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## REPORT

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### ACADEMIA AND INDUSTRY: THE COLLABORATIVE RESEARCH ARRANGEMENT

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University research collaborations with industry, including those between academic medical centers and large pharmaceutical companies, continue to attract a great deal of attention. A recent example is the announcement of a significant transaction by Beth Israel Deaconess Medical Center and Takeda Chemical Industries Ltd., potentially yielding in excess of \$13.7 million over its term,<sup>1</sup> and at the same time a questioning of whether large collaborative university-industry research transactions are fading away.<sup>2</sup> Whatever the trend, it seems unlikely that such arrangements will disappear, particularly if the rate of National Institutes of Health spending on research levels off.

This article focuses on the key elements of an academic medical center ("AMC") collaborative research agreement ("CRA"). Such agreements, typically between an institution and an industry collaborator, will continue to have the potential to not only be significant sources of income for an institution, but also, to provide an opportunity for real scientific exchange between basic and translational research efforts as well as a window to the commercial world. To satisfy both parties, however, it is important to be quite focused on the goals of the effort, and its scope and duration.

<sup>1</sup> Krasner, Jeffery, "Beth Israel Lands Research Deal," *Boston Globe*, Jan 10, 2003.

<sup>2</sup> "Last of the Big-Time Spenders?" *Science*, Vol. 299, Jan. 17, 2003.

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#### The Parties and the Research Program

While the parties to the CRA from an entity standpoint are easy to define, the specific researchers and the laboratories to be engaged are at its core. As a result, both sides should think through carefully who the key participating individuals will be. On the institutional side, this should result in a specific designation of one or more principal investigators ("PIs") and their laboratories, and the research efforts (the "Research Program") should be defined with as much detail as possible to ensure a clear meeting of the minds. Such program definition would include, for example, naming research areas by identifying the specific enzymes involved, the experimental model being used, the experimental plan or approach to be pursued (e.g., "a proteomics approach in conjunction with our specific transgenic or gene knockout mouse models"), and future study directions depending upon the results achieved. The definition of future study directions should include the extent of efforts to be taken in the event the desired goals are not achieved, or if for reasons that might not be easily predicted (e.g., Food and Drug Administration or National Institutes of Health intervention), a particular aspect of the Research Program cannot be pursued. If only a specific hypothesis or research aim is to be identified or tested, the description of the Research Program should state this. Provision also must be made to take into account the possibility of a change in PIs over the term of the relationship.

The collaborator should identify its team as well. This typically will consist of at least a named senior representative (e.g., the vice president for research), and may extend to a group, or even a scientific advisory board. Whatever the approach, there should be definition given with respect to such matters as:

a. an ongoing method of informed communication and collaborative scientific interaction that is not overly intrusive, yet meets the goals of the parties (e.g., "The collaborator's designated representative may consult informally with institution's representative regarding the Research Program on a reasonable basis.");

b. the need for formal reports (e.g., "Each of the named PIs shall provide semi-annual reports of the progress of their efforts under the Research Program. In the event a specific experiment is concluded, the results shall be communicated to the designated representative within 30 days of completion.");

c. the ability of the collaborator to request any changes in the Research Program over its course and any obligations to make such changes (e.g., "The parties shall confer in good faith with respect to any proposed changes to the Research Program. Absent agreement by both parties, there shall be no obligation to make such requested changes.");

d. commitments to host or attend scientific meetings; and

e. the commitments of the collaborator to provide directly or indirectly (e.g., through sublicenses) technology that may be necessary to effectively pursue or complete the Research Program.

Finally, in defining the Research Program, it will be important to recognize the mission of the institution as one to advance knowledge and the overriding need to conduct the Research Program, under the direction of the PI, in a manner consistent with the rules of the institution (e.g., conflicts of interest policies) as best suited to carry out the mission. And, of course, there can be no guarantees of results.

### Budgeting and Compensation

Detailed definition of the Research Program allows creation of matching operations and capital budgets, discussion of funding needs, and timing over the CRA term. The agreement reached should recognize the direct and indirect costs of the effort, as well as the increasing costs likely to be incurred over the term. An accounting system will be necessary that can separately account for expenditures of the funds in accordance with the approved budgets. A system also may be required for time and effort allocations. From the institution's perspective, however, there should be built-in flexibility to allow rebudgeting within cost categories, and some leeway on budgeted numbers within reasonable time periods. A provision addressing either significant savings ("can be retained by further research within the Research Program") or overruns should be included.

Where capital expenditures or use of the equipment is funded by the collaborator, the CRA should specifically set the terms for the agreed ownership (e.g., "Institutions shall retain title and ownership rights to all equipment or supplies purchased for, used, or fabricated in connection with the Research Program, whether or not funded in whole or in part with funds provided by the collaborator.").

The timing of payments is, of course, critical. In the ordinary course, the institution will want a significant initial payment in recognition of the costs already incurred to be able to create the Research Program, as well as in consideration of the exclusivity inherent in such arrangements. Ongoing payments, however, may well be based upon a wide variety of factors:

a. There may be a set of specific Research Program related payments, for example, the initiation of the various phases of the program.

b. The parties likely will agree to a series of commercial milestone payments based upon an agreed set of events.<sup>3</sup> Because it is often the goal from the collaborator's perspective to achieve results that can be commercialized, a trigger point within the CRA will be a grant of rights to the collaborator.

### Grant of Rights

In addition to scientific exchanges, the goal of industry-AMC collaboration is, of course, the development of commercial products. The typical model to implement this goal is a grant of exclusive rights to develop technologies, invention, drug targets, enzymes, patents, and the like. A collaborative arrangement, therefore, might provide an "exclusive option to negotiate an exclusive license to make, have made, develop, or sell or practice any invention created as a result of the Research Program during its term for twelve months after its conclusion."

The option term will be the subject of negotiation, as will the license terms. Typically, the CRA will set a defined period from the disclosure of an invention or process by the institution to exercise the option to license. A failure to timely exercise these rights and, thereafter, pursue patents and commercialization within an agreed time frame, should result in a waiver or forfeiture of the exclusive (or total) option right, and a revision of rights to license and commercialize to the institution. Where joint inventions are involved, the parties might agree that each will have the rights to license to third parties in accordance with an agreed royalty arrangement or a complete freedom to pursue development.

Exercise of any option right should be subject to two limitations. First, to the extent the Research Program is funded in part by other sources, the claims of such other sources must be considered. The most important of such sources would be NIH funding. In such event, consideration must be given to the mandate that "unique research tools" remain available to the greater research community.<sup>4</sup> Secondly, the institution itself will want to retain the right (free of cost or limitation) to use Research Program defined materials or inventions<sup>5</sup> in the ordinary course of its research and education activities.

Pricing for the execution of a license may adopt a variety of approaches, all designed to be enforceable, rather than be construed as mere "agreements to agree." Factors to be considered actually may resemble a grid, with floors and ceilings depending upon the particular product or application involved (e.g., therapeutic versus prophylactic products, relative contributions of the parties, market size, number of competitors, etc.). At the end of the negotiations, however, if agreement is

<sup>3</sup> It is beyond the scope of this article to explore the multitude of milestone payment arrangements that exist. Typical payment milestones would, however, at least be initiated upon an agreement reached to grant a license to the collaborator, through phased trials, and into actual marketing and distribution.

<sup>4</sup> Rights also must be consistent with Federal Patent Policy, 35 U.S.C. §§ 200 et seq.

<sup>5</sup> Inventions are "any invention or discovery, whether or not patentable, conceived or reduced to practice, in the performance of the Research Program."

not reached, there must be an agreed methodology for resolution of the necessary terms to have a binding agreement. Options might include an agreed dispute resolution process, or the ability to simply match (within 60 days) the terms at which the institution would grant a license to a third party following the conclusion of the negotiation period.

Finally, the parties actually may wish to provide a practical limitation to the scope of the potential revenue-generating arrangements—a limitation to rights to inventions that actually are patented. Hence, to the extent there are inventions that are not patented, such inventions might be available on a nonexclusive license basis to the collaborator.

### Term and Termination Provisions

The term of the CRA will be the product of discussions concerning a variety of factors, including:

- a. the length of time reasonably necessary to complete the research program;
- b. the price to be paid over the term; and
- c. the potential results of the various aspects of the program.

One common approach is to establish a base term (e.g., three to five years) with the possibility of extension based upon results and agreed-on additional payments.

The CRA should state whether the option period expires when the CRA terminates, or the terms and conditions under which it may be extended as well. If termination may be based upon the results of an (independent) scientific progress review, the conditions for that review should be evaluated at the outset.

CRA's will, of course, have standard provisions that cause terminations (e.g., material nonperformance), which may include the failure to agree on a replacement PI should that become necessary (e.g., departure to another institution). Without cause terminations during the initial term or base period are to be avoided, if for no other reason than to avoid wasting the effort required to put the CRA in place. One area, however, of increasing discussion as a grounds for termination is the reputation of the parties. While defining specific events that might allow for a "for cause" termination in this area can prove difficult, consideration can be given to some benchmarks such as loss of program certifications, NIH or other governmental orders affecting the ability to conduct research at the institution in any related area, and the like.

In the event of termination, notice periods—which allow the pursuit of other funding sources, adjustment of personnel workloads, and completion of related capital obligations—all are factors that must be considered.

### Intellectual Property Rights and Protections

The structure of the CRA typically will require that all inventions related to the Research Program to which the institution could claim ownership will, in fact, be owned by the institution. "Credit," authorship of related publications, and distribution of institution pro-

ceeds will be allocated in accordance with the existing policies on this subject.<sup>6</sup>

Because commercialization will be in the hands of the collaborator in the first instance, if the collaborator exercises its rights to license an invention, it will be responsible for pursuing the appropriate domestic and foreign patent applications. It will be the institution's responsibility to ensure an appropriate disclosure process to allow this to occur. If the collaborator indicates no desire to pursue intellectual property ("IP") protection, then the right to do so should pass to the institution. The costs of pursuing IP protection often will become a charge on future distributions, potentially up to agreed limits or over the course of an agreed time frame or revenue stream.

Notwithstanding those processes required to protect patent rights, and the provisions, which will be in the CRA to protect confidential information that may be exchanged, the CRA must provide the rules applicable to publications. This will require a process for review and comment by the collaborator of information for a limited time frame and with enough time prior to publication (e.g., 30 days from receipt) to review the material and request deletion of proprietary or confidential information, or to allow a patent application to be filed (e.g., allowing an extension of publication deferred for an additional period not to exceed 60 days).

### Administrative Provisions

*Use of Names, Publicity and Marketing:* The parties will need to reach agreements with respect to public communications regarding the existence of their relationship. Because of the nature of the institution, it is likely to require that "no press release, advertising, sales literature, or other statements or materials making any reference to the institution or its employees, affiliates, contractors, medical staff, or investigators, may be created or distributed without the express written consent of the institution." In this regard, the parties typically will agree to joint announcement of the collaboration, inventions, and even milestone achievements. The institution also typically will acknowledge the collaborator's support of the CRA-related Research Program and investigations in scientific publications and other scientific communications.

*Indemnification and Insurance:* The parties likely will agree on reciprocal basic indemnification commitments and insurance obligations. Indemnification obligations will need to be negotiated with respect to issues arising from licensing agreements or patents that arise from the Research Program.

*Dispute Resolution:* The parties will agree on a mechanism, location, and applicable law to address disputes. Because the desire is to achieve a long-term collaboration, it is desirable to require an initial referral of disputes to senior officials within each organization prior to the commencement of formal claim filings. Because of the nature of the potential disputes, and relative perceptions by the public of the parties, the institution likely will push hard for a local forum.

<sup>6</sup> See e.g., "The Research and Intellectual Property Policy," 1 MRLR 472, 10/16/02.