

Special Contractual and Intellectual Property Rights Considerations

Sponsored Research Agreements, University and Government Licensing, and Clinical Trial Agreements

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This article and portion of the program address contractual and intellectual property considerations that frequently arise in the drafting and negotiation of sponsored research agreements (“SRAs”), license agreements with universities (and other non-profit organizations) and the federal government, and clinical trial agreements. Each of these subjects is addressed separately, but most of the article and much of this portion of the program will be devoted to sponsored research, which is the driver for much of the innovation in the medical and life sciences industries. Article I below discusses SRAs in some detail; Article II focuses on a few key provisions of license agreements with universities and non-profits; and Article III is a very brief overview of clinical trial agreements, the terms of which are frequently dictated by the hospital (especially if it is a prominent teaching hospital) employing the clinical investigator. Included in the Appendix are a few model agreements and sample actual agreements (redacted, of course) and other relevant materials. A disclaimer: My background in this practice area is representing the pharmaceutical company. As a result, this article is biased towards that perspective.

I. Sponsored Research Agreements

A. The term “sponsored research” refers to research (also development) that is paid for by one party (the sponsor¹) and performed by another party, which presumably has expertise in the subject matter. For its money, the sponsor expects one or more of several things from the sponsored activity—new inventions, proof of concept, corroboration of results, product improvement, among others. The sponsor typically expects to own or have exclusive rights to the results of the sponsored work. The other party is typically a university or hospital (referred to for simplicity as industry-university arrangements), another commercial enterprise (industry-industry, such as big pharma-small biotech), or the federal government (industry-government).

B. The work covered by a sponsored research arrangement can range from a one-shot, short-term specific task (such as performing toxicology studies for a potential pharmaceutical compound) or a multi-year program related to a more general field of basic research (such as the applicability of variants of a certain category of peptides to the treatment of various disease indications). The former involve the payment of money by the sponsor for a discrete work product; the latter also involve the payment of money by the sponsor, but can also involve collaboration on the research, which can complicate the IP ownership issues.

C. Sponsored research is always² governed by a written agreement. Key provisions, found in almost all SRAs, regardless of the parties, are:

- * Scope of work and changes to the scope of work
- * Funding terms; budget
- * Reporting the results of the work
- * Ownership of, and rights in, the results of the work
- * Patent filing, prosecution and maintenance
- * Publication of the results of the work
- * Confidentiality
- * Liability, indemnification and insurance
- * Term and termination

D. Industry-University Sponsored Research

1. Sponsored research is a big business for universities and other non-profits, such as teaching hospitals and research institutions. According to the results of the FY 2000 survey of its members by the Association of University Technology Managers (AUTM)³, sponsored research expenditures by 190 members which responded to the survey was \$29.5 billion, of which \$18.1 billion came from the federal government and \$2.7 billion from industry. Sponsored research also bears considerable fruit. The respondents to the AUTM survey reported more than 13,000 invention disclosures (that is, reports of inventions from sponsored research), about 6,400 new U.S. patent applications filed, about 4,300 new licenses and options executed (two-thirds with startups and small businesses (fewer than 500 employees) and one-third with large businesses). The respondents had about 21,000 active licenses and options, of which about 9,000 yielded income (such as license fees, milestone payments and royalties) totaling about \$1.26 billion. Of particular interest to this audience, the respondents reported that almost \$64 million in legal fees was reimbursed by sponsors. Most of that probably went for patent work. Of course, the universe of sponsored research is larger than the AUTM membership (and not all of its non-profit members responded), so the actual total figures in all of these categories are likely much larger.

2. Principal provisions of the SRA

a. Scope of Work. This is usually described in some detail in an exhibit to the agreement. Provision should be made to permit the sponsor to change the scope of the work within reasonable limits and, in any event, to approve any change; the university⁴ should have limited or no rights to change the scope of work unilaterally. In a long-term collaboration, there may a joint scientific committee made up of representatives of the sponsor and the university. The JSC monitors the progress of the research and suggests changes to the scope of work based on that progress.

b. Tie up the PI. A sponsor usually provides funding to a university because it wants a luminary on the university faculty to conduct or at least oversee the research. The sponsor should have the right to

terminate the SRA if the principal investigator (PI) terminates her or his affiliation with the university. Often, the university has the option to propose a successor, but subject to the approval of the sponsor.

c. Funding and Budget. The funding is ordinarily tied to an agreed budget, which can be very detailed in terms of FTEs required to do the work and costs of supplies and other materials. Equipment, which is either loaned or gifted to the university, may also be included in the funding. The sponsor is interested in periodic payments (quarterly is common); the university is interested in a minimum commitment, usually of one year, especially if it is hiring post-docs to do much of the work.

d. The “encumbered” PI. Most PIs work in a lab with other faculty and/or post-docs. Exclusive arrangements (that is, arrangements where one sponsor funds the entire activities of a lab and, therefore, has rights to all of the output of the lab) with luminary PIs are rare. Most PIs and labs are “encumbered” with concurrent or prior sponsored research arrangements with other industry sponsors or with government funding (federal grants supporting basic research). It is critical to understand what, if any, “encumbrances” may be on a PI and to take necessary steps to assure that any other arrangements will not adversely affect the sponsor’s rights to the results of the work it is funding. Section 6 of the “Sample Industry-University SRA” included in the Appendix is one example of how to address this issue. See also section 15.a of the same agreement. Due diligence is very important here.

e. Ownership of Results. Most, if not all, universities have policies which provide that all inventions made with the use of university funding and/or facilities belong to the university, even if the funding is provided by a third party. Therefore, in a straightforward money for work sponsored research arrangement, the results are owned by the university and the sponsor has an option (usually exclusive) for a license, which may be either exclusive or non-exclusive, of the results of the research. In a collaborative arrangement, where employees of the sponsor are working collaboratively and in parallel with the PI on the research and sharing information, there are likely to be joint inventions. These are generally jointly-owned, with the sponsor having the right to license the university’s interest. The university generally has no rights in the sponsor’s interest in jointly-owned inventions, except perhaps a non-exclusive license limited to internal research work, usually within the scope of the RFA. The sponsor owns any inventions made solely by its employees, with the university generally having no rights. But see section 8 of the “Sample Industry-University SRA”. The parties to this agreement have been collaborating for many years, and this provision is an acknowledgement of the contribution of the university and its faculty to the “background learning” of the sponsor’s scientists that facilitated their inventiveness. Ownership of inventions is generally governed by the U.S. rules for inventorship of patents (in other words, ownership follows the inventors named in the patent application). A word of caution: Joint inventions may lead to jointly-owned patents. In the absence of an agreement to the contrary, each of the owners of a jointly-owned patent may fully exploit the patent for its own account without any approval of the other party required.

f. Sponsor Rights in Results. Generally, the sponsor is granted an exclusive option to license the results of the sponsored research. See, for example, section 7 of the “Sample Industry-University SRA” and the Guide to the Ownership, Distribution and Commercial Development of M.I.T. Technology (the “MIT Guide”), which is also included in the Appendix. The option must be exercised within a defined period of time after a triggering event, which may be the disclosure of the invention or the filing of a patent or other IP application covering the invention. The sponsor would prefer a later triggering event in order to permit more time to evaluate the invention, especially if a license fee is required at the time of signing the license agreement. Most university SRAs provide for the negotiation “in good faith” of a license “on usual and customary terms” (or similar language) at the time the option is exercised. The “Sample Industry-University SRA” is unusual in that a form of license agreement is attached and the range of royalty rates is set out in the SRA.

g. Reporting Inventions. The SRA must provide for the reporting of any inventions to the sponsor. Most university policies require faculty to report inventions to a university office (see, for example, the MIT Guide), but the sponsor must also receive notice in order to begin to evaluate the invention and to monitor the patent (or other IP protection) process. The SRA should provide that the PI and those working with her or him keep detailed and accurate records of the progress of the research. This is important not only with regard to the issue of ownership of results (especially if the PI is “encumbered”) but also for patent purposes. Good scientists know the importance of this practice.

h. The Patent Process. The SRA should specify which party is responsible for the preparation and prosecution of any patent applications and the maintenance of any patents that issue on inventions made during the course of the SRA (if a license is taken, this subject is picked up in the license agreement). In general, sponsors would prefer to control this process, but some universities insist that they control the process. If the university is responsible, the sponsor should negotiate for some right to review and comment on filings in advance. In addition, the sponsor should have the right to designate countries in which applications will be filed and, if the university fails or refuses, to undertake such filings (which would be in the university’s name). If the university decides to abandon an application or an issued patent, the sponsor should have the right to pick it up. In any event, the sponsor will pay all of the patent costs, including in some situations past patent costs.

i. Publication of Results. This subject epitomizes the tension between the conflicting missions of the university and the sponsor. As stated in the MIT Guide, an overriding policy is the “prompt and open dissemination of the results of M.I.T. research and the free exchange of information among scholars.” The Guide goes on to state that “technology transfer is . . . subordinate to education and research.” Therefore, “dissemination [publication] must . . . not be delayed beyond the minimal period necessary” to protect the rights of the parties (i.e., to file a patent application or make some other protective IP filing). Most if not all universities have similar policies. If it had its way, the

sponsor would require that all of the results be kept confidential until it chose to make them public. At best, the sponsor can expect to have the right to review and comment on any publication in advance (oral publications are problematic) and to have a delay in publication until protective steps have been taken. Ninety to 120 days overall from the first notice of the proposed publication is about the best that the sponsor can expect.

j. Representations and Warranties. Generally, the university disclaims any representations and warranties about the sponsored research other than to pursue the research with reasonable diligence and to conduct the research following current good laboratory practices.

k. Government Rights. Many universities receive government funding for research. Therefore, a sponsor is very likely to find that a PI and her or his lab is “encumbered” because of prior (which may affect the know-how of the lab) and/or concurrent funding in the same field in which the sponsor has an interest. Fortunately, the encumbrance of government funding is not that burdensome. The Bayh-Dole Act (P.L. 96-517, Patent and Trademark Act Amendments of 1980) created a uniform patent policy among the many federal agencies that fund research, enabling small businesses and non-profit organizations, including universities, to retain title to inventions made under federally-funded research programs.⁵ The act encourages universities to collaborate with commercial concerns to promote the utilization of inventions arising from federal funding. The trade-offs for letting universities take ownership of government-funded inventions are that the government retains a non-exclusive license to practice the invention throughout the world and the government retains march-in rights. The march-in rights give the government the right to take back the invention if it is not being effectively commercialized. I am not aware of any instance of the government exercising this right, although I have heard that it may have been threatened in one case. In addition, the act now requires, as a result of subsequent amendment, that any product covered by a government-funded invention that is sold in the United States must be substantially manufactured in the U.S. This may be problematic if the commercial licensee of the university is a foreign entity.

3. If a client is considering a sponsored research program at a university, one of the first steps in the lawyer’s preparation should be a visit to the university’s website. Most universities, especially those actively involved in sponsored research, post their technology transfer policies online. Many also have forms of their agreements online.

E. Industry-Industry Sponsored Research

1. These would typically be between big pharma, as sponsor, and small biotech or big biotech (one with cash), as sponsor, and small biotech. The principal reasons for the sponsor are generally one or more of the following: diversification of research activities; lead compound identification; taking over development of a lead that the other party is unable to pursue; or product diversification. These arrangements are often more collaborative than industry- university arrangements and can involve cross-licensing, co-marketing, and division of the research and development functions between the two parties based on their capabilities. The other party, usually a small biotech with one product or some research technology, enters these

arrangements for the funding to develop its product or validate its technology. If the arrangement is successful, it can be the springboard to the development of other products and services. The history of ArQule, Inc. (www.arqule.com) is a good example of a company that is progressing from a company with research technology to a developer of proprietary pharmaceuticals products.

2. The agreements covering these arrangements are as diversified as the arrangements themselves. The Sample Collaboration and License Agreement included in the Appendix is a redacted version of a real agreement. In this case, the sponsor engaged the biotech company to use its IP to identify a lead candidate for a specified disease indication. The agreement provides for a division of labor between the parties, with the biotech company responsible for the research phase, both parties participating in the pre-clinical program, and the sponsor, which is a big pharmaceutical company, responsible for the clinical and commercial programs.

3. The Sample Collaboration and License Agreement, as its name indicates, also includes a license and provisions regarding manufacturing. The elements of the agreement that govern the research and development programs are very similar to and involve the same considerations as those discussed above for industry-university SRAs. One issue that is generally not an issue in industry-industry agreements is publication of results. In the commercial context, the parties are able to agree to keep the results of the research confidential and to agree on how and when any results will be disclosed.

4. In these arrangements, due diligence on the part of the sponsor is also critically important, as often small biotech may have licensed in some of the IP that it proposes to license to the sponsor.

F. Industry-Government Sponsored Research

1. Our federal government has an established policy, supported by laws and executive orders, to transfer government-developed technology to the private sector, including industry. For an overview of government policy, laws and executive orders in this area, an excellent resource is the Green Book—Federal Technology Transfer Legislation and Policy prepared by the Federal Laboratory Consortium for Technology Transfer, which can be accessed online at www.federallabs.org.

2. One way that industry can access federal government technology is by sponsoring collaborative research at a federal agency or department. In the life sciences field, the National Institutes of Health (“NIH”) and the National Science Foundation research centers are probably the prime agencies.

3. Sponsored research with the government is generally conducted under a Collaborative Research and Development Agreement or CRADA. While each agency has its own form, they are generally substantively the same. The NIH/Public Health System model CRADA (“Model NIH CRADA”) is included in the Appendix.

4. With a couple of exceptions, the substantive provisions of a CRADA are similar to those of an industry-university SRA, as discussed above. Two significant exceptions are the grant of rights to the government in the sponsor’s IP that is developed in the course of the CRADA and the right of the government to grant third party licenses if the sponsor is not fulfilling its commercialization obligations (see sections 7.4 and 7.5, respectively, of the Model NIH CRADA).

5. As suggested above in the context of industry-university sponsored research, if a

client is considering collaborative research with a government agency, one of the first stops is the agency's website, which should include policies and forms. A suite of NIH forms, which are also available at www.nih.gov, are included in the Appendix.

II. University and Government License Agreements

[Author's note: A discussion, even a summary one, of the major provisions of license agreements is beyond the scope of this article and, indeed, of this program. A Sample University License Agreement is included in the Appendix. This is a redacted version of a real license with a university and includes all of the provisions that would customarily be included in a university license. A license with an agency of the federal government would be substantially similar, but would also include provisions relating to march-in rights, substantial manufacture in the United States, and reservation of rights for research purposes. See the NIH Model License Agreement included in the Appendix. The following section of this article and related portion of the program will address only the requirement to commercialize the subject matter of the license.]

A. The mission of a university and of our federal government is to make its research and knowledge available for the benefit of the general public. Stated differently, a university or the government does not want the subject invention of a license to "sit on the shelf" of a licensee.⁶

B. Therefore, a university or the government will often require that a detailed development and commercialization schedule be built into the license agreement. If the licensee fails to meet the schedule, it will be in default under the license and risk termination of the license, loss of exclusivity or some other penalty. See, for example, sections 13.02 and 13.05 of the NIH Model License Agreement. The solution in the Sample University License Agreement is somewhat unusual. It does not contain a specific development schedule (earlier licenses with the same university did), but does provide for increasingly higher annual license fees, which are intended to operate as a disincentive to the licensee to not develop the subject invention.

C. Typical development benchmarks for a pharmaceutical product, the achievement of which generally triggers a milestone payment to the licensor⁷, are some or all of the following:

- Identification of lead candidate for development
- Filing of IND or equivalent
- Completion of Phase I clinical trials
- Completion of Phase II clinical trials
- Completion of Phase III clinical trials
- Filing of NDA or equivalent
- Approval of NDA or equivalent

The development schedule requires the sponsor to achieve each milestone within a specified period of time (except for the first one, measured from the date of achieving the prior one). Given the unpredictable nature of the pharmaceutical development process and the severity of the penalty for failing to achieve a development benchmark (for example, loss of the license), these time frames are the subject of extensive negotiation.

D. In pharmaceutical licenses, the three phases of the clinical trial process are often used

as development benchmarks and/or triggers for milestone payments. The license agreement should be clear whether these are achieved by “completion” or “satisfactory completion”. The licensee would prefer the latter, as it would indicate that the development is progressing satisfactorily. The licensor, on the other hand, would obviously prefer the former because the licensor will be paid the milestone payment even if the licensee is not satisfied with the results of the clinical trial. In order to avoid the possibility of disagreement over what constitutes “satisfactory completion”, I have sometimes provided that commencement of the next phase of the clinical trials is deemed to evidence satisfactory completion of the preceding phase (e.g., commencement of Phase II clinical trials means that Phase I clinical trials have been successfully completed).

E. The lawyer should try to be creative in crafting “penalties” that are less severe than termination of the license for failure to meet development benchmarks, particularly in the later stages of the development process. Imagine a client losing a license agreement in its entirety for failing to achieve by a week a benchmark with a long performance time (a year or more is not uncommon for pharmaceutical development benchmarks) even though the client had diligently tried to achieve the benchmark throughout the entire period.

III. Clinical Trial Agreements

[Author’s note: These agreements govern the conduct of the clinical (human) trials that are a prerequisite to regulatory approval of a new pharmaceutical product or medical device. The terms of these agreements are often dictated by the site at which the clinical trial is being conducted, especially if the site is a prominent teaching hospital. On the other hand, if the study is to be conducted at multiple sites, it is advisable to have a template agreement for use at all sites in order to achieve some degree of uniformity. In this situation, it is advisable to craft a template agreement that the lawyer is confident will be generally acceptable to the most exacting (in terms of agreements) of the prospective sites. The Sample Clinical Trial Agreement (“Sample CTA”) included in the Appendix is an amalgam of CTAs used by several teaching hospitals. If a client is considering entering a clinical trial agreement, the lawyer should consult the hospital’s website or call the clinical trial oversight office to see if the institution has a model agreement. The following is a brief discussion of a few key terms common to CTAs.]

A. Publication of Results. A hospital’s mission in this regard is similar to that of a university—to publish the results of its work. This issue is generally dealt with in the same manner as it is in an industry-university SRA. See section 2.2 of the Sample CTA. In a multi-site study, publication of results by an individual site/PI is delayed, usually for up to 18 months after completion of the study by all sites, to permit a joint multi-site publication.

B. Who Owns What. The data from a clinical trial is collected at the site by the PI on case report forms (“CRFs”) approved by the sponsor. Generally, the sponsor owns the completed CRFs and all of the data from the study (which can have real value). The hospital owns the patient medical records, the PI’s research notebooks and related documentation, and all intellectual property resulting from the study, usually subject to an option to the sponsor to take a license of the IP. See section 2.1 of the Sample CTA.

C. Indemnification; Insurance. The sponsor generally must indemnify the PI, the hospital and its trustees, directors, officers, employees, etc. from all loss or damage incurred as a result of their undertaking the clinical study, except for loss or damage directly caused by their negligence, reckless misconduct or intentional misconduct or their failure to adhere to the terms of the protocol for the clinical trial or to the terms of the CTA. The sponsor will also undertake to cover the cost of care and treatment of any injury or side effect to any patient participating in the clinical trial (usually with offset for any health insurance recovery). The sponsor will be required to carry a specified amount of liability insurance specifically covering clinical trial activity of the sponsor.

APPENDIX

Copies of the appendices to the article are available upon request to Jaclyn Braga at jbraga@morse.law

I. Guide to the Ownership, Distribution and Commercial Development of M.I.T. Technology

II. Sample Industry-University Sponsored Research Agreement

III. NIH Model CRADA

IV. NIH LOI for CRADA

V. NIH Model Materials-CRADA

VI. Sample Collaboration and License Agreement

VII. Sample Industry-University License Agreement

VIII. NIH Model Patent License Agreement

IX. Sample Clinical Trial Agreement

Footnotes.

1 This article focuses on the commercial or industrial for profit company as sponsor, but it should be noted that our federal government provides enormous funding for sponsored research. See AUTM statistics below, for example.

2 I rarely use the word “always” when describing anything in the practice of law (there are generally exceptions to everything), but in this case I think the term applies.

3 According to its website, AUTM includes among its members more than 300 universities, research institutions and teaching hospitals.

4 When I use the term “university” I am also referring to hospitals and research institutions, the typical “other parties” to sponsored research arrangement.

5 Previously, the government owned the inventions and might license to the university, which in turn might sublicense to industry—a cumbersome process.

6 Conversely, in certain circumstances, a commercial licensee might want to do just that for defensive reasons, such as building a wall around patents it may already own or control or to prevent a competitor from having access to the subject invention.

7 This is because the achievement of the benchmark validates the value of the subject invention; milestone payments generally increase in size over the development schedule as the subject invention is proved “more valuable” as it approaches commercial realization.