Patenting and commercializing biotechnology inventions

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To someone with a viable invention and no production resources or finance, a patent can give options otherwise not possible. Patents attract capital, help source research funds and provide licensing opportunities. Yet patenting is an expensive business. Even though, filing a complete specification in India may cost only Rs 200, the attorneys' fee may amount to hundred times that figure! Since most therapeutic, diagnostic or food product inventions have no prospect of grant in India and since the market prospects are often better in another country, it makes commercial sense to secure patents in foreign countries. Even once a patent is granted, costs continue. Maintenance, renewals, defence and active exploitation of the rights, monitoring competitor activity, etc. will follow. The costs of pursuing patent protection must therefore be balanced against the holding of granted patents or pending patent applications.

Some pointers can prove helpful. One can begin by asking: Is the invention really *new*? Is it commercially attractive? Is there a market need for the invention or must it be developed? Is the invention a marked improvement over currently available solutions? Is the merit easily demonstrable? A great majority of patents are commercial flops. If the commercial value of the invention is low, patenting efforts should be abandoned. Also if the invention is in a 'hot' area, the likelihood of the technology advancing before the invention is granted a patent is very real. The cost may not justify patenting if protection is short-term. Another vital decision is at what point in time should the inventor initiate filing procedures without compromising the validity or the scope of the ensuing patent at a later date? Mostly these are business decisions and can benefit from the informed opinion of patent attorneys. There is also the folly of rushing too early to file a patent. Technology takes time to mature for markets. If one is not careful, by the time the technology is ready for commercial exploitation, its patent-life would have run out. This is more so for biotechnology, where regulatory approval takes several years of the patent life.

Of the various intellectual properties, utility patents and trade secrets are the most important in biotechnology. Several kinds of biotechnology-related products can be patented. These include: transformed cells, isolated proteins, mutant proteins and active-site portions of antibodies (*Cellular and molecular biology*); transgenic plants and animals (*Genetic engineering*); methods for preparing MoAbs, MoAbs with various specificities against various microbial antigens, hormones, endotoxins, etc. (*Hybridomas*); EIAs, labelled antibodies for scanning (*Diagnostics*); recombinant vaccines, antibiotics, therapeutic peptides, hormones etc. (*Biologicals, therapeutics*). Use claims can be handy when the processes are well known, and only say the microbe varies. All these inventions besides being eligible subject matter of patents, should comply with the conditions of novelty, utility, non-obviousness and enablement.

Using patents and trade-secrets simultaneously

While the trade-secret protects the invention by withholding information, the patent protects by disclosing information. Indeed, a trade-secret is an ideal form of protection as it does not cost anything and lasts forever, at least until it is discovered by reverse engineering. Trade secrets can be licensed out but prior to doing so, it is critical to enter into a confidentiality agreement with the potential licensee. Employees who must have access to such trade secret information must have express confidentiality obligations and be schooled against inadvertent disclosure.

Biological material can be replicated in large quantities from minute amounts of the starting material, be it clones, cell lines, gene sequences, etc. Loss of proprietorial control over the material can mean serious consequences to the owner of the material and therefore it is increasingly important to institute agreements by resident as well as visiting scientists on the use of proprietorial biological material. Cases of lost clones and cell-lines from publicly funded laboratories finding their way into private hands are not unheard of.

The hybridoma for the generation of specific monoclonal antibody against a specific antigen is often kept as know-how. The microbial strain disclosed in a patent and commercially exploited need not be the same, as improved strains are employed in fermentation. Media composition, culture conditions, isolation and purification processes for products can be maintained as know-how. Clinical data or toxicology data may also be withheld as know-how. Even when a patent application is to be filed, there may be ancillary technologies that need not figure in the application but are important to make the product that embodies the patented invention. These are better preserved as trade secrets than as patents. It may be possible to practise both patents and trade-secrets together and it is advisable to disclose only the minimal information mandated by the law for grant of a patent.

Licensing mechanisms

Where funds are scarce as in universities and most publicly funded research institutes, the decision to file a patent is itself risky. The obvious strategy then is to find a licensee who will bear or at least share patenting cost. Intellectual property administration and technology licensing are discreet but inter-related activities. New patterns of technology licensing relationships are emerging and these range from ordinary licenses, marketing partnerships to joint ventures. Research institutions that are publicly funded generally have primary commitment to public good followed by creation of knowledge. Pursuing these goals and simultaneously making some money off the research requires adequate policy decisions at the administrative level because technology transfer activities do affect the freedom of the faculty to the choice of the research project, the right to publish where and

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1. Mukundan, T. and Kishore, K., *Curr. Sci.*, 1991, **60**, 355–362.
2. Constantine. G., in *Biology of Bats* (ed. Wimsatt. W. A), Academic Press, New York. 1970. vol 1, pp. 319–322.

Acknowledgements should be brief. Footnotes are not allowed except to identify the corresponding author if not the first.

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when and also to the choice of collaborators. With biotechnology inventions in general, commercialization is capital-intensive. It is advisable for small research institutions to make a deal of some sort with a larger company which has the requisite resources for successful commercialization.

Licensing

Exclusive, semi-exclusive or non-exclusive licence may be opted. Licences may also be granted on the basis of territory or field of application. The stage of development of the technology, market size and the level of protection available influence licensing activity. The strength of the patent is a major factor in licensing negotiations. However, it is unwise to put away negotiations till grant of a patent as this would mean throwing away precious time for product-development and blunt a major competitive advantage. Market research, technology evaluation and patent search should precede technology transfer and licensing. The act of selecting the *right* licensee who is capable of developing and commercializing the invention needs to be repeatedly emphasized. Some traits one should be looking for in licensees include: (i) the capability for absorption of the invention and its adaptation to field use, (ii) financial strengths in case regulatory approval and development for the product is envisaged, and (iii) the motivation of the company to commercialize the invention. Often technologies are bought by companies to stifle competition to their own products. It is therefore desirable that one looks up the company's product line and ensure that there is no clash of interest. Some of this information can be obtained from the annual reports of the potential licensees, their business plans, the range of products they intend to bring out and the markets they compete in, etc. These can help compare potential candidates for negotiating a licence. It is almost improbable to find the 'ideal' licensee and compromises have to be made. The diverse objectives of the partners makes for a conflict of interest situation. Contentious issues often pertain to the:

Scopes of the licence; Value of the technology–quantum and timing of payments; Determination of milestones, terms of intervention; Indemnity and insurance, e.g. where biologicals for human use are involved.

A win-win attitude from the beginning of the partnership is essential. It should be realized that only when the invention is successfully commercialized, royalties would accrue. Industries must also on their part appreciate the limitations of research institutes and not view licensing negotiations as a one-time opportunity to seize advantage. Two related issues from experience, which in retrospect are very critical to successful technology transfer are, the incorporation in the licence document of a fool-proof reporting system to document the licensee's efforts at commercialization. This would aid the licensor initiate intervention procedures if progress is wanting. The second issue concerns ensuring meticulous royalty/sales record keeping. This will facilitate access of the licensor to audited royalty payment records. It must also be settled as to who in the partnership would bear the costs of infringement litigations if any, the company, the institute or jointly. Retaining know-how helps salvage the invention in case somebody succeeds in working around the patent. Technology-pricing is also tricky. If the technology will have a short life, it is a correct strategy to negotiate for substantial lumpsum payments in the first years. Companies on the other hand emphasize on milestone payments for any 'unproven' technology they may have taken up from the research institute. A reasonable compromise approach should be to spread the licence fee in instalments dictated by the various milestones achieved in the technology transfer process. The licensee not pursuing development of the invention towards its commercialization, has often been the cause of worry of many research institutes, including mine. If progress is not good enough, the institute should be in a position to call off the deal and find a new licensee early enough. Such intervention clauses have to be incorporated into the agreement. If the institute insists on annual licence maintenance fee, and if this quantum is increased over subsequent years, companies may by prompted to bring technologies from the back-burner and actively pursue development. Else if their interest has waned, they would request for termination of the agreement. Either way, for the institute it is better than the unpredictable wait. Successful licensing negotiations appreciate that every eventuality cannot be covered.

In the coming years technology licensing will be even more demanding. In order to be competitive, techno-enterprises may require major readjustments that call for operational flexibility and a fast response time – a trait normally not endowed to public funded research organizations. It is highly unlikely for scientists going about their usual chores to fully comprehend the implications of the law or business strategy. Their talents are best exploited in their own disciplines. The need for the hour is to nurture a band of technology transfer specialists, scientific 'dilettantes' if you may, with a hard nose for business. They should be able to sense research developments in their respective institutes that have potential for industrial applications and then successfully interface with the industry that requires this development. Most Western universities and research institutions have incorporated a technology licensing office within their organizational setup. Perhaps it is time we began to appreciate this fact and modify our approaches to suit the changing scenario.

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