

Principles for Effective Academia-Industry Collaboration in Pharmacoepidemiology¹

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Introduction

The complexity of biomedical research has led to increasing recognition that advances in human health can benefit from effective scientific interchange between academia and private sector institutions. Scientific collaboration between the private and public sector may inform all types of medical research, including pharmacoepidemiology. Though the potential value of academia-industry collaboration is generally apparent, all stakeholders recognize that research activities must be conducted in a manner that adheres to the principles of sound scientific methods and ethical requirements while, at the same time, acknowledging the missions and responsibilities of the involved institutions.

Marshalling the complementary resources and expertise available in academia, industry may support the advancement of human health, through the development and assessment of diagnostic and therapeutic interventions. Pharmacoepidemiology plays an increasingly important role in biomedical research, through assessment of the safety and effectiveness of preventive and therapeutic biomedical interventions. In spite of many successful examples, there have been high profile conflict of interest cases involving academia-industry collaborative research activities, which have stimulated discussion about the propriety of certain interactions between academia and industry [see e.g., 1], and have led both to greater public scrutiny of scientific research and to some hesitancy to collaborate between academia and industry.

The purpose of this document is to outline principles to be incorporated into academia-industry agreements, with recognition of common and different interests between the two groups and with the intent of creating a framework to facilitate collaborative pharmacoepidemiological research to advance human health. The document purposefully avoids providing specifics on how to implement these principles given that these will very much depend on the specific setting. While these guidelines focus on agreements between one academic institution and one company, it should be noted that the principles described in this document generally apply, with minor modifications, in multiple situations, e.g., when there are multiple sponsors or multiple academic centers involved in an investigational study or for academia-industry partnerships outside of investigational studies (e.g., academic Centres with multiple industry partners).

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(A) Transparency for Academia-Industry Collaborations

An essential component of a successful academia-industry relationship is a transparent and detailed research agreement establishing clear roles, responsibilities and rules of engagement. The Research Agreement should specify:

- the study/research question and scope of research and activities, including aspects related to protocol development and data management/programming
- study conduct in compliance with
 - the protocol
 - governmental laws, rules and regulations, including ethical considerations and human subjects protections if applicable
 - applicable medical privacy, personal data laws, regulations and public disclosure policies
 - Good Pharmacoepidemiology Practices set forth in ISPE guidelines
- study results including
 - periodic updates on study progress
 - interim results/reports
 - final study reports and
 - reporting to regulatory agencies or other agencies such as payer and HTA bodies
- data ownership, access to data, record keeping
- payments
- confidentiality
- publication including
 - applicable disclosure of protocols, results and manuscripts on publicly available registers
 - jointly determined publication plan including authorship and agreed review process for intended manuscripts and presentations
- timelines

(B) Conflicts of interest

Background

Academic institutions and their affiliated academic medical centers conduct research and training in pharmacoepidemiology and are relied upon by medical professionals, regulatory authorities, and the general public to conduct research properly to inform decision-making regarding the appropriate use of pharmaceuticals, vaccines, biologics, and medical devices. The pharmaceutical, vaccine, and device industries are responsible for proper development and commercialization of products, as well as safety monitoring and pharmacoepidemiology following licensure. To fulfill societal expectations, there is a shared responsibility between academia and industry to assure that pharmacoepidemiologic research is conducted in a manner that is optimally free from external bias.

“ Conflict of interest means a professional or personal interest sufficient to potentially influence the exercise of one’s judgment regarding any activity of a research project. Financial and commercial interests are the most easily identifiable sources of conflicts of interest, but conflicts can occur for other reasons, such as professional interest, personal or familial relationships, academic competition or beliefs.”[2]

While public attention on conflicts of interest in biomedical research has primarily focused upon the potential for financial inducements to influence scientific independence and physician prescribing behavior, there are other types of conflict of interest (COI) that may influence all fields of biomedical research, including pharmacoepidemiology, “for today’s scientists, the rewards of publicity in terms of future research funding and career advancement may mean considerably more than personal financial gains.”[3]

Interactions between industry and academia are scrutinized by the public. It is necessary for ethical as well as reputational concerns that researchers in both academia and industry assure that potential conflicts of interest are recognized and mitigated.

Issues that need to be addressed in the Agreement:

1. Transparency. Minimizing COIs through complete disclosure
2. Addressing nonfinancial COIs
3. Prescriptive approach (e.g. a check list) vs declaration of principles (defining COI)
4. How it aligns with ISPE Good Pharmacoepidemiology Practices[4]
5. Role of local institutional policies, e.g. an institution may limit industry research support to an investigator (uncommon), or other financial support, e.g. speaking / advisory board participation (common)
6. Adherence to local laws/regulations
7. Examples of potential COIs
8. Conflicts of interest vs. competing interests
9. Changes that may occur once the agreement is signed

(C) Confidentiality:

Domains and concerns related to confidentiality may differ between industry and academia, and collaborative agreements between these sectors must acknowledge and provide approaches to meeting their respective needs while simultaneously assuring that public health interests are not compromised.

Industry may provide academic collaborators with confidential information that is needed for the work proposed (e.g., to develop a protocol). A confidentiality agreement should be established prior to sharing any confidential information.

This confidential information may include proprietary product information which, if made public, could harm the commercial interests of the sponsor. Ideally, the sponsor should identify, in writing, information that it considers confidential. Further, the sponsor should be given an opportunity to identify the sponsor's confidential information (that they wish to remove) in manuscripts/presentations submitted by the academic collaborator.

Academic and industry collaborators share a common interest in conducting research to advance public health. Working within a regulated environment, industry-based researchers are required to submit to appropriate regulatory authorities certain product-related information that is of public health concern. As part of their professional responsibilities, academic researchers have an ethical obligation to report to appropriate regulatory authorities information which they believe may constitute a real or potential public health threat. Approaches to sharing data and study findings with regulators should be reflected in the Research Agreement.

Confidential information provided by academic collaborators to industry sponsors typically relates to proprietary tools and/or data (e.g. software, analytical methods, coding dictionaries). As is the case for industry, the academic collaborator should identify, in writing, information it considers proprietary. The sponsor should agree to appropriate restrictions on the use of collaborators' confidential information and vice versa.

(D) Conduct of the Study

The latest version of the full study protocol or the study proposal should be an attachment to the study agreement as well as a description of the system in place for documentation of changes to the original version of the protocol. An analytic plan should be described and included as an attachment to the study protocol. The protocol should include a description of plans for protecting human subjects and assuring privacy that satisfy governmental regulations. This would also include the process for ethical committee review (e.g. IRB approval). These and many other aspects of study conduct are covered in more detail in the Guidelines for Good Pharmacoepidemiology Practices.[4]

A steering committee and/or an independent advisory committee may provide value to ensure the integrity and independence of the study and should be considered. A description of the purpose and function of each of these committees should be provided as well as a description of the membership composition, the process for selection of committee members, as well as their responsibilities.

The agreement should include a description of the institutions involved as well as a description of the key personnel who will be conducting the project, services (e.g. database access and license agreement) and equipment which will be required to conduct the study. This includes a brief description of the roles of the personnel assigned to the project. Resumes of the principal investigators and other key personnel with major responsibilities are useful as attachments to the agreement.

The agreement or protocol should also include a description of the timelines for the study (anticipated initiation and completion dates, length of time anticipated for various aspects of the study including data collection and analysis) and the deliverables from the study.

It is recognized that, at times, a study may have to be terminated earlier than planned, or, conversely, extended beyond its original term. The processes for addressing such changes should be described, as well as the steps to be followed if these situations occur.

ISPE endorses the opportunity to register and publicly disclose hypothesis driven pharmacoepidemiology research protocols in a suitable public site, such as the ENCePP registry (also currently functioning as the EU PAS Register) or ClinicalTrials.gov. [4] The agreement should state whether and how the protocol should be registered and who will be responsible to do so.

(E) Publication

One of the core missions of public and private academic institutions is to advance knowledge for the benefit of the population at large. There is a common interest between academia and industry in assuring the validity of any research and a general obligation to disseminate and publish research findings of potential scientific or public health importance irrespective of results. To avoid delay in publication [e.g., 1], several institutions have put policies in place to ensure timely publication of study results [e.g., 5]. An example of an international guideline comes from the

Guideline on Good Pharmacovigilance Practices for Post Authorisation Safety Studies (PASS) published by the European Medicines Agency and the Heads of Medicines Agencies

[6]. Academic institutions across the world need to maintain the right to publish research results. Any research agreement between academia and industry should have language addressing a) who is responsible for dissemination of results; b) the right of academia to publish the research findings with or without concordance of industry investigators; and c) the right of the sponsor to review manuscripts prior to their submission for publication within a specified time. Authorship decisions, including the inclusion of coauthors employed by the sponsor, should follow guidelines established by the International Committee of Medical Journal Editors, recommending that authorship be based on the following four criteria:

- Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published; AND
- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.[7]

We here outlined basic principles to be incorporated into academia-industry agreements creating a framework to facilitate collaborative pharmacoepidemiological research to advance human health. These basic principles can be used to evaluate existing templates for academia-industry contracts or to create new ones.

References:

1. Pfeffer MA, Skali H. PRAISE (Prospective Randomized Amlodipine Survival Evaluation) and criticism [editorial comment]. *JACC: Heart Failure* 2013;1(4):315-7. <http://dx.doi.org/10.1016/j.jchf.2013.05.005>, last accessed March 16, 2017
2. Kurz X, Bauchau V, Mahy P, Glismann S, van der Aa LM, Simondon F; ADVANCE consortium. The ADVANCE Code of Conduct for collaborative vaccine studies. *Vaccine*. 2017 Mar 9. pii: S0264-410X(17)30242-6. doi: 10.1016/j.vaccine.2017.02.039. [Epub ahead of print]
3. Rothman K. Conflict of interest: the new McCarthyism in science. *JAMA*. 1993;269:2782-2784
4. Guidelines for good pharmacoepidemiology practices (GPP). *Pharmacoepidemiol Drug Saf* 2008;17:200-8. Also accessible at https://www.pharmacoepi.org/resources/guidelines_08027.cfm; last accessed March 16, 2017
5. from <http://vcresearch.berkeley.edu/research-policies/policy-guidelines-governing-openness-and-freedom-to-publish>, last accessed March 16, 2017:
 - Publication delays not exceeding sixty (60) days are acceptable so that a sponsor may review publications and (1) offer comments or suggestions and/or (2) determine that its proprietary data are not inadvertently disclosed. In either case, the final decision on content must rest with the author.
 - Delays not exceeding ninety (90) days also are permitted so that the University and/or the sponsor may screen proposed publications for possibly patentable ideas. If both sixty- and ninety-day delays are applicable, the total period of delay should not exceed ninety (90) days.
 - The Berkeley campus does not accept sponsored project agreements in which results and/or data generated by the University are owned by the sponsor and are not available for the University's scholarly purposes, including the sharing of information with other researchers.
 - Restrictions on the University's right to commercially disseminate tangible research results and products (such as biological materials, chemical compounds, computer software, mechanical specifications, drawings, and schematics) are acceptable only if (1) they apply to a tangible deliverable item specified in a grant or contract, and (2) there is no restriction on publication or noncommercial dissemination of the central research findings, including distribution of the results to other researchers for scholarly purposes.
6. EMA Guideline on good pharmacovigilance practices (GVP) Module VIII – Post-authorisation safety studies (Rev 1): http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500129137.pdf, last accessed March 16, 2017, page 15/16:
 - **VIII.B.7. Publication of study results**
 - For studies that are fully or partially conducted by investigators who are not employees of the marketing authorisation holder, the marketing authorisation holder and the investigator should agree in advance a publication policy allowing the principal investigator to independently prepare publications based on the study results irrespective of data ownership. The marketing authorisation holder should be entitled to view the results and interpretations included in the manuscript and provide comments prior to submission of the manuscript for publication.
 - **VIII.B.7.1. Regulatory submission of manuscripts accepted for publication**
 - In order to allow national competent authorities to review in advance the results and interpretations to be published, the marketing authorisation holder should communicate to the Agency and the competent authorities of the Member States in which the product is authorised the final manuscript of the article within two weeks after first acceptance for publication.
7. International Committee of Medical Journal Editors: <http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-the-role-of-authors-and-contributors.html>, last accessed March 16, 2017