

Transferring Biotechnology

Characteristic features and problems are outlined from U.S. perspective

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Many considerations in licensing biotechnology are the same as for licensing other advanced technologies. However, there are some very significant differences.

In licensing of any technology, including biotechnology, the underlying business purpose dictates the basic provisions and considerations for the licensor and the licensee to reach a mutually acceptable agreement. An underlying business reason exists for both the licensor and the licensee to enter into an agreement. Moreover, these underlying business reasons will mean a different strategy for the licensor than for the licensee. Important considerations for both the licensor and the licensee are what a license agreement provides to each.

Prior to entry into licensing negotiations in biotechnology, it is important for both the licensor and the licensee to consider thoroughly and evaluate their underlying strategy.

Important considerations for the licensor include

- The choice of the licensee and his capabilities.
- Scope of business interests of the licensor versus the business interests of the licensee.
- Business and technical ability of the licensee to meet the obligations set forth in the agreement.
- Government policies, particularly restrictions, on technology transfer.
- Tax considerations in technology transfer.
- Limitations on foreign currency convertability/transfer.

Importantly, the ability of the licensee to make the agreement a technological and commercial reality, mutually beneficial to both the licensor and the licensee.

Important considerations for the licensee include an evaluation of:

- The nature of the licensor's technology including the effectiveness and efficiency of the technology.
- The status of the licensor's technology and how far the technology has been developed by the licensor, e.g. lab scale, pilot plant, semicommercialization, regulatory approval, etc.
- Costs of production and use of the technology, for example, product profitability or process savings.
- Size of potential domestic and foreign market and

reasonably anticipated market share that could be developed.

-Potential licensee investment necessary to exploit the licensor's technology including anticipated research and development costs, regulatory approval expenses and capital investment expenditures.

-The costs of marketing necessary to exploit the technology.

-The novelty and uniqueness of the technology, including consideration of present and potential future alternatives to the licensor's technology.

-What patent position exists or is available, its breadth in terms of scope and geographic coverage and enforceability.

-What degree of exclusivity arises and to what extent exclusivity is dependent on a patent position and/or trade secrets.

-Are there any unique economic factors which might alter the commercialization of the technology.

-Are the potential products regulated by a government regulatory agency, and if so, what is the stage of the technology in relation to obtaining regulatory approval for marketing, i.e. has any first-stage or second-stage clinical testing been conducted?

License negotiations proceed markedly more smoothly in any licensing negotiation when both of the potential licensor and the potential licensee earnestly desire to enter into a license agreement. Also, the preparation of the actual license agreement to be executed by the parties proceeds more smoothly once all of the business factors such as scope of licensed rights, territories, royalty rates, and potential contingencies have been discussed and agreed to in principle. Further, license agreement negotiations are facilitated when both parties enter them on the basis that the license agreement should be "fair" to both parties. Often this requires the licensor to recognize the reasonableness of the licensee's position and, conversely, this requires the licensee to recognize the reasonableness of the licensor's position.

As one final consideration in licensing, it must be recognized that biotechnology licensing differs in one major respect from the licensing of all other types of technology, even high technology, since biotechnology relates to living organisms that are capable of reproduction.

Biotechnology has been broadly defined as including:

... any technique that uses living organisms (or parts of organisms) to make or modify products, to improve plants or animals, or to develop microorganisms for specific uses.¹

Since living organisms reproduce, licensing of technology

*Sughrue, Mion, Zinn, Macpeak & Seas, Washington, D.C.; paper presented at LES International Conference, Tokyo, 1985.

1. *Commercial Biotechnology: An International Analysis* (Washington, D.C., United States Congress, Office of Technology Assessment, OTA-BA-218, January 1984, page 3.)

involving living organisms and/or parts thereof involves many different considerations than are involved in licensing of more traditional technology. The living organism is literally the entire biotechnology "factory." A technology transfer can thus include a transfer of intellectual property rights where the development transfer involves patent, trade secret and/or know-how rights. The technology transfer can also involve a transfer of personal property rights where the development transfer involves biological materials such as organisms, cell lines or parts thereof, e.g. plasmids, gene constructs, expression or promotion vectors, etc. As a result, control by the licensor of the licensor's technology after licensing may be more difficult after transfer, and importantly, after a license termination where biological materials, i.e. the biotechnology factory, have been transferred. Thus, a licensor must consider the value of his intellectual property rights in relation to his personal property rights to assess the value of the biotechnology he is planning to license and his risks in doing so.

LICENSING PROVISIONS AND CONSIDERATIONS

The following provisions are considered appropriate for a high-technology license agreement and, specifically, unique problems and considerations that exist with respect to the licensing of biotechnology are discussed.

Introductory Clauses

In most instances, the introductory clauses, or as lawyers like to call them, the "Whereas" clauses, set forth the underlying desires and objects of the parties to the license agreement. They are in general relatively easy to formulate. Even so, they should be drafted with care since if the intent of the parties is ever an issue, these clauses in the license agreement may be relied upon for interpretation as to the intent of the parties to the agreement.

Definitions

The clarity of any license agreement, whether biotechnology or not, depends on whether the terminology used in the agreement is clearly defined and whether the definitions used have been fully considered and carefully drafted. Moreover, the ability to understand the provisions of the license agreement and the minimization of potential controversies in the future as to interpretations of the provisions of the license agreement are greatly dependent upon the clarity of the definitions used.

The definitions define the subject matter of any agreement. What is to be licensed and the obligations and the rights of the parties are set forth in reference to the definitions. Accordingly, in a biotechnology license agreement, the subject matter of the technology being licensed should be clearly defined.

The licensing of a biotechnology development may involve licensing of intellectual property rights, including patents, trade secrets and know-how, relating to the development and the licensing of the right to use and replicate biological materials such as microorganisms, cell lines, plasmids, DNA constructs, etc., and sometimes to sell them. As a result, clear, and preferably separate definitions as to the nature and scope of the intellectual property rights and as to the nature of and identifying characteristics of biological materials should be set forth in the licensing agreement.

Carefully crafted definitions are very important where the license agreement will grant rights of a different scope to various aspects of the technology. For example, the licensed technology may involve a monoclonal antibody produced by a newly developed hybridoma. The licensor may be willing to permit the licensee to make, use and sell the antibody. However, the licensor may only be willing to allow the licensee to make and use the hybridoma to produce the monoclonal antibody.

The licensor may not be willing to grant rights to the licensee to sell the hybridoma capable of producing the monoclonal antibody. In this situation, it is essential that the agreement specify the nature of and the difference in the licensed rights as to the monoclonal antibody and the licensed rights as to the hybridoma. Clear and separate definitions of the monoclonal antibody and the hybridoma producing the antibody facilitates the ability of the licensor to clearly establish the rights granted and the differences in the rights granted.

Clear and separate definitions are also needed to define different aspects of the technology being licensed where a different royalty base will exist depending upon how the licensed subject matter is utilized by the licensee. Definitions for "licensed biological materials," "licensed cell line," "licensed microorganism," and "licensed product" can be included to distinguish aspects of the technology.

Definitions

The agreement should define what existing patent rights and existing patent applications are included. If proprietary information such as trade secrets and know-how is involved in the licensed technology, a definition of the nature and scope of the proprietary information should be carefully considered and included. "Licensed patents," "licensed patent applications," "licensed trade secrets," and "licensed know-how" are appropriate definitions to include.

Further, since genetic engineering technology can be utilized by a licensee for production of end products or consumer products, to develop microorganisms and cell lines to produce end products, to produce products in bulk for subsequent utilization by a third party in producing the ultimate end product and to produce products which are used in-house in the operation of in-house processes, clear definitions as to (1) "licensed end products"; (2) "licensed basic genetic products"; (3) "licensed process improvement products"; and (4) "licensed bulk products" should be set forth.

In biotechnology, to explain these concepts further, "end products" are basically products which are used by the ultimate end user where the products are destroyed in use, the products are consumed in use, or the activity is eliminated in use. Examples include insulin, vaccines, antibodies, hormones and other biological active materials.

Basic genetic products include recombinant DNA (rDNA), plasmids, gene constructs, chimeras, and microorganism transformants.

Process improvement products can be products which improve a process and result in a cost saving. For example, if the technology provides the ability to produce an enzyme for use in an in-house process that is less expensive than or is more efficient than enzymes from other sources, this would result in a cost savings and a process improvement.

Bulk products are basically those products that are pro-

duced in bulk and are to be sold to another manufacturer for further processing rather than directly to an end-product user. These types of products could be monoclonal antibodies, hormones and vaccines that would be produced in bulk but ultimately transferred to another manufacturer who would market them, for example, in a kit form or in a unit dosage form for ultimate end use by the consumer.

Clear definitions as to the nature of these types of products need to be set forth in the license agreement since the nature of the rights granted may differ and field-of-use restrictions and/or different royalty rates may apply to each.

Restrictions

In addition, if the licensed rights involve territorial restrictions or field-of-use restrictions, the geographical territory and the specific field or fields of use, with exemplification in the agreement or in an appendix to the agreement where necessary for clarity, are important definitions to consider. If territorial limitations are extensive, it may well be desirable for these definitions to be set forth in a separate section of the license agreement.

In summary, the definitions included in a license agreement are extremely important and thorough, and deliberate consideration of the definitions included is crucial for both the licensor and the licensee. Definitions to be included in the agreement are generally arrived at during negotiations between the parties as the license agreement is being put together. As a result, the legal and technical ramifications of the definitions under consideration as to the licensed technology need critical review by the licensor and licensee both from the standpoint of breadth of the licensed technology and activities permitted and from the standpoint of restrictions on the licensor's and licensee's flexibility as to technical and commercial activities "in competition with" the licensed technology.

Ownership of the Licensed Technology

In addition to the definitions discussed above, it is highly desirable for the agreement to set forth that the licensor has title to the technology and any tangible biological materials involved and to insure that the licensee recognizes that title to the licensed technology lies in the licensor.

Ramifications as to title need to be considered as to the licensing of technology where the underlying technology involves transfer of a unique plasmid, transformed microorganism, etc., containing, for example, a rDNA sequence developed by the licensor. Although the rDNA sequence developed by the licensor may be well defined in the agreement, who owns or has rights to the "remaining DNA" of the unique plasmid or transformed microorganism containing the rDNA sequence may not be well defined. Thus, the relative rights of the licensor and licensee as to title to a discovery of a unique or commercially advantageous characteristic in the "remaining DNA" needs to be taken into account.

As a result, if the biotechnology licensed involves the use of biological materials such as vectors, DNA constructs, plasmids, transformant microorganisms or cell lines, hybridomas, etc., it is highly desirable to set forth that the licensor has full title to these biological materials and all parts thereof and, potentially, even title to the

licensor in products produced from biological materials. The agreement should define the licensor's ownership in the transferred biological materials. The agreement should also clearly set forth who has title to variants, mutants, improved DNA constructs, vectors, transformant microorganisms, cell lines and hybridomas that might ultimately be developed therefrom or importantly, may arise out of the licensee's efforts. Otherwise, title may be dependent on who developed such, or who has custody and control over such.

Rights, Ownership

The licensee should insure that the licensor has full right, title and interest in the technology being transferred, including any unique organisms, cell lines, plasmids, etc., involved in the technology transfer. The licensee should determine whether the technology was developed through funding by a governmental agency. If so, can the licensor transfer full rights on an exclusive basis, and are there are limitations on the length of time a licensor can grant exclusivity?

In the United States, often a university licensor has developed technology using U.S. Government funding, such as funding by the National Institutes of Health or the National Cancer Institutes. While U.S. law permits universities to take title to such inventions and to license and exploit them, restrictions may exist on the university as licensor of technology developed in whole or in part with U.S. Government funding.

It is of particular importance for the licensee to insure as to any microorganisms, cell lines, plasmids, etc., included in and transferred with the technology that the licensor has full ownership rights in these biological materials. Full ownership rights and the ability of the licensor to license and transfer them for use may be more important than any intellectual property rights involved in the licensed technology. Otherwise, clouds on the title to the underlying biological materials necessary to exploit the licensed technology may exist leading to controversies and litigation of the type involved in the Genentech/Hoffman LaRoche/University of California litigation on the KG-1 interferon cell line and the University of California-San Diego/Hagiwara hybridoma litigation. The derivation of any biological materials being licensed should clearly be explored by the licensee to assess the nature of rights he is being granted and whether they, in fact, can be granted.

These areas should be discussed and resolved during licensing negotiations. The potential licensee should satisfy himself that the licensor has full rights to license and transfer the biotechnology, or if less than full rights, the extent of the rights the licensor has.

As protection, the licensee should insure that the license agreement contains warranties and representations that the licensor has the ability to transfer the rights to the technology being licensed. Otherwise, the licensee may find himself without easy recourse as to the obligations, particularly monetary payments, commercialization obligations, etc., to the licensor that the licensee has assumed under the terms of the agreement.

Nature of License Rights/Grants

The license agreement should set forth whether the licensee is granted exclusive rights or nonexclusive rights

to the technology. If part of the technology is to be exclusively licensed and another part of the technology is to be nonexclusively licensed, this should be clearly set forth and delineated.

Any territorial restrictions should be recited and, further, any field-of-use restrictions should be well defined in the license grant. Territorial restrictions as to the United States are specifically sanctioned by U.S. patent statutes (35 U.S.C. § 271). Geographic limitations as to particular countries or areas of the world are permissible under U.S. antitrust principles if they are a result of the exercise of valid patent rights and are not for the purpose of a simple division of world markets to lessen competition.

Field-of-use restrictions, e.g. where a license on a biologically active compound would limit its use to veterinary applications, to human applications, to certain product types, etc., are legally proper and enforceable and do not violate U.S. antitrust laws where the restrictions on use are inherently within the scope of the U.S. patent rights granted.

The licensed rights should clearly define whether the rights are granted as to the licensor's then-existing developments, issued patents and pending patent applications. This can be easily accomplished by listing the licensed patents and pending patent applications in an appendix to the agreement. The agreement should also define the rights of the parties as to future improvements by the licensor upon which patents might issue or patent applications be filed. Does the licensee receive rights under these future patents and applications or must a new agreement be negotiated and entered into?

4 Further, the license agreement should define whether the licensed rights extend to an affiliate of the licensee. That is, may the licensee sub-license an affiliate? If so, a clear definition of what constitutes an affiliate of the licensee should be a part of the agreement.

Definitions

Importantly, the licensed rights should define whether the licensee will receive the full scope of rights, i.e. to make, use and sell in all fields of use and in all territories or whether there are any restrictions on any of these activities, restrictions as to certain territories or restrictions as to fields of use. For example, if the underlying technology involves a transformant microorganism, cell line or hybridoma, does the licensee have the right to sell such or is the license limited to simply marketing the products produced by the microorganism, cell line or hybridoma.

Thus, the nature of rights granted and their scope as to existing and future patents and applications, as to existing and future trade secrets and know-how and as to any existing and future underlying biological materials should be clearly and separately delineated, particularly if the scope of the rights licensed differs as to these aspects of the licensed technology.

In the event the licensee is granted territorial rights or worldwide rights, and if it becomes necessary for an affiliate of the licensee in a particular country to enter into a license agreement directly with the licensor because of the rules and regulations of that particular country, the license agreement should provide that the licensee's affiliate will be so licensed directly. Obviously, from the licensee's standpoint, the licensee should insure that the

so licensed affiliate should not be required to pay an additional license agreement fee or down payment. The obligation of the licensed affiliate generally is only to pay whatever royalties the licensee in the basic agreement would be required to pay as to comparable activities.

Residual Rights

It is also important for the license agreement to set forth whether the licensor retains any residual rights as to the licensed technology. For a truly exclusive license to the licensee, no residual rights as to the technology or its utilization should remain in the licensor as to a specific territory or as to a specific field of use. However, if the intent is for the licensor to retain rights, then the scope of these retained rights should be clearly set forth in the license agreement.

In summary, the nature of the licensed rights should be clearly defined in unambiguous terms. In most instances, the nature of the licensed rights will be set forth in relation to the definitions of aspects of the technology licensed as to rights licensed under patents, know-how and trade secrets and biological materials and the scope of the rights licensed as to each aspect should be clearly set forth. The rights licensed as to each aspect may be coextensive but the rights licensed may not be.

Title to the Technology Licensed

The license agreement should clearly set forth that the licensor has title to the technology licensed, including clear title to any patents and pending applications, to know-how that might be concomitantly transferred and to any transformants, cell lines, hybridomas, etc., involved. The licensee should insure that no clouds on the licensor's title exist.

In the United States, particularly where a university or other research institution is the licensor and the technology being licensed has been funded in whole or in part by United States Government research funding, residual rights as to a royalty-free license to the United States Government or its contractors exist. Further, until recently, a limitation existed on the time for which an exclusive license could be granted on technology developed using United States Government funding—generally eight years from the date of execution of the agreement or five years from the date of the first commercial sale (unless the licensee is a small entity, i.e. 500 employees or less (full-time, part-time, or temporary on a weighted-average basis), as defined by the United States Small Business Administration, in which case a full patent term exclusive license could be granted). This was changed in 1984 and presently exclusive license agreements for the full patent term may now be granted to any licensee regardless of size on any United States Government-funded development to which the university or research institution takes title. However, the former time limitations may apply to licenses and sub-licenses in effect before this change.

Also, the licensee must recognize that under certain circumstances, the United States Government may force the issuance of additional licenses on technology funded by the United States Government and as a result the license would then become nonexclusive. The United States Government under certain conditions has "march-in" rights as to technology developed with U.S. Government

funding. All of these factors ultimately may affect the exclusivity provided to a licensee even if the licensor is willing to grant an exclusive, nonrestricted license to the licensee on technology developed with U.S. Government funding. The licensee should therefore assess the possibility of future nonexclusivity in determining the value of the technology.

Title in Licensor

As discussed above, from a licensor's standpoint, it is highly desirable to set forth that title to any biological materials such as genes, DNA constructs, vectors, plasmids, transformants and cell lines is in the licensor. Also, the licensor should consider whether, if these replicable biological materials are transferred to a licensee, what type of transfer is involved.

In some instances, an outright sale of these biological materials may be advantageous. In other instances, the licensor may wish to transfer these materials with payment therefor on an installment basis. The ultimate price of the transfer then is paid over a period of time. Advantageously for the licensor, the price of the transfer can be based on the ultimate commercial market value which these materials provide to the licensee. In other instances, the licensor may clearly wish to set forth that as to these biological materials, they are basically leased and no transfer of title to the licensee occurs.

Any potential tax implications and any potential antitrust problems in the various licensed countries should be considered in reaching a decision on the nature of the transfer of biological materials.

Rights to Future Inventions

The license agreement should clearly define whether the licensee is being granted rights to future inventions within the scope of the licensed technology and, if so, what these rights are. Obviously, from a licensee's standpoint, a licensee would wish to insure that a license on future developments within the scope of the licensed technology and covering products that might arise out of the licensed technology are or will be granted to the licensee with no additional payment therefor.

If additional payment is required for these future developments, the license agreement should provide for this to insure that the licensee knows what its potential obligations could be and that the agreement defines the licensor's obligations in licensing future developments and patents and patent applications thereon, etc. It may be difficult to negotiate royalty rates on future unknown developments. Use of a "window," i.e. establishing a maximum and a minimum within which the parties agree the royalty rate will be, is one approach to this.

Future Developments

License agreements often provide that future developments and improvements, whether patentable or not, which are within the scope of the licensed technology inure to the benefit of the licensee without any additional payment of up-front money or increase in royalty rate. These future improvements, particularly if patentable, may extend the term of the agreement if the term of the agreement is defined in relation to the expiration of any patents involved. While the licensor receives no additional

payment for his future improvements in this case, the licensor is benefited because the obligations of the licensee to pay royalties on the technology covered by these future inventions is extended until these new patents expire. The licensee benefits because his exclusivity is potentially extended.

The license agreement should also specify whether a license on any improvements made by the licensee in the licensed technology are granted back to the licensor. In general, grant backs on either an exclusive or nonexclusive basis are not a violation of U.S. antitrust laws as long as their overall effect is not anticompetitive. Fewer antitrust problems are considered to arise if the grant back to the licensor is nonexclusive in nature.

License Issue Fee

Most license agreements provide for a down payment or up-front money to the licensor upon execution by the licensee or within a certain period of time after execution. This can be a one-time payment or, depending upon the circumstances, can be a payment in installments set forth with specific reference to calendar periods or with respect to specific, well-defined benchmarks of a technical, scientific or regulatory approval nature. The amount of this down payment can be quite varied and will depend on the value of the technology from a commercial and technical standpoint.

Considerations as to the amount of the down payment or up-front money include the nature and scope of the licensed technology, its stage of development vis-a-vis commercialization, any governmental regulatory approval for marketing that might be required and the costs involved and whether such has already been obtained, and importantly, the commercial potential of the technology and the degree of exclusivity the technology provides. Use of a commercial consultant or a market survey may be helpful in establishing what amount is reasonable as to the licensed technology.

The up-front money paid to the licensor may be apportioned between patent rights, trade secret and know-how rights and biological material rights. Apportionment may be beneficial from a tax standpoint, and the tax implications of such should be considered.

Royalties

The provisions as to the royalties payable from the licensee to the licensor are very important and should be drafted with care. Considerations include:

—Whether royalties are to be calculated on a percentage basis, generally defined with respect to sales, or on the basis of the number of units sold of various products or uses within the scope of the technology licensed.

—Whether different royalty rates are involved depending on use of the licensed technology by the licensee, e.g. one rate as to end products, another rate as to genetic products, a third rate as to bulk products, etc.

—Whether any minimum annual royalties, often included where the rights licensed are exclusive to the licensee, are involved, and if so, when do they begin, e.g. in the first year of the license, after regulatory agency approval, after the first commercial sale, at a set period of time after first commercial sale.

—Whether a straight royalty based on sales or number of units sold is to be used or whether a sliding scale royalty dependent on volume is to be employed. A sliding-scale

royalty is beneficial to both the licensor and the licensee in that a reduced-royalty percentage for increasing sales is advantageous to the licensee and provides the licensor with potentially larger royalty income, even though at a reduced percentage. With a sliding-scale royalty, there will be an incentive for the licensee toward maximizing his sales or use to benefit from a reduced royalty rate.

—Whether any of the initial license issue fee or up-front money, as well as any of the yearly minimum royalties, are creditable against future royalties. Obviously, credits of up-front money against future royalties are advantageous to the licensee in that his initial down payment or up-front money is potentially recoverable but are also advantageous for the licensor since there is an incentive to the licensee to commercialize and to maximize his commercialization to achieve credit.

—Whether the royalty base is with respect to sales, number of units sold, or some other indicia which are easily and clearly defined from an accounting standpoint.

—Whether more than one royalty can accrue if the technology is covered by more than one patent or application or whether only one royalty is paid regardless of the number of patents or patent applications covering the product or use of the technology.

—Whether, if the product is produced in a “patented” country but the sales occur in a “patent-free” area, how the royalty is to be defined. In this situation, the royalty base can be calculated as if the sales were in a “patented” country or a reduced-royalty rate can be employed.

—Whether the royalty rate is reduced in the event of a loss of exclusivity due to the presence of competition or due to patent invalidation. The reduction can be triggered if the market share of a competitor rises above a certain percentage in the product area involved. With respect to licensed technology that may involve preeminent government rights or government compulsory licensing, a reduction in royalty rates can be provided in those instances where a change in exclusivity arises. A reduction in royalty rates can also be provided for in the event of an invalidation or revocation of previously existing patent rights or claims.

—Whether there is to be a different royalty base on “patented” products from “unpatented” products. Is the royalty base on “patented” products to be payable on the basis of coverage by only issued patent claims or does coverage by pending application claims result in the product being considered a “patented” product? This is an important consideration. In many instances, due to deferred examination in many countries where patent applications related to the licensed technology are on file, patent rights may not well vest until some 6 to 10 years after many foreign patent applications are filed. Until patent issuance or until some patent rights vest, obviously the licensee has no way of enforcing his exclusivity. However, from a licensor standpoint, he will wish to insure a higher royalty rate as to “patented” products in the event that potential patent rights exist due to a pendency of a patent application covering the subject matter licensed in that country of concern.

—Whether transfers, for example, from the licensee to an affiliate of the licensee for ultimate resale, are to be royalty bearing or non-royalty bearing. Many license agreements provide that if the ultimate licensee affiliate is obligated to pay a royalty on the basis of sales as is the licensee, the transfer from the licensee to the licensee's

affiliate is non-royalty bearing.

—How currency exchange conversions based on sales in countries other than the home country of the licensor are to be handled. A specific provision as to currency exchange conversion into home country currency can be provided for by reference to the currency exchange rate quoted on the last day of the applicable period of time for which royalty payments on sales would be due. Also, what happens if export of a foreign currency is prohibited or restricted should be considered.

—How often royalties are to be paid, annually, semiannually, or quarterly. In general, most license agreements provide for a quarterly or semiannual payment of running royalties.

—Whether the royalty rate is reasonable considering the royalty basis, the period of time royalties accrue, the value of the technology, the stage of development of the technology, and the potential market and profitability of the technology.

—If the license is nonexclusive, whether the royalty rates are comparable to those granted other licensees.

Compliance with Applicable Government Regulations

The licensor should insure that the licensee will conduct any of his activities in accordance with applicable government regulations, i.e. not only those that are mandatory but also these that are voluntary. In the United States, any research on rDNA involving United States Government funding must be conducted in accordance with the applicable National Institutes of Health guidelines for research involving rDNA molecules.

A licensee of a university or research institution where the licensed technology was developed with United States Government funding is generally required in the license agreement to adhere to these guidelines. This is so even though an industrial or commercial concern in the United States is not legally obligated to follow these guidelines in its rDNA research. Also, additional government regulations involving approval for marketing of foods and medicines, applicable worker health and safety regulations, and recommendations by the Center for Disease Control of the U.S. Public Health Service as to biological safety and containment procedures, etc., exist. The licensor should minimize his liability as to the use of the licensed technology by requiring his licensee to adhere to those regulations and the license agreement should include a relevant provision to this effect.

Product liability litigation is increasing, particularly in the United States. Under emerging principles of law, the licensor can be held responsible for the licensee's activities as to the licensor's technology. As a result, the licensor should require the licensee to follow applicable government statutes and regulations.

Further, a requirement that the licensee adhere to any voluntary guidelines, such as the voluntary guidelines published by the Centers for Disease Control on biological material containment, would be desirable since it is anticipated courts in the United States may interpret these voluntary guidelines as setting forth the minimum standard of care which must be exercised. Provisions of this type are desirable to attempt to minimize the licensor's liability by the licensee's use of the licensed technology.

Best Efforts

The major benefit to the licensor of a license arrange-

ment is generally not the license down payment or the up-front money but rather running royalties which will accrue from a commercialization of his technology. As a result, from the licensor's standpoint, it is highly desirable for the license agreement to provide that the licensee will use his best efforts to commercialize the technology. This is particularly true where the licensee is granted an exclusive license.

It is difficult to define "best efforts" in a manner that is acceptable to the licensor and the licensee other than in general terms. The utilization of best efforts can be defined where appropriate as achieving certain technical or business benchmarks within specific periods of time. In general, "best efforts" provisions are arrived at as a result of negotiations between the licensor and licensee.

Remedies to the licensor for lack of compliance with best efforts include a monetary payment, imposition of minimum annual royalties after the lapse of a reasonable period of time, a right by the licensor to terminate the agreement or, alternatively, a conversion of an exclusive license into a nonexclusive license. A conversion from an exclusive to a nonexclusive license is probably not a desirable solution from the licensor's standpoint since this prevents the licensor from subsequently granting an exclusive license to a new licensee.

Hold Harmless Provisions

Because the licensor has no control on how the licensee will use his licensed technology and because biotechnology is relatively new, biotechnology license agreements should definitely provide that the licensee agrees to hold the licensor harmless as to any damages which might arise out of the utilization of the licensed technology. This coupled with the requirement that the licensee adhere to governmental regulations and voluntary guidelines established by governmental agencies, which are more and more being interpreted by courts in the United States as the minimum standards of care as discussed above, is considered essential in licensing biotechnology.

At present, it is unclear what are the potential risks for a licensor in a new, untested technology and what potential product liability questions might arise. However, there is a developing tendency for courts at least in the United States to attribute liability to a licensor if his technology gives rise to injury.

Hold-harmless provisions are thus essential to minimize the licensor's exposure, and indemnification provisions in a licensing agreement are a prerequisite in a number of U.S. states for an action by the licensor against a licensee as to liability imposed on the licensor. Thus, the licensee should be required to defend and indemnify the licensor as to any damages and losses for personal injury, death or property damage arising as a result of the licensee's activities as to the licensed technology. This is in addition to requiring the licensee to comply with applicable government statutes and regulations as well as voluntary guidelines discussed above.

Confidentiality

Most license agreements involving high technology require that the licensor's confidential and proprietary trade secret and know-how information transferred to the licensee be held confidential. The licensee's obligation as to confidentiality generally does not extend to transferred

information known to the licensee prior to disclosure, to information in the public domain or to information that becomes part of the public domain through no fault of the licensee. These are generally acceptable provisions in a biotechnology agreement.

However, in biotechnology licensing where replicating or replicable biological materials are transferred to the licensee, the licensor must specifically limit the licensee's ability to transfer any such biological materials to a third party for any use. Such transfers, even for research purposes, basically result in the licensor's loss of control as to the biological materials and difficulty in policing their use by a third party transferee. Accordingly, the biotechnology license agreement should prohibit the licensee from transferring replicating or replicable biological materials to third parties, without the written consent of the licensor.

Where a university is the licensor and university research personnel are the principal developers of the technology to be licensed in an agreement, the licensee must recognize the need of the university research personnel to publish. As a result, confidentiality obligations generally are more limited in this type of agreement.

Often, the provisions set forth that confidential information and research results obtained pursuant to the agreement will be held confidential and submitted to the licensee for review as to any developments that might be considered patentable by the licensee. The licensee must decide within a certain period of time, often 45 days or 90 days, after receipt of the information whether to seek patent protection prior to publication or disclosure of the information developed. This attempts to balance the need to publish and the need to patent developments arising out of the agreement.

Payment and Reports/Records

Just as with other license agreements, license agreements in biotechnology should contain provisions setting forth how royalty payments are to be made, the timing of such payments, how the payment is calculated, submission of reports on the royalty basis, e.g. on net sales or number of units sold, how the royalty rate was applied to the royalty basis, and, if the royalty rate differs depending upon the nature of the product sold or used, a breakdown as to products should be included in the licensee's report. The licensor must be able to verify that the appropriate amount of royalty has been paid; and provisions providing the licensor with the right to inspect the licensee's records. The licensee should thus be required to retain records for a minimum period of time, for example, from one to three years, and to make them available to the licensor or an accountant appointed by the licensor at reasonable periods of time and at reasonable intervals to insure royalty payments to the licensor are correct and that the basis for payment can be monitored.

Prosecution of Patents/Responsibility Therefor

In general, it is the obligation and privilege of the licensor to file for and prosecute patents and pending applications on the technology transferred in the license agreement. A biotechnology license agreement should set forth the specific rights and obligations as to parties on prosecution and maintenance of existing patents and pending and potential patent applications and on filing of new patent applications worldwide or in the licensed territory or area

if territorial or field of use restrictions exist. Since the licensee will commercialize the technology and since the licensee has control over the type of commercial products that will be marketed, the licensee should also be able to at least review and consult with the licensor as to the claim coverage of any pending patent applications involved in the agreement.

Specifically, the license agreement should set forth who bears the expenses of patent maintenance and of prosecution of patents applications, who selects the countries in which patent applications on present and future technology are to be filed and, in the event of a nonexclusive license, if the costs of prosecuting patent applications and patent maintenance are to be potentially shared by all licensees. The agreement should specifically provide who has the obligation as to payment of maintenance fees and annuities and as to meeting any working requirements.

Where a licensor grants a number of exclusive licenses in different fields of use and with multiple country application filings, it is recognized that review of patent application prosecution by and input from various licensees can complicate patent prosecution procedures for the licensor. The licensor may decide the only reasonable way to handle this is to simply keep his various licensees informed as to the status of patent prosecution in the territory in which each licensee is licensed.

Supply Provisions

In addition to a running royalty and minimum annual royalties discussed above, it is often highly advantageous for the licensor, particularly where the licensor is a small emerging company, to supply to the licensee a portion of the licensee's requirements as to the products to be marketed. This provides the licensor with additional income on his technology. The licensor then benefits from the profit on the materials or components actually supplied to the licensee in addition to the running royalties due and payable by the licensee on sales of the licensed products. This is an approach whereby the licensee can reduce his up-front money payment to the licensor in return for an agreement by the licensee to purchase some of his product requirements from the licensor.

For example, where a bulk product is to be supplied and the end product requires government regulatory approval prior to marketing, a supply provision provides the licensor with the ability to produce and sell products to the licensee without the attendant expense of obtaining government approval before marketing.

Supply provisions can be included in the agreement if they are voluntary, are basically mutually beneficial or are at the request of the licensee. These provisions should set forth the amount to be supplied as well as a basis for establishing the sale price of the materials supplied to the licensee. The sales price of product provided by the licensor to the licensee can be based on a formula which takes into consideration the actual costs of the product, overhead expenses as well as a reasonable profit to the licensor thereon. The percentage can be based on minimum percentage, for example 300% of the licensor's fully allocated manufacturing costs. To protect the licensee, a cap can be placed on the sales price at a price no greater than a percentage, for example 350% of the licensee's similarly calculated fully allocated manufacturing costs of like products. Alternatively, the basis for the

sales price of the product by the licensor to the licensee can be a percent of the sales price of the licensee's end product.

Publicity

In general, limitations should be included in the license agreement as to the publicity that can be generated by any party as to the underlying license agreement. Where the licensor is a small company and the licensee is a large one, it is often highly desirable for the licensor to publicize the license agreement. Publicity provides the licensor with credibility in the industry and further publicity can materially affect the price of the licensor's stock and the ability to attract potential investors.

However, problems can arise as to publicity on entry into a license agreement. Disclosure may be necessary if the licensor is a state university due to applicable "sunshine laws" requiring a university's relationships be of public record. Disclosure of certain information as to the agreement and its effect on company business may also be necessary to satisfy United States Securities and Exchange Commission regulations.

As a result, the license agreement should describe any limitations as to publicizing the license agreement and should provide that the text of any public announcements by one party are to be approved by the other party. The license agreement should state that if applicable governmental regulations or statutes, such as securities regulations or "sunshine laws," require disclosure that a party may disclose information as to the license agreement as required by governmental regulations or statutes.

Know-How Transfer

Specific provisions need to be included in the license agreement to establish how know-how possessed by the licensor is to be transferred to the licensee. In the event the licensor has technology with which the licensee is not familiar, it may be necessary not only initially to educate the licensee but also a continuing technical relationship between the licensor and the licensee may be essential to insure that the licensor's know-how can be best used by the licensee for commercialization. Also, the extent to which the know-how can be disclosed to and transferred among licensee's affiliates and within licensee's research and development organization should be set forth. The license agreement should establish a mechanism for this technology transfer, how it is to occur and, if it is to continue during the agreement, what the costs of this technology transfer are and how the licensor is to be reimbursed for this technical assistance of the licensee.

Assignability

In general, in high-technology areas such as biotechnology, the license agreement prohibits granting of sublicenses by the licensee, except to licensee's affiliates, and sets forth that the agreement is nonassignable without the consent of the licensor. The obvious reason from a licensor's standpoint for assignability only with the licensor's consent is that the licensor needs to know at the outset who his licensee is. Only in this way can the licensor insure that the potential licensee is appropriate to handle, develop and commercialize the licensor's technology. The only acceptable exception to this restriction on assignability might be where the entire business of the licensee or licensor is acquired by a suc-

cessor in interest.

In the event that sub-licensing rights are to be granted, whether any approval of a sub-licensee, for example, a nonaffiliate of the licensee, of the licensee by the licensor is required should be included in the agreement. Further, if the rights under the agreement can be sub-licensed, the sub-licensee should be required to assume all of the obligations binding upon the licensee. If rights are sublicenseable, it should be recognized that only those rights licensed to the licensee can be sub-licensed. Moreover, the agreement should define whether any portion of the royalty from the sub-licensee to the licensee flows to the licensor. The licensor should avoid any situation where a licensee could potentially sub-license but no royalty income flows from the sub-licensee to the licensor.

Warranties/Representations

Desirably, the licensor should make no warranties as to the validity of any licensed patents or pending patent applications.

Biotechnology is in an early stage of development and numerous applications may well be on file in various countries of the licensed territory and may issue into patents. As a result, the licensee's freedom to practice the licensed technology could be adversely affected. Yet, at the time of entry into the agreement, the licensor may not be aware of this. Thus, the licensor should make no warranty that the practice of the licensed technology, even including that covered by issued patents, would not constitute an infringement of the patents of third parties.

Further, it appears to be commonplace in biotechnology agreements to set forth that the licensor makes no express or implied warranties of merchantability or fitness for purposes as to the technology licensed. This is highly desirable since, if the licensed technology involves a license to use a biological material such as a microorganism or cell line, the licensor could be considered the manufacturer of such thereby incurring liability as to damage flowing from use by the licensee of the licensed biological material.

Infringement by Licensee

For the licensee's benefit, the license agreement should provide for the situation where the practice of the licensed technology or sales of products produced thereby might result in an infringement of the patents of others. This is true even though the licensor makes no warranty of noninfringement of the patents of others by practice of the technology licensed.

In the event that the licensee should discover that the practice of the licensed technology or sale of products under the licensed technology, or a situation should arise in the future that the practice of the licensed technology or sale of products under the licensed technology results in an infringement by the licensee, the licensee or the licensor may seek to obtain a settlement with the third party, before or after litigation with the third party patentee, so that the licensee can continue to practice the licensed technology.

Any settlement expenses or royalties paid to such a third party patentee by the licensee to continue to be able to practice the technology could be offset against royalties due and payable by the licensee to the licensor. Generally, a cap is placed on the ability of the licensee to offset against royalties due and payable to the licensor so

that the offset does not exceed 50%, and sometimes not exceed 33%, of the running royalties due and payable by the licensee to the licensor.

Infringement of Licensed Patents

Obviously, a serious problem from an exclusivity standpoint for the licensee in a patent-based agreement is competition in the licensed area. Where there is an infringement by licensee's competitors of the licensed patents, the license agreement should provide that the licensor will seek a discontinuance of such infringement by the third party. With an exclusive biotechnology license agreement, the agreement should also set forth that in the event that the licensor decides to take no action in seeking a discontinuance of the infringing activities of third parties or is unwilling to initiate litigation to protect the licensee's exclusivity provided by the licensed patents, the licensee has the right to act on behalf of the licensor to seek a discontinuance of the infringement, either by settlement or by litigation. Who bears the costs of litigation should be set forth and, if the costs of litigation are to be borne by the licensee, whether any of those litigation costs can be offset against royalties due and payable to the licensor. The rights to any damage awards in the event of a successful litigation should be included in the agreement.

With a nonexclusive licensee, generally the licensee should insure that it is the responsibility of the licensor to police infringement and prosecute infringement of the licensed patents. The agreement may provide that even though this is the licensor's responsibility, the licensees will bear the litigation costs incurred by the licensor since this is necessary to protect their exclusivity. An appropriate offset with a cap against royalties due and payable by the various licensees to the licensor could also be included.

Antitrust/Tax Implications

It is beyond the scope of this presentation to include a detailed discussion of antitrust and tax concerns in the licensing of biotechnology. It should be noted that biotechnology licenses are subject to the same antitrust and tax concerns that are involved in the licensing of any other technology. Considering the international nature of many biotechnology licenses, it is important to remember that U.S. antitrust laws do not distinguish between transfer or use of technology within or outside the U.S. in agreements involving a U.S. licensor or a U.S. licensee. Further, all foreign patent owners are subject to the jurisdiction of U.S. courts as to actions affecting patents or patent rights (35 U.S.C. § 293).

As a result, the antitrust/tax implications as to the provisions of a biotechnology license agreement need to be kept in mind by the licensor and the licensee.

Statutes and Regulations Affecting Biotechnology Transfer and Commercialization

Both the licensor and the licensee should be aware of governmental regulations that have an impact on the ability to transfer intellectual property rights and materials involved in biotechnology. Regulations protecting public health and safety often exist relating to shipment and transfer of biological materials such as microorganisms, viruses, cell lines, etc. For example, in the United States a broad range of statutes and regulations

exist relative to interstate and international transfer of biological materials. In the United States, transport of biological materials within and into the United States is regulated by the Department of Agriculture, the Department of Transportation, and the Department of Health and Human Services, Public Health Service. Thus, the ability to transfer interstate within the United States or to import into the United States biological materials, which underlie the licensed technology and may well be necessary for its practice, must be considered by the parties to the agreement.

The parties should include provisions in the biotechnology license agreement to take care of the contingency that transfer or importation may not be possible or may be delayed, relieving, delaying or mitigating the licensee's obligations under the agreement. Regulations also exist relative to worker health and safety administered by the Department of Labor, Occupational Safety and Health Administration requiring a safe and hazard-free environment for workers. The U.S. Food and Drug Administration, Department of Health and Human Services, also regulates the marketing of drugs, food additives, animal feed additives, etc., in the United States, and approval prior to marketing is required.

Similarly, the U.S. Department of Agriculture regulates veterinary biologicals. As a result, if the licensed technology involves marketing a product requiring U.S. Food and Drug Administration or U.S. Department of Agriculture approval, the license agreement should delineate whose responsibility it is to obtain such approval. If it is the licensee's responsibility to do so, how expeditiously must he seek approval? Does the licensor have any obligation to assist the licensee in this approval process and, if so, to what extent?

Also, under U.S. law, bulk drug substances and drugs that have not been approved by the Food and Drug Administration cannot be exported from the United States. A drug substance is defined as an active ingredient intended for treatment or prevention of disease. It cannot be exported from the United States unless it is to be used in manufacturing a Food and Drug Administration approved drug or unless it otherwise meets the requirements for export of a drug. Drugs can only be exported if they are Food and Drug Administration-approved. They are subject to a Food and Drug Administration investigational new-drug application, or assurance of the manufacturer of the drug or a foreign government official that the drug will be used only for investigational purposes and the drug can be used legally in the country importing the drug.

Export Controls

As a result, if the technology transfer involves the necessity for export of drugs presently manufactured in the United States, the above Food and Drug Administration regulations must be considered since they may delay implementing the transfer of technology from the licensor to the licensee or may dictate manufacture outside of the United States to implement the technology transfer. Provisions in the license agreement should provide for this type of contingency.

The United States also has export controls on technology and commodities, administered by the U.S. Department of Commerce, Office of Export Administra-

tion, based on reasons of national security. Biotechnology and biological materials as commodities being transferred to a foreign license are subject to these export controls. Control is based on the nature of the technology or commodity for which export is being sought and the location to which export is being made.

Export licenses are required for virtually all exports, whether technology or commodity, from the United States. A general license exists if the technology/commodity falls within one of the enumerated classes in the regulations and no export license is issued. Otherwise, a validated license for export is needed. This requires the filing of an application and, if a validated license is granted, the export is authorized under the specific conditions set forth in the validated license grant. While not time consuming, delay in technology transfer can be encountered since the issuance of a validated license takes anywhere from one to three months.

Many biological materials such as most viruses, all fungi and many common bacteria require a validated license for export from the United States. Inactivated, attenuated and relatively harmless bacteria can be exported under a general license, but review of United States export control regulations is necessary to insure a general license for export from the United States. U.S. export control regulations as they apply to biological materials are currently under review.

If the biological materials have the potential to produce toxins or are highly effective and debilitating as to human or animal/plant life, resulting in potential military applications, export may be more difficult and may turn out to be impossible.

Appropriate provisions in a biotechnology license agreement to provide for the above contingencies need to be considered and may be necessary to protect the parties to the agreement.

Miscellaneous Provisions

The license agreement should also contain the following additional provisions, generally present in license agreements. These provisions do not appear to involve aspects that are particularly unique to biotechnology.

1. Most-favored licensee clauses — These provisions set forth in the case of a nonexclusive license, that no other license would be granted by the licensor on terms more favorable than those granted to the licensee or, if so granted, these more favorable terms are available to the licensee.

2. An arbitration clause — This type of clause provides for settlement of disputes by arbitration, what rules of arbitration are to be used and who bears the cost of arbitration in the event a dispute has to be settled in this manner. Voluntary arbitration of patent validity and infringement issues arising out of a contract is now specifically provided for by U.S. patent statutes. (35 U.S.C. § 284).

3. The term of the license agreement and how the license agreement is terminated prior to this term — Generally, the term of the agreement extends until the last-involved patent expires or extends for a period of 10 years or longer. In 1984, the U.S. patent statutes were amended to provide for a patent term extension up to five years as to patents on products regulated by the Food and Drug Administration (drugs, biologics, antibiotics, medical devices, food additives and color additives) and as to patents on methods of manufacturing and using these

Food and Drug Administration regulated products where delay in marketing was occasioned by the time necessary for Food and Drug Administration approval for marketing.

While the extension is requested in the name of the patentee, the agreement should set forth who has the right to, who has the responsibility for and who bears the expense of obtaining such a patent term extension as to patent rights involved in the licensed technology. Further, either the licensor or the licensee generally has the right to terminate the agreement upon a breach by the other. Often the licensee has the right to terminate the license agreement voluntarily with 60 days' or 90 days' prior notice to the licensor.

4. No waiver or breach — This provision generally provides that a waiver by one party as to a breach by the other party does not constitute a waiver of any other breaches.

5. Entire agreement clause — This clause generally provides that the agreement sets forth all of the terms and conditions between the parties and replaces any prior written or oral representations or agreements between the parties.

6. Applicable law — This provision generally establishes the provisions of the agreement will be interpreted under the laws of a particular country or state.

7. Notice — The manner of notice and addresses of the various parties to which notice can be given is set forth.

8. Separability clause — In the event a provision of the agreement is held invalid or unenforceable, this provision sets forth the invalid or unenforceable provision is considered to be separated out of the agreement and the remaining provisions in the agreement between the parties remain in full force and effect.

9. Government-approval clauses — Generally, this type of clause provides that, in the event any government approval is necessary as to the agreement or its terms, such will be obtained and the agreement is not effective until the necessary governmental approval has been obtained.

10. Tax provisions — If any taxes must be paid by one

party, the taxes will be paid and the party paying the tax will notify the other party that such has been paid.

11. Marking clauses — This type of provision sets forth that any goods produced under issued or pending patents will be so marked to thereby provide notice to third parties as to the existence of patents or pending applications on that product. Notice may be needed in the event of infringement litigation as to patents licensed under the agreement as a starting point for measurement of damages as to the activities of third parties if infringement is held to exist.

12. Use of trademarks — These provisions generally authorize or prohibit the licensee from utilizing the trademarks of the licensor in the licensee's advertising or promotional effort.

SUMMARY

In many ways license agreements in biotechnology do not greatly differ from license agreements in other areas of technology. However, as pointed out, in certain instances licenses on biotechnology do indeed differ. Attention should be directed particularly to the discussion on issues unique to biotechnology, so that an appropriate license agreement acceptable to both the licensor and licensee arises.

As one final comment, while the above can be considered to be a checklist, by no means should it or any license agreement presently available be used as a form. Use of form license agreements and the like are generally a substitute for thinking. In most instances, there will be uniqueness about each licensing arrangement. This will require individual consideration by the parties and negotiations between the parties to insure that appropriate provisions acceptable to the licensor and licensee are included and that the license agreement can be produced after agreement in intent has been reached by the parties with a minimal amount of time and expense involved to the parties.