's family member being given access to a specific research protocol or investigational treatment opportunity.

For single patient treatment use protocols, the Principal Investigator must confirm with the Office of Planned Giving that the patient and/or patient's family member has not given a gift to fund a specific protocol for which the individual or individual's family member is being considered for treatment.

In the event that any gifts are identified that may constitute an ICOI, the matter will be evaluated by the IRB in considering the project approval, with input from other offices as appropriate, including the HRAC and the Conflict of Interest Standing Committee.

Payments Related to Licensing, Technology Transfer, and Patents. In connection with the submission of a protocol to the IRB, Investigators are required to disclose in parallel to the Research Integrity Office (RIO) any interest in intellectual property that is the subject of a copyright, issued patent, or a patent application (regardless of whether the intellectual property has been patented, licensed, or assigned to the University) if such intellectual property is being tested, evaluated, or developed in, or if its commercial value could be affected by, the human subjects research. In the event that licensed or optioned intellectual property is identified, the matter will be evaluated by the IRB with input from other offices when appropriate, including the Penn Center for Innovation.

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<sup>5</sup>Such equity might include warrants and options.

The application to the IRB requires a certification by the Principal Investigator as to the accuracy of all information contained in the application, and imposes on the Principal Investigator a continuing obligation to report, to the extent known, any modifications to the content of the application.

### **Financial Interests of Institutional Leaders.**

Senior Leadership. Annual financial disclosures submitted by the Board of Trustees, the President and other senior officers, the Provost, the VPR, and the Deans will be reviewed by the Office of General Counsel. If it is determined that any disclosed interests could reasonably give rise to a potential ICOI related to human subjects research, the matter will be referred to the RIO for initial consideration and possible referral to the VPR, or other appropriate institutional official.

Department Approvers of Submissions to the IRB. The department chair or his/her designee (Department or Division Approver) must affirm in the application's departmental certification page that s/he has no Significant Financial Interests (SFIs)<sup>6</sup> related to the protocol. In those circumstances where such an SFI may exist, the IRB will be notified for rerouting of the application to a different Department or Division Approver.

Other Individuals who have Responsibility for Review and Approval of Human Subjects Research. Financial disclosures submitted by the IRB Chairs and IRB senior leadership, and other school-based personnel with responsibility for the oversight of human subjects research will be reviewed by the VPR. In the event that any such individual is determined to have a potential or actual financial conflict of interest (FCOI) related to a protocol, said individual will not be permitted to participate in the review and approval of that protocol.

### **Process by which Potential ICOIs Related to Human Subjects Research are Reviewed and Managed**

Potential ICOI matters will be referred to the VPR by any individual or office. The VPR will determine whether the matter may be handled administratively or if it warrants review by the HRAC.

Administrative Review. Examples of circumstances that may warrant administrative review include: situations where there is a low risk that objectivity in the approval, conduct, evaluation or reporting of research will be impaired by the potential ICOI; where there is established precedent based on prior review of an analogous ICOI; or where the matter has been previously reviewed by an advisory committee.

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<sup>6</sup>SFIs are defined in accordance with the *University of Pennsylvania Policy on Conflicts of Interest Related to Research*, effective August 24, 2012.

The Research Integrity Office will be responsible for initiating the administrative review. The RIO will obtain relevant factual information, including the protocol and where applicable, informed consent, the source and value of the ICOI, and any individual FCOI. The RIO will consult as needed with the IRB, Office of Research Services, Penn Center for Innovation, PSOM's Office of Clinical Research and other University and School-based offices to obtain this information. The RIO will provide a summary of this information to the VPR. The VPR will be responsible for determining whether an ICOI exists, whether it is manageable, and if so, any required ICOI management plan. In cases where individual Investigators have an FCOI under management related to the same research, the VPR will determine whether the ICOI is sufficiently managed by the Investigators' management plan or whether additional ICOI management is indicated.

ICOI management plans (if applicable) will be provided to the responsible parties for implementation. Documentation of the VPR's final ICOI determination will be provided to the IRB and other responsible parties, as applicable.

Human Research Advisory Committee (HRAC) Review. The VPR may refer matters to the HRAC that are determined not to qualify for administrative review. The HRAC will serve in an advisory capacity to the VPR and will make recommendations as to whether an ICOI exists, whether it is manageable, and if so, the components of the ICOI management plan. If it is determined that the ICOI is not manageable, the research will not be conducted at Penn.

External Advisory Board (EAB). An External Advisory Board (EAB) will be constituted by the VPR composed of no less than three knowledgeable experts who do not hold appointments in any form, past or present, at the University of Pennsylvania and are not themselves conflicted with regard to the conduct of the research or participating entities. In addition to providing advice to the VPR upon request, the EAB will be responsible for the periodic review of the principles reflected in this guidance, including making recommendations for modification as it deems appropriate.

## **Management Principles**

The management of ICOI will adhere to the following General Principles. These Principles will be periodically reviewed and, as necessary, modified in concert with the recommendations of the EAB.

- 1) Investigators with an FCOI will have a management plan in place, according to policy.
- 2) The IRB assesses disclosures to human subjects in the Informed Consent document related to an ICOI.
- 3) The management of an ICOI involving human subjects research should take into account relevant factors such as:
  - the magnitude and nature of the institution's financial interest;

- the extent to which the institutional financial interest could be influenced by the research and vice versa;
- the nature and design of the research, including whether the research involves a unique patient population or an institutional facility or other resource that would be difficult to duplicate, or a particular technical or professional skill on the part of an Investigator;
- the degree of risk to human subjects, and vulnerable populations, and whether safety or other factors will be diminished if the trial is done elsewhere;
- the degree to which the risk of bias may be mitigated.

Potential management requirements might include, but are not limited to:

- Removal of the institutional leader from oversight or recusal from decision making related to the research project
- Reduction or elimination of financial interests
- Additional required disclosures in public presentations and publications, and to other centers participating in a jointly conducted research project.
- Use of an external IRB
- Use of an external, independent DSMB
- External monitoring (particularly of endpoint assessments)