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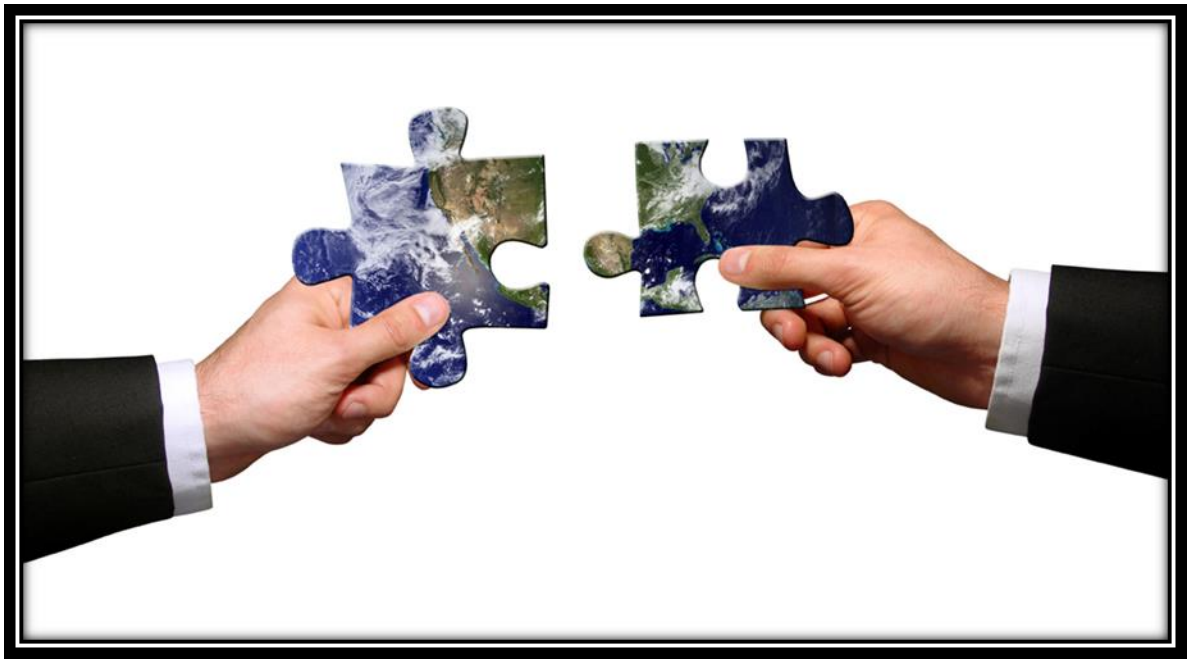
Collaborative Research



Office for the Protection of Research Subjects (OPRS)

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This series of booklets is adapted from the Collaborative Institutional Training Initiative (CITI) Responsible Conduct of Research online course available at www.citiprogram.org

Also available in the RCR Series:

Using Animal Subjects in Research

Conflicts of Interest and Commitment

Peer Review

Data Management and Acquisition

Human Subjects Research

Mentoring Student Researchers

Research Misconduct

Responsible Authorship and Publication

About the Source Material

The Collaborative Institutional Training Initiative (CITI) web based education program, developed by the University of Miami and the Fred Hutchinson Cancer Research Center, offers training in Human Subjects Research, the Responsible Conduct of Research, and Good Clinical Practice. CITI is currently used by over 1130 participating institutions and facilities from around the world and offers online course material in more than seven different languages. CITI RCR was developed with public funds and thus allowed access to material used to create these booklets.

Introduction to Collaborative Research

This booklet discusses the multiple factors that are contributing to the increase in research collaborations and the attendant complexity where ethical and/or regulatory concerns arise. Technology such as e-mail and video teleconferencing ease communication across countries and nations. Federal laws, such as the Bayh-Dole Act, promote the commercialization of patentable technologies developed at universities thus allowing relationships between academia and industry to grow. Private and federal funding sources like the National Science Foundation and National Institute of Health explicitly encourage collaborative and multidisciplinary projects to move knowledge from the lab to commercialization or clinical application. While some researchers look within their own discipline to gain complementary expertise, save time, or decrease expenses, others collaborate with researchers outside their own field to answer research questions. The multiplicity of institutions, departments, disciplines and researchers increase the potential for both knowledge and unique issues of sharing research. Case studies and reference lists have also been included in this booklet.

What is Collaborative Research?

Over the past 50 years, research collaborations have increased across all disciplines. The term collaboration initially referred to researchers working together within the same discipline, within an institution or in different institutions.

Collaborations can be as simple as one researcher sharing reagents or techniques within the same lab or they can be as complex as multi-centered clinical trials that involve academic research centers, private hospitals, and for-profit companies studying thousands of patients in different states or countries.

High-energy physics, the human-genome project, the social impact of computing and telemedicine illustrate increasingly complex areas of scientific and engineering inquiry. As the scope of scientific inquiry enlarges, researchers are increasingly collaborating in larger groups and are working with investigators who are educated and skilled in other disciplines and fields.

Forms of Collaborative Research

Multidisciplinary/cross-disciplinary research is collaborative research that involves researchers working within or across disciplines, either within an institution or in different institutions. A physician working with an engineer to manufacture a new imaging device is an example of a cross-disciplinary research project. When the pharmaceutical industry works with a medical center to perform a clinical trial of a new drug, it is collaboration between industry and academia. All of these interactions create different expectations and require a variety of modes of communication to ensure that the collaboration is successful.

The Challenges of Collaborative Projects

Researchers assume certain additional responsibilities when embarking on collaborative projects. These responsibilities arise from the burdens of:

- Increasingly complex roles and relationships
- Aligning the differing interests of the collaborators
- Meeting institutional requirements
- Managing cultural differences

- Managing regulatory/ compliance differences

Paying special attention to these added burdens can help collaborative projects run smoothly. A written Memorandum of Understanding can allow the collaborating parties to formally outline the goals and expectations of each party. (For a guide to writing a Memorandum of Understanding visit: http://www.fcc.gov/pshs/docs/clearinghouse/DHS-MemorandumOfUnderstanding.pdf)

Differences between Collaborators

In any relationship, people have different styles of communicating. Some researchers are more formal, while others are more laid-back and relaxed.

One collaborator may believe that peer-reviewed papers should be short and should use a limited amount of data. Another collaborator may believe that more data should be collected and a narrative of the research should be developed before anything gets published. This kind of disagreement can occur with collaborators in the same field or in different fields. The tradition of the discipline can also affect who should be an author on a paper. In many fields, people who have not contributed substantially to the intellectual process of the research are not included, while, in other fields, people get authorship if they participated in the research at any level.

Different research disciplines also have varied approaches and work habits. For example, different types of work may follow different timetables. Biomedical laboratories can run 24 hours a day according to the experiments, while other disciplines may have more routine, 8- to 10-hour days. A middle ground must be established. Investigators in one field should not assume that their colleagues in another field will automatically adjust schedule to the other's discipline.

Researchers also often speak different languages. Technical jargon exists in sub-specialties within, and across, all disciplines. It can be challenging for researchers to create terminology that can be understood across many disciplines.

Whether researchers work easily together or not, formal written agreements are necessary for managing grants, contracts, publications, and data ownership.

The crucial point is to presume nothing and to put everything on the table for discussion as early in the relationship as possible.

Sharing Data and Results

The free exchange of information at scientific and scholarly meetings and in publications allows researchers to build upon the work of their predecessors and contemporaries. In

commercial enterprises research data can have profound financial repercussions so it must be carefully vetted before it is published. When academic and business researchers work together on projects, each party has to come to an agreement about how data and materials will be shared. Most institutions do not permit sponsors to interfere with or delay a research publication. Some universities are willing to permit sponsor input in exchange for funding, access to industrial ideas, and opportunities to train students in commercial types of research endeavors.

Collaboration Concerns

Industry Sponsored Trials

Prohibitions to the publication or even sharing of data developed in industry-sponsored drug trials performed by investigators at academic research centers has become front-page news. *The New York Times* reported in 2004 that medical-school researchers funded by a pharmaceutical industry had sought access to unpublished data in an antidepressant trial. They hoped to determine whether the drugs increased the risk of suicidal behavior in children. The drug company denied the researchers access to the data and would not allow them to communicate with other researchers who had participated in the same study at other institutions. A *New York Times* editorial about the case suggested that it may now be time for all institutions to negotiate contracts with drug companies that would "ensure researchers' access to data and the prompt publication of results."

Collaborating across Institutions and Nations

Universities throughout the nation and the world have different policies regarding the disclosure of potential conflicts of interest. While one medical center might not allow a researcher to be involved in the clinical trials of a drug he or she developed, another institution might permit it as long as certain management safeguards are in place.

International collaborations raise concerns about differing standards of treatment for research subjects in developing nations. In his presentation "Ethical Issues in International Collaborative Research," Reidar K. Lie of the NIH Department of Bioethics contends the quality of care given to subjects in poorer countries should be equal to that of the richer ones, even if different standards of care in the recipient country would more easily identify differences in how subjects respond to the intervention (from CITI module).

Managing and Accessing the Data

Research collaborators should clarify who will hold primary ownership of the data once the project has been completed. Before research has begun it is important to form an agreement regarding:

- Which party or parties will be responsible for the data
- How the data can be used for future investigations
- What restrictions will be placed on sharing the data
- How credit will be given for subsequent publications

Collaborators may have reasonable expectations about contributing to one or more publications once the research has been completed. These issues should be delineated in a collectively signed memorandum of understanding to reduce the chances of misunderstandings and disagreements.

Concluding or Continuing a Collaboration

Any combination of factors may influence a collaborative group's decision to conclude or continue an affiliation. The desire to continue a collaborative project should be weighed against the rationale and cost of continuing the collaboration and the likelihood of producing a meaningful contribution to a field of study.

The decision to conclude, continue, or modify a collaborative relationship can be made during one of the following stages of the research process:

1. During conceptualization
2. During implementation
3. Following implementation

The decision to continue or conclude may be predetermined by the end of the funding interval or stipulated in a Memorandum of Understanding (MOU).

Sometimes the research simply "runs its course" and the investigators conclude that further work in the area will not be a good use of their time. Collaborators may lose interest in the project because they have discovered other opportunities or have switched their individual research focus.

Despite having an MOU agreement, a situation may arise that causes researchers to reconsider their decision to conclude a collaborative effort. Researchers may decide to continue collaborating if their research yields unanticipated findings that might

significantly advance a field of study. A new research direction could necessitate re-conceptualizing the original project and recruiting additional collaborators with a different set of research skills and expertise.

Ways to Enhance Collaboration

In his book Scientific Integrity (2000), Francis Macrina identifies six key components for successful collaboration. They are:

1. Communication

In collaboration nothing should be assumed. If two researchers exchange data, personnel, or materials without a formal agreement in place, they risk encountering major disagreements in the future. Once a relationship is formally established, data, ideas, and personnel issues should be discussed. Communication is central to establishing, maintaining, and even terminating a collaborative relationship.

Communication is particularly important in collaborations between academia and industry. Special requirements may be imposed on the publication of material or on inventions and patents. Whether a student can participate in such an academic-industrial project must be resolved early. Also, patent lawyers, technology-transfer administrators, and marketing personnel from industry need to establish a common ground for communication.

2. Discussion of goals and roles

Parties to a collaboration should define goals in a way that complements each other's work. Formally setting goals allows researchers to express their desires and expectations.

Coordinating the effort among the participants requires management and communication. A project coordinator or manager has to be designated at the outset, especially when multiple laboratories or groups of researchers will be involved.

When a research project changes direction, the potential impact on the participants needs to be addressed. It is likely that authors may be added or eliminated. Researchers also have to determine when a collaboration is over.

3. Discuss authorship in advance

Different disciplines have varying standards for determining authorship. The criteria for authorship has to be established beforehand so all parties know what to expect. With authorship comes responsibility, so collaborators need to determine how they will deal with the differing expertise levels of each author. Who will actually write the manuscript and be responsible for the input from collaborators has to be established.

If the research changes direction, someone expecting authorship might be disappointed, so the evolution of a project has to be considered. Finally, who will be included in acknowledgments should be addressed.

4. Discuss data and material management in advance

The issue of who owns data is governed by the type and source of funds used to support research. Investigators and institutions also have rules for the custody and retention of data. The NIH and the NSF allow grantee institutions to own data. Most pharmaceutical sponsors do not allow this.

The transfer of materials among collaborators is subject to so-called "**Material Transfer Agreements**," or MTAs, developed by administration offices. MTA's ensure a university's rights are protected when specimens or reagents are shared with colleagues or private entities.

An MTA is a research contract between a provider and recipient of research materials which governs the terms and conditions under which the material may be used. An MTA protects the intellectual and other property rights of the provider, and generally addresses:

MTA's include:

- Limits on the use of the material, usually for non-commercial research purposes
- Prohibitions on the redistribution of the material
- Conditions of use, including prohibitions of use in animals or humans
- Conditions for publication, usually with provisions that the manuscript must be seen by the donor before submission for publication
- A hold-harmless cause, meaning that the donor has no liability resulting from the use of the material
- The issue of the return of unused materials

There are two main types of MTAs; incoming and outgoing. MTAs at academic institutions fall into these categories:

1. transfers between academics or non-profit research institutions
2. transfers from industry to academia
3. transfers from academia to industry

USC is a member of the Uniform Biological Material Transfer Agreement which was developed by the NIH to encourage the signatory institutions to share research materials. USC MTAs need to be reviewed to ensure compliance with USC policies, principles and guidelines, and all MTAs need to be signed by an authorized representative of USC. Review and approval of MTAs is conducted by the Senior MTA Administrator of the USC Stevens Institute (http://stevens.usc.edu/mta.php).

5. Discuss intellectual property issues in advance

All investigators want to be able to protect results that might have potential commercial application. Disclosing results too early could hinder collaborators from obtaining patent protection. All parties should know institution and granting-agency's policies regarding intellectual property and patent procedures.

6. Managing accountability

Each institution must abide by certain regulations, policies, and laws. Researchers working with animals, humans, or hazardous substances must conform to the appropriate regulations, policies, and laws. Basic researchers might have access to patient data from the clinical arm of a study and must be aware that they need to maintain the confidentiality of patients and personal health information. Also, clinicians should inform bench researchers of the potential hazards of certain human tissue samples. Researchers also need to inform one another of any potential conflict of interest that they might have in the project.

The Institutional Role in the Collaborative Process

A. Technology Transfer Office

Most universities have a **Technology Transfer Center** or similar office. Technology Transfer Offices are responsible for identifying and patenting new inventions and copyright materials, including software. The office helps inventors develop the necessary documentation for patents and other kinds of protection. Although the university owns the intellectual property, the Technology Transfer Center works with the principal investigator to develop the best possible deal to benefit the university and the inventor, as both may receive licensing revenues (At USC, consult USC Stevens Institute for Innovation http://stevens.usc.edu/)

B. Contracts and Grants Offices

Contracts and Grants Offices (http://dcg.usc.edu) deal with contract and grant administration. Contracts and Grants submit sponsored project proposals to all agencies (whether governmental or private) and to negotiate and accept awards based on these proposals.

If an investigator with an ongoing grant enters into a collaboration with a researcher at another institution and money is involved in the transaction, a subcontract is written and managed by the Contracts and Grants Office.

If collaborators within an institution apply for a grant together, they are both included in the personnel section of the grant.

If collaborators from different institutions apply together for a grant, they must decide who will be the prime institution and who will be the secondary institution, a subcontract will have to be made. Material-transfer and intellectual-property agreements also come into play.

C. Clinical Trials Offices

The Clinical Trials Offices provide many support services to clinical investigators, freeing them to focus on their research.

The major responsibilities of the office include:

- Maintenance of an efficient administrative unit capable of quickly negotiating and executing Clinical Trials Agreements
- Management of ongoing clinical research contracts, including account control, collection and distribution of clinical funds, and computerized management reporting tools to monitor these activities
- Project control and financial services, such as the formulation and review of clinical-trial budgets
- Stimulation of new clinical research activities
- Improvement and support of the institutional infrastructure for clinical research

Bridging institutional lines, the Clinical Trials Office represents the institutions involved and also acts as the administrative unit for pharmaceutical and diagnostic companies when exploring the clinical-trial possibilities and when negotiating a Clinical Trial Agreement.

At USC, contact Health Research Association (HRA) (www.health-research.org).

Conclusion

Research collaborations allow researchers to answer questions they wouldn't be able to if they worked alone. The challenges for the investigators engaged in collaboration is a need to understand what the project's main goal is, and what role each collaborator must play in order to achieve that goal. While collaborators may work independently from each other at certain stages of the research, they should always be cognizant of the project's larger picture. They can increase the likelihood of a positive outcome by clearly delineating roles and responsibilities, developing management plans and fostering cooperation and a sense of fairness and accountability.

Case Studies

I. A Collaboration Formed Overnight

Sharon, Ben, and Terra are young faculty members at different universities who happen to meet at an evening reception at a large international neuroscience meeting. The three start talking about their respective research interests and before long it is clear that they share a common interest in learning disorders. However, the new friends come from different scientific backgrounds. Sharon has a Ph.D. in electrical engineering and works at the cutting edge of brain imaging technology. Ben is an educational psychologist interested in pre-school children in inner cities. Terra has a Pharm.D. and has been conducting experiments on the physiologic effects of alternative medicines.

As late night turns to early morning, the newly met trio begins to see some benefits from working together. They start to sketch out a multidisciplinary grant proposal. The scientific hypotheses quickly fall into place, but before long the three realize that there are some logistical problems that will need to be solved before the collaboration can move forward. How would you help these three faculty members who are unsure how to answer these questions:

1. *Who should submit the proposal and through which university? Since they will be studying children with learning disorders, will they need to obtain IRB approval?*
2. *They realize that "intellectual property might be generated from this project. Will it be necessary to adopt a formal agreement to prevent problems later on?*

II. Collaborators Who Become Competitors

Drs. Smith and Jones are junior faculty members in the Education Department at Podunk University (PU) decide to set up a small business to develop and market a new tutorial for high school students that will help them prepare for the SAT exam. The product will be developed based on the focus group research done by the pair at PU. Together they prepare a grant application to further develop the concept. They submit the proposal under the US Government's Small Business Innovative Research (SBIR) program. Before the application is reviewed, however, Jones decides to accepts a job at a start-up company in another state, that develops educational software.

The application receives a good score, but, not quite good enough to be funded.

Nine months later, at a subsequent study section review meeting, the reviewers notice that the original application has been resubmitted by Dr. Smith with changes reflecting their earlier critique. They also note a remarkably similar new application, from Dr. Jones who changed jobs and on behalf of his new employer, the software company. This new proposal from Dr. Jones makes no mention of the original collaborative proposal, but, it contains much of the same language and the project summary is nearly identical to the original.

1. *How could this situation have been prevented?*
2. *How should the reviewers respond to similarities in the two proposals?*

III. Interdisciplinary Study of Terrorism

A group of investigators in various behavioral sciences and public health have been collaborating on an interdisciplinary project, across several institutions, to understand the causes of terrorism and to determine ways to prevent it. The U.S. Department of Homeland Security has funded the research. While all the investigators have been excited about working together on such an important topic, a few issues and problems with regard to the interdisciplinary collaboration are beginning to emerge.

1. What are some of the challenges that can emerge for researchers working in different disciplines?

One researcher had an opportunity to visit Pakistan and interview young people in a terrorist training camp using a tool developed by the investigators. He also decided to hire a local health worker to draw blood from the subjects to compare hormone levels with age-matched controls in the United States. Before he went away, though, he did not consider asking the young people for their consent to participate in the research project, since in his prior research he had relied on anonymous databases from which he extracted data and he had not had experience in getting consent.

2. What could the collaborative team have done beforehand to ensure that informed consent was obtained?

After he returned home, other difficulties arose when he discussed his findings with the five co-principal investigators at his institution. Half of them thought that the research should be published immediately, while the others thought that the results should be given to the government in confidence, because of the timeliness and nature of what was found.

3. How should the researchers resolve the issue of what to publish?

But, even within the group of people wanting to publish, disputes arose concerning which journal the data should be sent to, with each person arguing for his or her own discipline's peer-reviewed publication. Moreover, when a key collaborator at another institution heard about the findings indirectly, she felt slighted and angry that he hadn't been asked to take part in the discussions.

4. How could this situation have been prevented?

5. What should the research team do to resolve their dispute?

Resources

Writing Guide for a Memorandum of Understanding:
http://www.fcc.gov/pshs/docs/clearinghouse/DHS-MemorandumOfUnderstanding.pdf

US Department of Health and Human Services Office of Research Integrity Tutorial on Collaborative Research:
http://ori.dhhs.gov/education/products/rcradmin/topics/colscience/open.shtml

CITI Program
www.citiprogram.org

Grants for Collaborative Research in Humanities:
http://www.neh.gov/grants/guidelines/Collaborative.html

USC Office for the Protection of Research Subjects:
https://oprs.usc.edu/

National Science Foundation Funding Opportunities:
http://www.nsf.gov/funding/

Macrina, F. (2002).Scientific Integrity: An Introductory Text with Cases. 2nd Ed. American Society for Microbiology Press

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