

# Licensing an Aid to Pharmaceuticals

*A review of R&D activities indicates licensing offers an important vehicle for marketing drug products*

BY SALVATORE R. CONTE\*

## A. INTRODUCTION

\$930 Million! This is the estimated commitment to research and development in ethical pharmaceuticals (human and veterinary) financed or conducted domestically and abroad by the U.S. pharmaceutical industry for 1974. The sum reflects a 13% increase over the \$824 million spent in 1973, a 50% increase over the \$619 million spent in 1970 and a 165% increase over the \$351 million spent in 1965<sup>1</sup>. Projected into 1975, the amount spent for global R&D by U.S. headquartered firms will easily exceed one billion dollars!



S. Conte

Compared to sales, the R&D allocations over the same 10 year period show a fairly constant annual R&D-to-Sales Ratio (percentagewise) of about 11-12%, although a decrease has been noted recently due to the distressed condition of the economy. In 1973, the R&D/Sales Ratio decreased to 11.2% from the previous year's 12.1%.

In general, about 75-80% of the pharmaceutical industry's R&D funds are allocated to basic research and the development of new drugs with the remainder allocated to activities focused on improving or modifying existing products.

In the search for new drugs, thousands upon thousands of compounds are synthesized and screened each year from which, with luck, a dozen or more completely new and different drugs will evolve. There are estimates that 4,000 to 6,000 such compounds are made for every ultimate commercial product. Responsible for the low number of marketable drug entities are the rather extensive governmental procedures and requirements, particularly regarding evidence of both safety and efficacy, that precede the marketing of a new drug under existing federal legislation. Indeed, it can easily cost from \$2 million to \$6 million for each salable drug and take years to complete.

During the 1965-74 decade, only 158 new synthesized drugs were introduced into the United States, not all of which had their origin in American research establishments. For example, of the 11 new entities introduced in

\*General Counsel, Johnson & Johnson.

1972, 6<sup>1</sup>/<sub>2</sub> originated in this country; of the 19 new entities introduced in 1973, 13 originated domestically; and of the 18 introduced in 1974, 12<sup>1</sup>/<sub>2</sub> originated here.<sup>2</sup> Shared research with a company abroad accounts for each half-product.

Considering the large number of pharmaceutical firms in the U.S. — which may be divided between the 115 major research-oriented members of the Pharmaceutical Manufacturers Association (PMA) and the more than 500 small to medium-sized non-PMA companies doing little or no research — and considering the very small number of new drugs marketed each year, it is evident that no one company can statistically be assured that its R&D effort will be successful in bringing to fruition even one salable product.

Such uncertainty and risk has led management in recent years to supplement its R&D effort with an aggressive search outside its own enterprise, both here and abroad, for compounds having potential, if not proven, pharmaceutical applications. The search has become even more intensified as a result of the recent downturn in the economy and its consequent "belt-tightening" in both short-term and long-term research budgeting and programming. It is more economical to spend a portion of one's time, effort and money on an "out-of-house" search for a probable drug candidate than to rely solely on an "in-house" R&D program. Management simply cannot afford to gamble that its R&D expenditures will actually or consistently provide it with new drug entities.

One of the ways of implementing this supplemental approach to one's own research activities is through the mechanism of licensing, which provides the licensee with the right to use some technology, whether it be know-how, a particular development, a patented product or the like, in return for some consideration to the licensor, generally a royalty based on sales resulting from the licensed technology.

## B. WHY LICENSE?

Although it is easy to understand why a pharmaceutical company might be eager to seek a license from the owner of a successful or potentially promising drug product, is it reasonable to believe that such a product would be available for licensing? Considering the intense competition to come up with one of those precious few new drugs each year, why would a particular enterprise having a marketable product or a promising lead even consider making it available to another? Indeed, the main goal of a company's R&D effort is for the self-commercialization of derived developments, not for licensing others.

There are, however, valid motivations to license (disregarding any compulsory licenses imposed under statutory authority or court ordered decrees). Such motivations

are generally founded in simple economic good sense. A few examples will suffice:

1. A particular concept may be beyond one's resources. An instance would be the discovery of a new compound having certain pharmacological properties by a small company whose limited financial and human resources prohibit it from carrying on the research effort required to obtain the necessary governmental approval for marketing. An interested licensee with the wherewithal for appropriate development is an answer.

2. A particular concept may be extraneous to one's normal business activity. For example, a manufacturer of agricultural chemicals finds that one of his compounds has potential human medicinal activity. Without developmental and marketing capabilities for drug products, what is such a manufacturer to do? Unless he wants to invest in and enter the pharmaceutical business, licensing offers him an answer.

3. A particular concept may be one of low priority among the many projects on a company's agenda competing for development. Economies of time might indicate licensing as a more suitable alternative to putting the idea on the shelf to await future development.

Many other situations can be exemplified. Suffice it to say that licensing opportunities are available within the pharmaceutical industry and that the challenge is there for management, whether as potential licensor or licensee, to seek out and take advantage of these opportunities.

### C. OBJECTIVES

20

Whether as licensor or licensee, it is important to clearly understand what you expect to gain from entering into a license agreement. Although somewhat obvious on its face, the importance of this statement cannot be over-emphasized since the objectives to be realized will strongly govern the choice of a licensing partner and the conditions of the agreement. A few of the main objectives underlying pharmaceutical licenses are:

1. *Cash Return:* The licensee profits from his commercialization of the licensed pharmaceutical and the licensor receives his financial reward from the licensee by the payment of monies, e.g., an initial lump-sum or royalties over the term of the license. With a maximum cash return through royalties in mind, the licensor must look for a licensee who can afford the cost to commercialize the drug and who is willing to expend an aggressive marketing effort for optimal distribution and sale.

2. *Product Exchange:* Instead of money, the *raison d'être* for licensing is often a cross-licensing of products. This objective has been particularly prevalent during the past decade. The relatively low number of available new drug entities has put a premium on a *quid pro quo* type of arrangement. The marriage between licensing partners, therefore, may depend on what each brings to the nuptial negotiating table. For example, a company looking for entry into the cardiovascular market may have to offer access to its anti-inflammatory agent in return, notwithstanding the competition so created.

3. *Market Extension:* Licensing may be used to reach new markets. For example, with over 40% of the world-

wide market for human pharmaceuticals being the United States, licensing offers a foreign company without a U.S. marketing organization a sensible outlet for the exploitation of its drug products through an American licensee. Similarly, a domestic pharmaceutical company may license others abroad in order to accomplish regional or worldwide marketing of its drugs. In either event, the licensor should look for a licensee having proven marketing capabilities in the particular licensed territory. If the licensee is to also perform the function of making the particular drug locally, the licensor should assure himself that the licensee's manufacturing facilities are both adequate and available, and if not, that the licensee can afford the cost of any requisite capital investments.

4. *Export:* The licensor may wish to maximize usage of its own manufacturing facilities and broaden its base as a supplier of bulk chemicals by exporting the particular drug in bulk form to its foreign licensees who will then formulate, compound and manufacture the desired finished dosage forms (e.g., tablets, capsules, suspensions, injections, etc.). In such case, a licensee must be found who is willing to purchase the bulk drug from the licensor, rather than being a self-manufacturer.

### D. LICENSING PACKAGE

Before embarking on a licensing venture, the licensor should have a complete understanding of what the license package contains and its relative value. Generally, the package consists of one or more of the following: industrial property rights, such as patents and trademarks; technical and commercial know-how; and governmental registrations or approvals for marketing the drug or applications for same.

How strong is the patent protection? The chances of the patent withstanding an attack on its validity and the remaining years of patent protection are important factors with regard to likely competition. Is there a valuable trademark associated with the product for use by the licensee? To what extent are relevant trade secrets or know-how essential to the licensee? How long are these likely to remain confidential? How much will the know-how save the licensee in time, money or research effort? In many cases the know-how is at least as valuable as any patent protection and often even more so.

These and other similar questions should be answered in order to determine the value of the package to be licensed.

#### Technical Status

In addition, the technical status of the particular development or invention will influence the manner of licensing the package. For example, is the particular pharmaceutical entity fully developed and approved for marketing by government authorities? If so, no additional laboratory or clinical work might be contemplated and the license agreement could be a relatively simple authorization to the licensee to commercialize the drug product upon payment of a royalty.

If the pharmaceutical entity, however, is in an early or intermediate stage of development, further intensive research, such as, for example, short- or long-term toxicity

and teratology studies in animals, and clinical investigations in humans, will be required before governmental approval for marketing can be obtained. Whether the licensor or the licensee or both jointly will undertake performance of the additional research will have to be provided for in the license agreement.

With non-pharmaceutical types of technology, it is generally very difficult to sell a license on a development which still requires considerable effort to complete, particularly, if there's an element of risk on the final outcome. The licensor, therefore, very often completes or agrees to complete the licensed development. With pharmaceuticals, however, it is not surprising to find that the licensee, rather than the licensor, will undertake such effort.

It previously was seen how the lack of either resources or capabilities to complete a particular development can motivate one to consider the licensing of a potentially useful drug. Such a potential licensor would naturally be reluctant to enter into a license agreement under which he assumes that very burden which prompted him to look for a potential licensee in the first place. Rather, he will seek a licensee who has the available money and facilities to complete the necessary research, the willingness to devote those resources to the project and a full awareness that ultimate success in obtaining a salable new drug entity is unpredictable.

Providing the existing data indicates medical and commercial potential, such a licensee, seeking to supplement his own R&D program and anxious to obtain access to a likely chemotherapeutic candidate, should not be hard to find. Depending upon the amount and expense of additional research to be done, the licensee can attempt to recoup his investment, either in whole or in part, by negotiating for some type of reimbursement should commercial success be achieved, for example, by crediting all or part of his expenses against future royalties or by a lowered royalty rate.

#### E. SECRECY AGREEMENT

Once management has decided to go the license route and the licensing package has been formulated, what approach and specific considerations should be taken into account for subsequent negotiations?

Of immediate concern is how to go about enticing a prospective licensee. Unless the particular drug to be licensed is enjoying proven medical and commercial success, in which case several prospects will very likely be beating a path to the licensor's door, some way must be found to give a prospective licensee a look into the licensing package so that he can determine his interest in it. This immediately presents a problem, particularly when the subject pharmaceutical is at an early stage of development or is still awaiting issuance of appropriate patent coverage. The prospective licensee would of course like to consider all of the licensor's available data. The licensor, on the other hand, must protect his proprietary information in the event the prospect does not take a license. How can the two get together?

The problem is usually solved by a secrecy agreement under which the licensor makes a disclosure of his information to the prospective licensee and the latter obligates himself not to use the information or disclose it to others for a reasonable period of time, say from three to seven

years, depending upon which party has the greater bargaining position.

As some measure of protection for the prospective licensee's own research activities, standard exclusions from his obligation of secrecy are usually provided for in the agreement, such as any information in or which enters the public domain, any information which is "in-house" before disclosure by the licensor and any information lawfully obtained from other parties.

#### Disclosure

The disclosure generally comprises most of the licensor's available technical information, such as, for example, the chemical identity of the drug, any pharmacological, toxicity and teratological data in animals and any human clinical data. The status of patent coverage including a copy of any relevant patent applications may be included. Such disclosure should give the recipient a fairly comprehensive idea of the drug's medical and commercial feasibility, the amount of research and development work still required before a salable product can be obtained and the measure of exclusivity likely to be enjoyed against possible competitors.

At the secrecy agreement stage, synthetic or manufacturing data is a relatively less important part of the disclosure unless particular problems are inherent in the production of the drug or its dosage formulations. Such problems should definitely be brought to the prospective licensee's immediate attention. If it is believed, for example, that production will be plagued by such factors as high cost, scarcity of reactants, low yield, low purity, heat or moisture instability or the like, the interest of the prospective licensee in acquiring a license may quickly wane or expire, regardless of the chemotherapeutic merit of the drug.

On the other hand, open and frank discussion of any such difficulty at the outset could pave the way for a possible joint solution.

After the prospective licensee's review of the confidential information is completed, generally within a prescribed period of, say, 60 to 90 days, and assuming he is now interested in and willing to acquire a license, the parties are then ready to open negotiations and discussions of the appropriate operating conditions of their future relationship.

#### F. PRE-MARKET STAGE: OPTION AGREEMENT

Although licensing in the pharmaceutical industry covers the spectrum of technological subject matter as in other industries, for example, products, processes, engineering know-how, secret formulations, etc., it most often relates to a newly synthesized compound or series of compounds having some chemotherapeutic potential but still requiring further research and development before commercialization is possible. The negotiating parties, therefore, must address themselves to the task of defining their relationship during this pre-market period in addition to the usual license arrangements.

Will the licensor or prospective licensee perform the required research? If the particular pharmaceutical entity is in an advanced stage of development, the licensor may wish to complete the project himself, in which event only the terms of the proposed license remain to be negotiated.

By offering the prospective licensee a fully marketable product, a relatively higher royalty rate is commandable. More often than not, however, the pharmaceutical entity is in an early or intermediate stage of development and, for reasons previously indicated, the prospective licensee undertakes the remaining research burden. For purposes of this discussion, in order to explore certain pre-market aspects of the licensor-licensee relationship, the latter situation will be assumed.

For such situation an option (to take a license) form of agreement is often employed. An option is a contract to keep an offer open during a defined time period. A license is an agreement which authorizes a party to practice some right owned by the licensor in accordance with the terms of the agreement. With regard to their pre-market relationship, the option agreement should provide that the prospective licensee, or optionee, be given the opportunity to evaluate the particular compound and perform the required research during which time he is assured of a continuing offer to acquire a license for commercialization of the drug from the prospective licensor.

### Terms Negotiated

The terms of the particular license in question are often fully negotiated at the same time the option is agreed upon and a copy of the license agreement is either incorporated into the option agreement or attached as an exhibit. Provision is usually made that written exercise of the option by the optionee acts to effectuate the particular license. Alternatively, the parties may wish to postpone negotiation of the license terms until after the optionee actually decides to take a license. This often occurs when the ultimate success of the particular project is deemed marginal. The optionee, however, should insist that certain essential terms of the license be agreed upon at the outset in order to discourage the licensor from increasing the ante should the project's success be realized. As a minimum, the following ought to be predetermined: the nature of the license (e.g., exclusive, sole or nonexclusive); the territorial scope of the license (e.g., worldwide, selected countries, U.S. only); the royalty rate (e.g., a certain percentage of net sales); and the term of the license (e.g., life of the patent, specified number of years).

Of mutual concern to both parties is the ultimate commercial realization of the pharmaceutical candidate. Of paramount concern to the licensor, however, is that the optionee discharge his assumed responsibility for completing the developmental program with diligence. For most pharmaceuticals, the time between synthesis of a compound and a salable product averages three to five years and a seven-to-10-year span is not rare. During this time the life of the licensor's patent coverage and its concomitant value regarding exclusivity in the marketplace is constantly diminishing.

In order to induce acceleration of the optionee's development program, the option agreement should provide for payment of a reasonable option fee to the licensor, generally known as "front-end" money. In effect, an option fee is an expression of good faith on the optionee's part and a "best efforts" type of provision. The fee can be a lump-sum payment or payable over the life of the option. Fees ranging from \$25,000 to \$50,000 per year are fairly common, depending upon the particular stage of development of the potential drug at the time of the op-

tion. If the optionee subsequently elects to take the license and commercializes the drug, all or part of the option fees can, if so negotiated, be credited against payment of future royalties. Should the optionee elect at any time during the option period not to take the license, the fees previously paid are forfeited.

The optionee can be expected to argue that he should not be expected to carry the burden of an option fee in addition to the significant costs he will experience in furthering development of the drug. The licensor ought to realize, however, that, although such costs are considerable and unavoidable, they do not ensure diligence. The payment of an additional \$50,000 per year can be quite effective, therefore, in prompting the optionee to achieve marketable status for the drug as quickly as possible, even if he be permitted to recoup the option fee from future royalties.

In most non-pharmaceutical option agreements, a specific term is set in which to exercise the particular option, for example, three months in which to acquire a franchise, six months in which to buy certain realty, etc. Before the end of the prescribed period, the optionee either does or does not exercise the option. If he doesn't, the option lapses.

### Time Period

When dealing with pharmaceuticals, however, the limitation on an optionee to a definitive time period may not be practical or feasible. The *sine qua non* for marketing a drug in the United States is the fulfillment of all requirements regarding safety and efficacy prescribed by the U.S. Food and Drug Administration (FDA) under our federal laws. This involves submission to the FDA of certain data, obtained according to established "phase studies" on animals and humans, in a New Drug Application (NDA) which must be approved before marketing can occur. Accordingly, exercise of the option to acquire a license is usually made contingent upon the optionee successfully obtaining the requisite NDA approval. Other countries have similar versions of regulatory compliance.

In this regard, the licensor must recognize the uncertainties of medical research. For example, test results may be inconclusive or otherwise not acceptable to the FDA so that additional studies will be needed, or the FDA may insist on different types of animal or human studies based on recent advancements in the state of the art. All this requires time, and accordingly, it is difficult to set a prescribed option term in which the NDA approval is sure to be obtained by the optionee. Accordingly, some estimate is attempted which is presumed sufficient for the optionee to obtain his NDA approval if all goes as planned, say 1-3 years, again depending upon the stage of development at the time of the option, with provision for extension if such approval is delayed due to governmental requirements.

### G. MARKETING STAGE: LICENSE AGREEMENT

Assuming FDA approval is or is about to be obtained and the option will be exercised, some form of a license agreement must be entered into which sets forth the continuing relationship and respective understandings and obligations of the parties during the marketing stage. The legal, structural, and technical aspects of drafting an ap-

propriate license agreement fall within the general discipline of contract drafting and should obviously be left to those specialists in this area. As a matter of general principle, a licensor and a licensee are free to contract as they see fit, provided the ultimate license is not one in restraint of trade or afoul of any other antitrust provision under applicable laws.

A license constitutes permission given by the owner of a certain right to another to invade that right free from legal recourse. A license thus makes an action lawful that would otherwise be unlawful. With pharmaceuticals, the usual rights of a licensor upon which licensing is based are those derived from patents and know-how. Typical licensed know-how includes all chemical and biological information and data owned by the licensor and, in particular, any animal or human data which would be useful to a licensee for submission with his NDA. Trademarks may also be included, particularly in situations where the licensor has an established trademark for a product in one area (e.g., the United States) which the licensee would like to utilize in his exploitation of the product in another market (e.g., in foreign countries).

In the following paragraphs, some key provisions and related concerns in pharmaceutical licenses are described.

#### 1. *Grant*

The most important provision in a license agreement is the "granting clause", under which the precise nature and scope of the particular license is defined. Whether the license is a patent, know-how, or trademark license, or some combination of these, whether the license is exclusive, sole or nonexclusive, whether the make, use and sell trinity is whole or partial, and whether the territorial extent of the license is domestic, regional, or worldwide, will be set forth in the granting clause. If the licensee is to be granted sublicensing rights, i.e., the right to sublicense others, this must also be included. The licensee normally acquires no right to grant sublicenses unless this right is expressly stated in the agreement.

Under an "exclusive" license, the licensee is conveyed all rights, except for legal title, to the particular patent, know-how or trademark, as the case may be, in order to utilize same in his commercialization of the product in the licensed area. Such a license precludes even the licensor himself from utilizing those rights in that area. A "sole" license is similar to an exclusive license except that the prohibition against the licensor is removed. The licensor retains a personal shop-right to also utilize whatever rights are granted to the licensee. A sole license, therefore, is an exclusive license save for a retained personal license in the licensor. Under a "nonexclusive" license, the licensee is merely granted the right to utilize the particular patent, know-how, or trademark with immunity or freedom from suit by the licensor. The licensor may license others or even compete himself with the non-exclusive licensee.

#### Fair Balance

With pharmaceuticals, as with all other licensed products, the license agreement must reflect a fair balance between the desired aims of the negotiating parties and the input each brings to the negotiating table. We have seen that it is often the case where a prospective licensee undertakes the burden of bringing an early "lead" to the status

of a salable drug. This being so, the licensor can hardly expect such licensee to be satisfied with a nonexclusive license. The reason is obvious: the prospective licensee would be foolish to agree to expend the required time, effort and money in R&D and then find that he has to subsequently operate in the face of competition from other non-exclusive licensees granted by the licensor. The prospective licensee, therefore, should strive to obtain an exclusive license or, at least, a sole license.

Should the licensor have no intention of ever marketing the licensed drug himself, as, for example, the agricultural manufacturer referred to previously in Section B, he ought to be favorably disposed to granting an exclusive license. On the other hand, if one of his objectives is to use the licensed drug as an entree into the pharmaceutical business, or, if already in the business to expand his drug line, then the grant of a sole license, whereby the licensor retains co-marketing rights, is probably the best a licensee should hope to obtain.

Nonexclusive licenses are generally employed when a licensor with a salable NDA-approved drug desires to expand the market as quickly as possible. Such an instance could arise when the NDA approval is obtained during the latter years of patent protection. By receiving royalty income for the remaining short life of the patent from several nonexclusive licensees, rather than from one exclusive licensee, the licensor might be able to better maximize his financial return.

#### 2. *Consideration*

Of paramount importance to the licensor is the question of consideration to be paid him for the license. Consideration may take many forms. It may be a lump-sum payment or several specified installments over a period of time. It may be a cross-license to a patented invention of the licensee, or a combination of money coupled with a cross-license.

Very often the consideration is a running royalty expressed as a certain percentage of the licensee's "net sales", which is generally defined as the selling price of the drug less certain common deductions, for example, allowances for returned or outdated goods, credits or discounts, and the like. For the licensor, such consideration permits him to continually share in the profit derived from the licensee's commercialization of the licensed drug over the life of the license. For the licensee, considering that from several hundreds of thousands to millions of dollars may ultimately be paid to the licensor over the course of the license, such consideration permits him to realize a financial return from which the royalty is gradually paid rather than be confronted with the payment of a large equivalent sum at the outset of the license.

What is an "appropriate" amount of royalty will depend upon such factors as the contribution each party has made toward commercialization of the drug, the anticipated market for the drug, the estimated profits to be realized, the past relationship, if any, between the parties and, ultimately, the relative bargaining strength of each party. As a very general rule-of-thumb, however, pharmaceutical exclusive licenses often carry a royalty of from 10% to 15% of the licensee's net sales, and 20% or more is not unknown in exceptional cases; for sole licenses, a royalty of from 7% to 10%; and for nonexclusive licenses, from 4% to 7%. Obviously, whatever the percentage, the amount of royalties paid must be reasonably set for max-

imum enjoyment of the license by both parties. Licensing means cooperation! An onerous royalty can only serve to deter the licensee from fully exploiting the sale of the drug and too low a royalty will not bring the licensor the fair return he is entitled to.

### 3. Annual Minimum Royalty

We have seen how the requirement to pay a substantial fee each year of the option period may be imposed on a prospective licensee to stimulate diligence of performance during the pre-market stage. Similarly, during the market stage, the obligation to pay an annual minimum royalty may be used to stimulate exploitation of the licensed drug. The objective of the licensor in a royalty-bearing license is a maximum cash return over the term of the license. Accordingly, the imposition of an annual minimum royalty is a reasonable burden on the licensee to ensure that he accomplishes at least enough sales of the licensed drug each year to cover the specified minimum royalty. In effect, an annual minimum royalty constitutes somewhat of a "best efforts" type of provision.

As a general rule, the annual minimum royalty is set at 25-50% of the forecast earned royalties. A simple approach is to set a figure that will be same over the life of the license, for example, \$50,000 per year. Alternatively, the annual minimum royalty can be escalated to a maximum figure, in order to account for expansion of the market during the early years until the usual market plateau is achieved, for example, \$15,000 for the first year of the license, with \$10,000 increases for the second, third and fourth year, and \$50,000 from the fifth year on.

## 24 Delay Minimum Royalty

Under certain circumstances, it may be reasonable to remove any obligation of an annual minimum royalty for the first and even the second year of the license, for example, to enable the licensee to undertake plant capitalization or production costs without being burdened with an additional obligation of paying out a specified minimum royalty at the same time, which royalty might not be actually earned during the early years of the license when distribution and medical acceptance of the drug may be slow in getting established.

An annual minimum royalty is usually provided for in exclusive and sole types of licenses since the licensor, in such licenses, has to rely on only once licensed partner to provide him with royalty income. With nonexclusive licenses, however, an annual minimum royalty may or may not be prescribed, although it would seem prudent for the licensor to require payment of at least a small annual minimum royalty to keep the license alive even when the licensee fails to make sales and no earned royalties are realized.

In the event the licensee fails in a particular year to pay earned royalties at least equaling the specified annual minimum royalty or to make up the difference, the licensor should have the right to terminate the agreement or, alternatively, to convert it to a nonexclusive license if the agreement was exclusive or sole. In either event, the licensor will then be free to look for another licensee.

### 4. Royalty Credit

Provision should be made in the license agreement to

credit any or all previously paid option fees, if so negotiated, against earned royalties or against any portion of the annual minimum royalty that may have to be accounted for.

### 5. Best Efforts

Should the license agreement contain an annual minimum royalty provision, the licensor must decide whether or not to rely solely on such provision to define the extent of the licensee's obligation to exploit the licensed drug. If the annual minimum royalty is high enough, for example, 50% or more of the forecast earned royalties, such may suffice to safeguard the interests of the licensor without further commitments required of the licensee. More often than not, however, the annual minimum royalty falls well below 50% of the anticipated royalties, and, without further duties expressly set forth in the agreement, the licensor may not be heard later to complain that the licensee failed to maximize sales, as long as the licensee meets the specified annual minimum royalty.

The situation could arise, for example, that during the course of the license, the licensee for some reason fails to exploit the licensed drug to its maximum potential. It may be that a competitive chemotherapeutic agent has recently evolved from the licensee's own R&D program. The question then arises: Should the licensee terminate the license in order to concentrate on his own development with resultant unshared profits or should he maintain the license but on a limited scale merely sufficient to meet the annual minimum royalty requirement? Rather than face release of the licensed drug to a competitor by terminating the license, he may choose the latter alternative and maintain the license.

Notwithstanding an annual minimum royalty therefore, and particularly in the absence of one, the licensor may wish to impose some type of "best-efforts" provision on his exclusive or sole licensee to prevent such an unfavorable development. Such a provision delineates the reasonable measure of activity expected from such licensees. A nonexclusive licensee is generally not required to undertake any obligations beyond the payment of royalties derived from his sales. With an exclusive or sole licensee, however, the licensor's royalty income is entirely dependent upon the market performance of a single partner. Certainly, the licensor ought to expect that such a licensee will exploit the licensed drug to the same extent had it derived from his own R&D program. Accordingly, it is not unreasonable for the licensor to require an exclusive or sole licensee to achieve not only a minimum quantum of sales but also to exercise a reasonable measure of activity towards optimum commercialization of the licensed drug.

### Typical Conduct

A typically prescribed course of conduct is that the licensee use reasonable efforts to create a market for, to promote, maintain and supply a demand for, and to obtain maximum sales of the licensed drug throughout the licensed territory. Further amplification of these goals may be prescribed, e.g., the expenditure of a specified budget each year on promotional activities, the establish-

(Please turn to Page 61)

the other hand there is a need to understand that technological contracts are excellent vehicles for strengthening the technological capabilities of the recipient country. Furthermore, these agreements are to be evaluated on the basis of economic and commercial criteria in order to properly ascertain the magnitude of problems and to create and maintain a receptive climate for technology and foreign investment into the developing countries.

The author wishes to give due recognition to UNIDO for providing a highly qualified expert assistance to the Mexican Government that made possible the establishment of an efficient system, and allowed important savings and benefits for the economy as a whole. And to encourage other developing nations to support the efforts of UNIDO in the field and to rely on technical assistance projects from UNIDO in the future.

## Licensing an Aid to Pharmaceuticals

(Continued from Page 24)

ment of adequate manufacturing facilities within a certain time, etc. The relative bargaining strength of the parties will determine the ultimate degree of commitment by the licensee.

Not only should the agreement set forth the objective criteria constituting "best efforts", but it should also prescribe the remedies available to the licensor for breach of such criteria by the licensee. As with failure to meet the annual minimum royalty, the licensor ought have the option of terminating the license or of converting it to a non-exclusive license.

It should be realized that, the more specific the contract language is in delineating the efforts and goals desired of the licensee, the fewer difficulties will be encountered by the licensor in an attempt to enforce the "best-efforts" provision or his remedies for its breach. Careful draftsmanship, therefore, is essential to avoid any uncertainty or vagueness in the characterization of what constitutes "best efforts" by the licensee.

### 6. NDA Access

As noted previously, it often occurs that the pharmaceutical entity to be licensed is not in a final stage of development and that subsequent completion is to be undertaken by the licensee. In such instance, the licensee should not be too surprised if, in addition to royalty compensation, the licensor demands the right to use for his own purposes any relevant R&D information and data evolving from the licensee's efforts as further consideration for the license. Of particular importance, for example, would be any animal and clinical data generated by the licensee that could be utilized by the licensor in obtaining his own governmental approvals to market the licensed drug.

If the intended license is exclusive, the licensor would obviously wish to use such data outside the licensed territory. Should the license be sole, which implicitly provides for licensor competition, use of the data both outside and within the licensed territory would be desirable to the licensor. Accordingly, if the licensed territory comprises the United States, the licensor would probably seek the right of access to any approved NDA subsequently obtained by the licensee including the right to use any of the licensee's data contained therein in order to support the

licensor's submission of his own NDA.

Such a demand is almost sure to bring cries of woe and dismay from the licensee. Why should he agree to complete development of the drug only to have the fruits of his labors shared with the licensor? Without some understanding on the licensee's part of the rationale behind such demand, and, perhaps, without some modification of the demand on the licensor's part, his reaction may well be justified.

### "Giant Step"

The licensee must realize that the license agreement opens up a new field to him or permits him to sell a product which he otherwise would not have. Furthermore, even though he may have to expend a considerable amount of additional money and effort before marketing can be achieved, the license puts him far ahead in savings of time and capital. He completely sidesteps the synthetic, screening, selection, and testing program from which the pharmaceutical entity evolved. It is for this valuable "giant step" forward with a new field or new drug that the licensee is being asked to share his efforts with the licensor.

The licensor, on the other hand, should be willing to acknowledge the licensee's contribution in achieving marketable status for the licensed drug. Such acknowledgment can take a variety of forms. For example, upon actual use of the licensee's data, the license could provide for a reduction in the royalty rate, or, reimbursement to the licensee for part of the direct or out-of-pocket expenses incurred in accumulating the data. Another approach is to provide the licensee with a specified "lead time", sufficient to bring him a reasonable return on his development costs and a secure market position, before the licensor will be permitted to use the data, say six months or one year. Another alternative is a de-escalation approach, such as: in the event the licensor makes use of the licensee's data within one year from the date the licensee obtains his NDA approval, then the licensee will be reimbursed with up to 50% of his out-of-pocket costs; if used by the licensor within the second year, such reimbursement will not exceed 25%; and if thereafter used, no financial reimbursement will be due the licensee. Obviously, the fairness and negotiability of any of these "variations on a theme" will be determined by the particular circumstances and equities involved.

### 7. Grantbacks

Many licenses provide that improvements made by the licensee relating to the licensed drug, for example, a new method of synthesis, a new end use, an improved formulation and the like, are to be communicated to the licensor and made accessible to him. Such "grantback" provisions have varied in the past from a mere nonexclusive right to use the improvement, for example, in areas outside the licensed territory, to an exclusive right to use or a full assignment of ownership rights worldwide. The latter, however, have lately come under close scrutiny as a possible misuse of the basic licensed patent. The arguments are made that such grantbacks merely serve to further secure and increase the licensor's patented monopoly and to dampen the licensee's incentive to develop improvements, thereby constituting effective impediments to competition. Consequently, such grantbacks must be ex-

amined in light of patent misuse holdings and prevailing antitrust laws. Less restrictive grantback provisions, such as the grant of only a non-exclusive right to the improvement, should not encounter patent misuse or antitrust difficulties in and of themselves, particularly if the license contains a reciprocal requirement by the licensor to make available any improvements he develops to the licensee. Absent any provision in the license agreement regarding improvements of either party, no right to same is acquired by the other.

#### 8. *Term of License*

With a patented drug product, the license will ordinarily continue for the life of the patent. Although shorter periods may be mutually agreed upon, a patent license can not exceed the expiration of the patent. If know-how and/or trademarks are included, the license with regard thereto may be for a specified term either shorter or longer than the patent license, depending on the circumstances. Consider, for example, a drug for which NDA approval is received at a time when only a few more patent years remain. An agreement should be possible which comprises both a patent license for a specified royalty until expiration of the patent and a know-how license covering access to and use of the very valuable and confidential information in the NDA for a separate royalty for a reasonable number of years which might extend beyond the life of the patent.

#### 9. *General Provisions*

There are many other provisions frequently included in license agreements that are standard regardless of the particular technology, pharmaceutical or otherwise, being licensed. For example, clauses governing (i) the manner and time of making royalty payments, (ii) the procedures to be followed in the event of third party infringement of either the licensed patent or trademark, (iii) the permissible excuses for nonperformance, i.e., "force majeure", (iv) the separability of certain clauses from the agreement if subsequently declared or adjudged "null and void", (v) the means by which the parties can get divorced and terminate the agreement, (vi) the confidentiality, (vii) arbitration, (viii) assignability and (ix) governing law aspects, and other clauses may have to be negotiated and agreed upon. They should not, however, present any unusual or unique problems merely because the subject of the license is a drug product.

#### NOTES

1. Annual Survey Report, 1973-74, of the Pharmaceutical Manufacturers Association, 1155 Fifteenth Street, N.W., Washington, D.C. 20005.

2. New Products Parade, February, 1975, by Paul de Haen, 11 West 42nd Street, New York N.Y. 10036.

## *Brazil: Technical Assistance Pacts*

(Continued from Page 25)

(a) INPI's broad powers to evaluate the need for acquiring any technology, and to inspect and follow up the progress of technology transfer and absorption; (b) prohibition of market limitations with some reservations for protecting pre-existing commitments with respect to third-party rights and national or international laws including, presumably, the U.S. export regulations limiting re-ex-

portation; and (c) the prohibition of relieving the supplier of technology from responsibility for third-party actions arising from faults or defects in the subject matter of the technology covered. The latter, which is also applicable to the patent and trademark license categories, if strictly interpreted may abolish the traditional concepts of performance guarantees and limited patent infringement claim defense or hold harmless commitments.

#### **Former Categories**

Taking the three formerly "Technical Assistance" categories individually, let us consider first category (c), contracts for supplying industrial technology. This category is defined in terms of acquisition of intelligence and technology not protected by industrial property rights recognized in Brazil. Perhaps the most significant of its provisions calling for follow-up in INPI's future actions for practical implementation, is the broad requirement that these include not just the technical data and supporting documents and instructions, but also technological development methods used in obtaining these data. Could it be that INPI will ultimately interpret this as meaning that the supplier should deliver also some of its R&D know-how?

Category (d) is defined in terms of agreements covering technical-industrial cooperation for acquisition of intelligence, techniques, and services required for the manufacture of industrial plants and equipment and capital goods. This may be the most important under the directives of Brazil's Second National Development Plan, and some provisions appear to be accordingly more generous. An example is the renewable five-year term for contracts. Some provisions are nevertheless ambiguous. For instance, if a patent is involved, it must be granted free but otherwise subject to the provisions of the patent license category. It remains to be seen whether in the final implementation this disadvantage can be offset through calculation of the amount for the overall contract price.

Category (e) covers agreements for specialized technical services, thus confirming that INPI's authority can be invoked even if no technology transfer is involved. Only the final implementation will show to what extent we are facing a new precedent. But at least one favorable precedent discernible in the provision applicable to transactions up to \$20,000. A registration application can be based on final invoice without preliminary proceedings.

The concluding part of the act subjects contracts in other categories and other contractual conditions and terms not specifically contemplated or incorporated in it, to submission for preliminary study by INPI before issuing its necessary directives. This provision is quite broad on the face of it, because it may include also apartment leases and change of address clauses. Only final implementation will reveal the practical and reasonable limits to be applied.

Although final implementation of the act will ultimately provide important detailed information, it is fair to assume that INPI will be devoted to answering the call of Brazil's Second National Development Plan for *effective* transfer of technology, aimed at gradually evolving conditions for creating the country's own technology potential. This would appear to be the basic guideline, and will undoubtedly result in INPI's retaining its great discretionary powers.