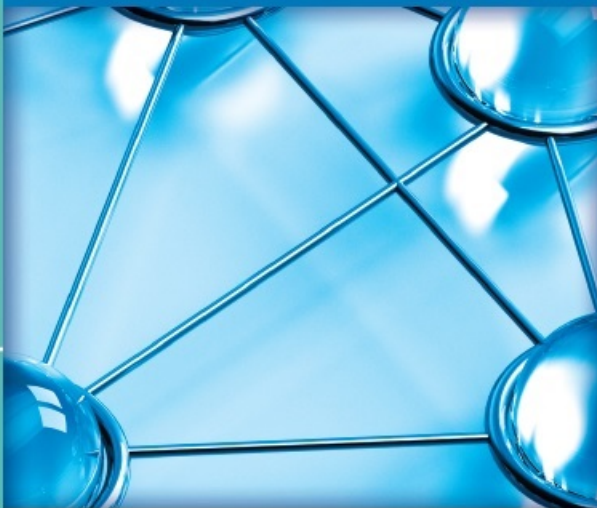


Principled Partnerships Quick Guide

Unlocking and Speeding Innovation



University Industry
Demonstration Partnership

Principled Partnerships: Unlocking and Speeding Innovation

FAQs for Universities and Industry

Introduction The phrase “financial conflict of interest” is commonly used to raise concerns regarding academic-corporate engagement—especially in the life sciences. The term “Principled Partnerships” was coined by the American Association of Medical Colleges (AAMC) as a more descriptive way to describe engagement between universities and companies.

Principled Partnerships stresses that relationships between academia and industry, for the commercialization of technology and development of solutions for society, are to be promoted rather than avoided. Concurrently, universities and companies strive to ensure that activities are conducted in a way that financial interests do not affect the objective conduct of research.

These FAQs were developed with the intention of framing the issue so that partners, the public, and other interested parties have a clear understanding of why university-industry research partnerships are crucial and how potential financial conflicts can be effectively addressed and managed.

WHY DO UNIVERSITIES AND FOR-PROFIT COMPANIES PARTNER?

Companies and universities possess complementary missions, resources and assets, and they partner to help each party advance its own mission via the exchange of scientific expertise. Experience shows that it is nearly impossible for any single entity to discover, develop, and successfully commercialize a product. Different expertise is honed in diverse environments, and each side provides unique resources to the undertaking of bringing new technology to market.

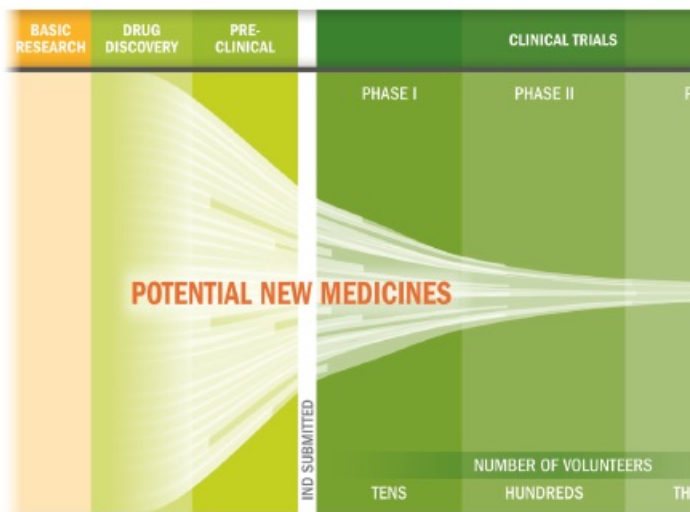
Although economic development is gradually becoming part of the research university mission at some institutions, universities do not have sufficient resources in manufacturing, pricing, marketing, distribution, or access to markets to be successful.

Without basic science, innovation is limited. Without commercialization, society at large would not receive the benefits of discovery and innovation. Principled Partnerships are crucial to advance technology in general and patient care in particular. And although health care is highlighted in this discussion, the same principles hold true in other research environments.

Collaboration should be encouraged and policies developed by the participating entities to support the flow of scientific information, and to reward innovators with appropriate protections for their intellectual capital.

THE BIOPHARMACEUTICAL RESEARCH AND

From drug discovery through FDA approval, developing a new medicine takes at least 10 years and costs an average of \$2.6 billion.* Less than 12% of the candidate medicines that make it into Phase I clinical trials are approved for marketing.



Key: IND: Investigational New Drug Application, NDA: New Drug Application, BLA: Biologics License Application

* The average R&D cost required to bring a new, FDA-approved medicine to patients is estimated to be \$2.6 billion over 10 years, including the cost of potential medicines that do not make it through to FDA approval.

Source: PhRMA adaptation based on Tufts Center for the Study of Drug Development (CSDD) Briefing: “Cost of Developing a New Drug.” FDA Infographic, “Drug Approval Process,” <http://www.fda.gov/downloads/Drugs/ResourcesForYou/Consumers/UCM28>

WHAT IS A KEY DIFFERENCE BETWEEN RESEARCH AT A UNIVERSITY AND RESEARCH AT A COMPANY?

Creating new knowledge is an important part of the university mission. Universities invest heavily in the research facilities and infrastructure needed to conduct basic research. Willingness to do early-stage research is part of academic culture.

University-based research is an open-ended activity that doesn't have an end goal of a saleable commodity. Most research is focused on fundamental findings (how and why things work), or "basic" research, rather than applied research (although basic research can lead to applications). For example, human subjects research and investigator-initiated clinical research at universities often identify potential new biochemical pathways or characterize new ways to use existing drugs, but often the studies are not large enough to bring products to market.

An example of basic research leading to applications is NMR (nuclear magnetic resonance). Developed by chemists to understand the structure of chemicals by measuring the vibrations of atoms exposed to magnetic fields, an application was developed when the NMR machine was enhanced with computer technology to create the magnetic resonance imaging (MRI) machine. The MRI takes pictures of the bone and soft tissues of the body, without the use of radioactivity. (Science, Medicine and Animals, National Academies of Science Press, 2004)

Applied research in areas such as engineering, computer science, and mathematics often focus on unique situations or early innovative technology that may not be economically feasible for the market. Companies, with shareholder obligations to return profit on their research and development assets, place a high priority on focusing their investment on research initiatives with the potential to lead to a product that can be commercialized successfully.

WHAT IS THE DEFINITION OF A FINANCIAL CONFLICT OF INTEREST IN RESEARCH?

The U.S. Public Health Service regulations define a financial conflict of interest in research as a "significant financial interest" that might affect the design, conduct, or reporting of research. The newest regulations from the federal government, regarding objectivity in research and investigator financial interests, focus on ensuring transparency, institutional oversight, and the management of investigators' financial relationships with industry.

The purpose of the regulations is to ensure that there is no reasonable expectation that publicly funded research will be biased by an investigator's personal financial interest. Additionally, some institutions have decided to make public all financial transactions between their faculty/physicians and industry. The relationships that are disclosed should not be automatically construed as negative, but instead should be viewed as what they are: an accounting of work and relationships. In fact, these disclosures can be an opportunity to clarify and highlight collaborations.

DEVELOPMENT PROCESS

It takes an average of 10 years on average and costs an average of \$1.3 billion to get a new drug to market. Only 1 clinical trial will be approved by the FDA.



License Application

the past decade (in 2013 dollars), including the cost of the many

g a New Drug." Nov. 2014. Tufts CSDD & School of Medicine., and US 393.pdf (accessed Jan. 20, 2015).

In an era when important research ideas exceed available funding, academic and corporate investments can be optimized and shared through principled partnerships.

ARE UNIVERSITIES MADE AWARE OF THE FINANCIAL INTERESTS (AND THEREFORE POSSIBLE CONFLICTS) OF THEIR FACULTY?

Yes. As mentioned earlier, federal regulations require that universities develop policies and procedures for the disclosure of certain financial arrangements. The faculty member discloses information to the designated officer or committee at the university, according to specific criteria and whenever financial interests change.

WHAT ABOUT COMPANIES?

Similar policies and procedures are promulgated by industry with the same goal of ensuring that partnerships advance objective science and that collaborations are free from bias. When these goals are met, the public (and prescribers, in the case of drug development) can have greater trust that products will perform as promised.

CAN POTENTIAL CONFLICTS BE PREVENTED AND THE PUBLIC TRUST PRESERVED?

Acting in one's own interest is human nature. Therefore, avoiding conflicts of interest is less practical than identifying, monitoring, and arbitrating conflicts of interest. As the federal language says, potential or actual conflicts should be "reduced, managed, or eliminated." At the same time, potential conflicts of interest cannot be allowed to undermine the goals of a principled partnership.

All participants in research partnerships want the output of their work to be based on objective science. This is the only way the product or technology will perform as promised, and for the real benefits and risks of the product to be understood.

WHEN SHOULD PRINCIPLED PARTNERSHIPS IN CLINICAL RESEARCH BE DISCLOSED TO PATIENTS OR CONSUMERS?

Experience shows that partnerships should be disclosed in nearly every instance, and as early as possible. Transparency engenders trust, by ensuring that partners live up to their commitments to be ethical and keep the public good a high priority. Transparency has to include information explaining the activities involved and include descriptions of oversight and mitigation, when needed.

WHAT IS THE PHYSICIAN PAYMENTS SUNSHINE ACT?

A 2007 study indicated that 94 percent of U.S. physicians have received payments for various purposes — consulting,

Management/Resolution by academic and industry collaborators

01

Understanding what each party seeks and receives from any partnership

02

Formal disclosure of personal financial or other relationships for investigators and faculty researchers involved in project

03

Review by organizational and other representatives as needed, to assess and provide recommendations for managing these relationships

04

Recommendation by independent officials on how to address any situation

05

Management/Resolution by academic parties in conjunction with their institutions, as well as management plans by industry

06

Appropriate contract mechanisms that reflect proposed workplan and management plan

research, gifts — from industry — (Campbell EG, Gruen RL, Mountford J, Miller LG, Cleary PD, Blumenthal D. A national survey of physician-industry relationships. *N Engl J Med.* 2007;356:1742-1750).

The Physician Payments Sunshine Act, a provision of the Affordable Care Act, requires exchanges of value (including payments for research) from pharmaceutical and medical device companies to physicians and teaching hospitals must be reported for posting on a public website. In addition, certain ownership interests have to be reported.

The Sunshine Act, implemented as the Open Payments Program of the Centers for Medicare and Medicaid Services (CMS), focuses on a national database for beneficiaries, consumers, and providers to better understand relationships among physicians, teaching hospitals, and industry. CMS hopes that it will promote transparency by publishing the financial relationships between the medical industry and health care providers (physicians and hospitals). The disclosure thresholds begin at \$10.

WHAT IS THE FEDERAL POLICY PROMOTING RESEARCH OBJECTIVITY?

Promoting Research Objectivity is the federal Public Health Service (PHS) language for Principled Partnerships and encompasses the financial conflict of interest in research regulations. Institutions applying for or receiving funding from any of the U.S. Public Health Service agencies (NIH being the most prominent) must comply with these regulations: Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought (42 C.F.R. Part 50, Subpart F) and Responsible Prospective Contractors (45 C.F.R. Part 94). Many colleges and universities are recipients of PHS funds and are subject to these regulations.

The National Science Foundation (NSF) also has robust conflict of interest policy which can be found in the Proposal and Award Policies and Procedures Guide Part II Section IV. A. These policies have been applied to recipients of NSF grants for many years and were updated in December 2014. Under the new Uniform Guidance, 2 CFR Part 200, federal agencies will be updating their policies on conflicts of interest.

WHAT ABOUT FDA REGULATIONS? HOW DO THE FDA AND PHS/NIH REGULATIONS FIT TOGETHER? HOW DO THEY VARY?

The regulations differ in the thresholds levels for disclosure, time periods covered by the disclosure, and public reporting requirements areas. It is not just FDA and NIH that have been propagating regulations in this area; codes of conduct, ethical guidelines, best practices and advisories have already been put in place by a number of stakeholders serving the biomedical research and health care communities, including professional and trade associations. A sample list can be found at <http://www.ndhi.org/physician-industry-collaboration/resource-materials/>.

The federal policy Promoting Research Objectivity only applies to recipients of Public Health Service funding—most often universities, research hospitals, and free-standing research institutions. However, it can also cover businesses and their investigators and employees who participate in activities sponsored by PHS Agencies (<http://www.usphs.gov/aboutus/agencies/hhs.aspx>).

While it is important that objectivity and addressing potential conflict of interest assumes a prominent position in partnerships, the downside is that multiple, differing policies have been created. The result has been fragmented and sometimes conflicting policy requirements that make it challenging for those who consider participating in these Principled Partnerships. Some members of the academic, corporate, and non-profit sectors have argued that harmonizing private and public policy regulations and policies is necessary to ensure that policies can support, rather than interfere with, truly Principled Partnerships.

WHAT ARE THE MAJOR DRIVERS BEHIND THE FEDERAL CONFLICT OF INTEREST REGULATIONS?

The major concerns are over the potential use of public funds for private benefit and the risk of biasing research.

HOW ARE PARTNERSHIPS' POTENTIAL CONFLICTS IDENTIFIED BY UNIVERSITIES?

The activities of university researchers are subject to a myriad of federal, state, and local government laws and regulations as well as the policies of the universities that employ them. These regulations and laws describe who and what situations are to be disclosed, when and to whom the disclosures are made, how and when disclosed situations must be managed, what disclosed information must be made public, and the consequences of failure to comply with regulations and laws. Additionally, faculty researchers must adhere to the guidelines, ethics, and norms of their individual professional associations.

Under the federal regulations of the Public Health Service, researchers must disclose all personal financial interests (e.g., consulting or advisory fees, travel and accommodation, equity interests in publicly traded companies, royalties, etc.) that are valued at more than \$5,000 and are related to their institutional responsibilities. For ownership interests in private companies, e.g., start-up companies or private companies, researchers must disclose any equity interests.

Again, it is important to note that disclosure of financial interests does NOT mean bias or conflict can be assumed, simply that the federally defined thresholds for disclosure have been met. Each university must review these disclosures and determine whether they are related to a specific research project.

Most universities have established a committee comprised of faculty from several schools who possess a significant and diverse sets of skills,

to determine if a financial interest could be a financial conflict of interest. Factors that these committees examine to determine whether a financial interest is related to a research project include:

- If the entity where the researcher holds an interest sponsors their research project.
- Whether that entity produces products (equipment, software, compounds, drugs, devices, etc.) or services used in their research project.
- Whether that entity is developing a product or service that the research project is designed to evaluate or develop.
- Whether a consulting activity is in an area that overlaps with or is the main subject of the research.



In addition to implementing policies compliant with the federal regulations, institutions are also required to prepare guidelines that outline their process for determining whether a disclosed financial interest is a potential financial conflict of interest. Here is an example of guidelines that an institution might use in making a determination of a potential or actual FCOI:

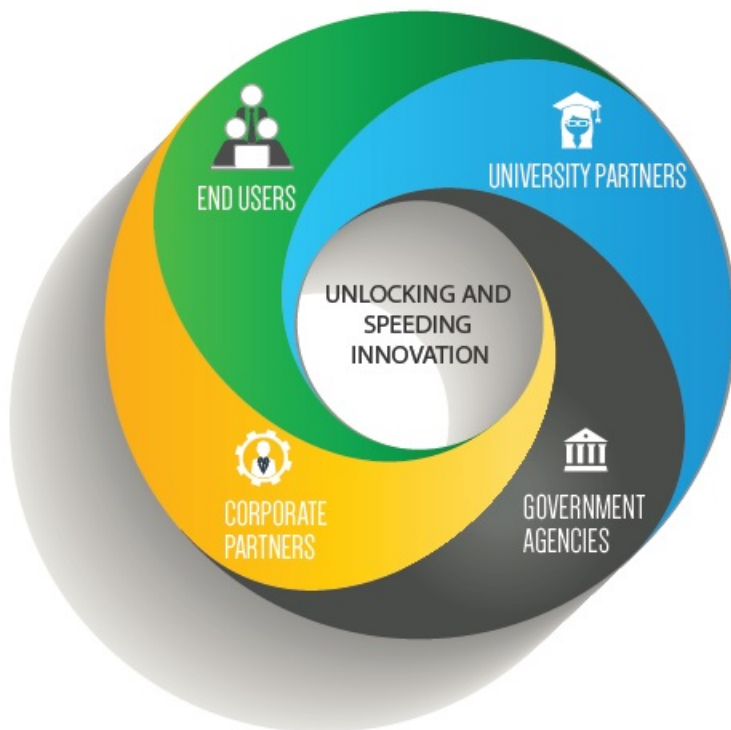
When a recipient institution determines that a financial conflict of interest exists, it must devise a plan agreed upon with the investigator to manage, eliminate, or reduce the conflict of interest. A variety of tools are used to manage an investigator's financial interest. These could include the following: mandatory disclosure, annual monitoring, revision of study design, revision of researcher's duties, oversight from an independent reviewer, reduction of the financial interest, divestment of the financial interest.

Similar processes are in place with industry partners, and many of these provisions are incorporated into contracts governing these collaborations.

WHY DOESN'T GOVERNMENT JUST PAY FOR ALL RESEARCH?

Historically, industry is the largest supporter of research and development (R&D), as distinguished from research alone—the government's traditional role. Industry also serves as an increasingly important investor in academic R&D.

Scientific advances now take place in a larger context or "innovation ecosystem," requiring many different sets of expertise to be involved in more stages of the process. Multiple channels of funding ensure all sectors of society have input into the research process. Collaboration across sectors often results in better scientific findings.



Useful Links

- 1 NIH Policy, including the regulations 42 CFR Part 50, Subpart F and 45 CFR Part 94 <http://grants.nih.gov/grants/policy/col/>
- 2 Quick reference guide to the Sunshine Act: <http://www.policymed.com/2013/02/physician-payment-sunshine-act-final-rule-quick-reference-guide.html>
- 3 The federal policy Promoting Research Objectivity <http://www.usphs.gov/aboutus/agencies/hhs.aspx> <http://www.ndhi.org/physician-industry-collaboration/resource-materials/>
- 4 The New England Journal of Medicine, Sunlight as Disinfectant — New Rules on Disclosure of Industry Payments to Physicians: <http://www.nejm.org/doi/full/10.1056/NEJMp1305090>
- 5 The New England Journal of Medicine, The Sunshine Act — Effects on Physicians: <http://www.nejm.org/doi/full/10.1056/NEJMp1303523>
- 6 Centers of Medicare and Medicaid Services: Open Payments website: <http://www.cms.gov/Regulations-and-Guidance/Legislation/National-Physician-Payment-Transparency-Program/index.html>
- 7 FDA Policy: <http://www.fda.gov/AboutFDA/Transparency/Basics/ucm222231.htm>

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