1 Bringing your technology to market

As the births of living creatures at first are ill shapen,
so are all innovations, which are the births of time.

Francis Bacon
Essay: Of innovation 1625

Introduction

We are living in exciting times. The pace of technological development in the 1980s and 1990s has been and will be heralded as a veritable revolution, whether this be in biotechnology, materials science, microelectronics or other 'high' technology fields. With this has come the need to incorporate novel information into products and services and hence, new industries have been born. This book focuses upon the biotechnology industry which, due to its fragmented nature, conveys unique characteristics that should be considered in commercial exploitation. However, it is hoped that the general principles that are described will be applicable to other fields and be of use to anyone wishing to take their technology to market. This book will be of relevance to academics at all levels, to university administrators, to entrepreneurs and to those wishing to enter the technology transfer business.

The technology gap

Molecular and cell biology is revolutionising many aspects of everyday life, allowing the coercive engineering of novel drugs, detection of genetic defects and disease states, making agricultural and industrial processes both more cost effective and friendly to the environment as well as making improvements in the quality of foodstuffs, amongst others. The US was first to realise the potential of this technology and some of the companies that arose in the early days are now familiar names, Genentech, Amgen and Cetus for example. In 1993 there were over 1200 US biotechnology companies, producing an entirely new range of

medicines, foods, etc. Europe has been slow to explore the potential of these new technologies, for reasons that may in part be reflected by our cultural and historical caution. The UK biotechnology industry is probably 10 years less mature than that of the US. This is manifest in the income generated, the number of biotechnology associated companies that have been formed and subsequently 'gone public' and the amount of capital that has been invested. In spite of this, the UK academic community (often funded by the taxpayer) is highly productive. How can this success be translated into products and services that will contribute to the gross national product and individual wealth? Obviously a prerequisite for successful commercial productivity is a research community that keeps generating new technologies. However, in other areas such as the transfer of technology from academia to industry, a positive attitude towards the protection of innovation via patenting and a favourable environment for the financing of ventures and mechanisms to facilitate the introduction of new products, i.e. helpful regulatory and approval procedures, are all necessary. It is in the protection of intellectual property and technology transfer that Europeans must pay particular attention. If we get these right, then the potential wealth and enthusiasm that will be generated will no doubt ensure the necessary positive funding and regulatory environment. Since these areas are are fundamental to bringing your research to market, they will be the focus of this book.

The benefits to society of the commercialisation of academic research have been considerable, and the protection of the intellectual property that arises therefrom allows monetary proceeds from the research to be returned to the originating institute, thus ensuring more research, more jobs, more progress. US universities have been particularly adept at realising the commercial opportunities (e.g. the original Cohen–Boyer patent for genetic engineering that was granted to Stanford University), whilst the equivalent in Europe has been variable in quality and bereft of quantity. There is currently an unfair burden on the taxpayer, who is expected to pay for the research yet inevitably sees a fraction of its true value as a commercial social benefit, since the results are either patented in other countries or highly trained staff seek employment overseas. Some may say that a portion of this research is of such an esoteric nature as to be irrelevant. It is by increasing the interactions between academia and industry that we can reverse this trend and demonstrate that the research has true value to society (Fig. 1.1). It will then be much easier to justify funding. We must also look closely at our attitudes towards science in the market place, since this also presents a considerable barrier. Thus the first hurdle is not legal, but psychological. For example, mechanisms for commercialisation of research are often in place in UK universities yet British academics rarely use them; reactions range from general reluctance to hostility. In addition, there have been several examples of inexperienced academic staff entering into agreements with industrial collaborators only to find that they are severely compromised at a later date and have ended up with a 'deal' that severely under-compensates. Historically, there has always been an attitude that relates to

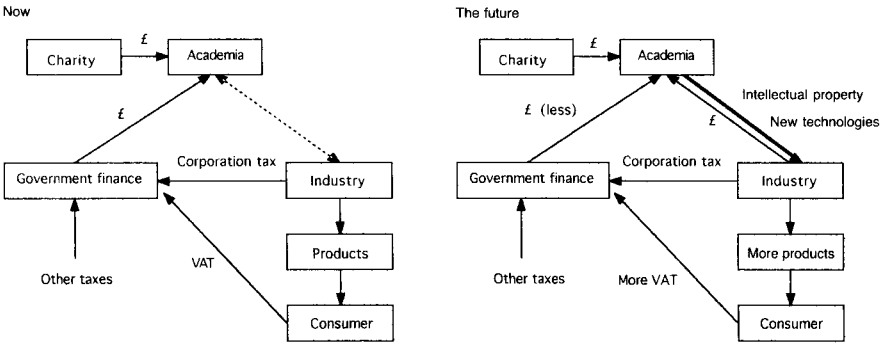

Fig. 1.1. Development of the UK research triangle: now and in the future?

the purity and superiority of non-applied research, which is partly due to both the erroneous perception of lower quality science in industry and partly due to the uncompromising selective processes in our education system. Such misperceptions must change if we are to assume our place in the technologically competitive twenty-first century.

There is a general perception that there is a shortage of finance for biotechnology ventures in Europe and especially in the UK. There is no doubt that compared to other sectors, biotechnology represents a high risk business and usually investors hope that a few extraordinary products will compensate for the large number of failures. The climate is now becoming less favourable, as too many new drugs are either not having the desired clinical effect or are causing unacceptable side effects. Derivation of a product from natural sources (e.g. gene cloning) does not mean that it should be easier to gain regulatory approval for it. Many companies have fallen in the rush to get such products into the market. In addition, several new 'biotechnology' drugs have been shown to have a much narrower range of applications than have been indicated in their respective business plans, with a concomitant reduction in market potential. Investors are cautious about the uncertainties in biotechnology patent protection, being aware of the immense drain upon resources that a patent battle would require, and indeed are concerned about the recent US legislation to limit the prices of pharmaceuticals. This may make European and Japanese companies more attractive in some respects, but the major demand for new therapeutic agents is undoubtedly of US origin. However, not all good ideas will necessarily involve therapeutics and thus require such stringent clinical trial and regulatory regimens; there are a great number of opportunities in related fields (e.g. research reagents, bioprocessing, hybridoma and other antibody technologies, bioelectronics, diagnostics).

Overall, the cash requirements in the biotechnology sector are likely to increase significantly in the next few years as the number of new companies increase and,

for those involved in therapeutics, as clinical trials are performed and regulatory approval is sought. Delays in the latter processes result in a costly loss of patent protection time. There are four crucial factors that will contribute to the direction of any particular company, aside from the important availability of finance and regulatory approval, these are: (a) the size of the potential market and the probability of aquiring a significant share of this market; (b) the relative abilities of the management team; (c) the degree of technological advantage in the chosen field; and (d) the intellectual property position, i.e. whether the retained 'patent wall' is sufficiently strong to protect the company, especially in the US where the market is largest. Opinion is divided on the extent of competitive advantage afforded by protection of intellectual property, since there is discordance between the European, Japanese and US patent offices in both consideration of genetic modification and overall patent policy. The plethora of small companies that are all developing innovative new products but may lack sufficient resource to take these through clinical trials suggests that over the next few years there could be a significant number of strategic alliances, closely followed by merger and aquisition. For those individuals with access to novel biotechnologies and the will to commercialise, it is expected that there could be a concurrent significant financial gain. What is required therefore, is an understanding of how to transfer this new technology (patents, know-how, samples, products, information and processes) to the commercial environment, in a way that is acceptable to both the body which is paying for this to happen and that which owns the assets. It is not an activity that the average academic is likely to enjoy, since there will be a drain on time, a need for communication to people who are not directly involved in your field and the probability of only a small proportion of benefits from these efforts returning to the originator. However, it can be a rewarding if not cathartic experience, since the lines of communication that will be established will help focus your ideas and provide new avenues to funding.

The first objective of this book is to examine the parameters that affect the protection of your intellectual property and the mechanisms of the patent process. Second, consideration is given to negotiation techniques and the further development of ideas in the commercial sphere, including an indication of the difficulties that will be encountered in the valuation of the idea. Third, the licensing of the technology and the start up of a new company are examined, as are the financing and managerial issues associated with development of the venture.

2 So do you really have something of value?

Protection is not a principle, but an expedient.
Benjamin Disraeli.
In a speech made on 17 March 1845

The concept of intellectual property

Before proceeding to take your technology to the market place, you should first consider its protection. There is no point spending effort and time in entering a market when competitors could easily copy your idea and sweep you aside with a better integrated or superior marketing strategy. Legal protection may not stop this, but at least you will have some form of redress and a platform from which to build. Whilst the emphasis in this book will be placed upon the biotechnology industry, it is well to remember that the rapid fluxes inherent in this industry lead to a similar rapid evolution of the intellectual property position.

Intellectual property (IP) is the driving force of any business. Businesses acquire assets in the form of buildings, labour, etc. and these have a tangible value. However, what differentiates businesses is their ability to turn these assets into greater profits. This requires 'know how', the techniques, experience and awareness to turn the assets to best advantage. This is in part inherent in the expertise of the staff that have been employed but is also resident in the intellectual property. This is the protectable part of the 'know how' and is the source of added business value. The right to use intellectual property (an intellectual property right or IPR) is responsible for the establishment of markets, for generating loyalty, for controlling the industry and above all, for generating profit. IP is, of course, difficult to value and this in part reflects our human need to assess value in terms of things we can see. Success is often seen as an active production line, a series of oil rigs, a well equipped facility on a science park, i.e. we naturally equate profit to the successful deployment of the labour force and capital resources. However, the differentiation between products often lies in the concepts and designs, i.e. the trigger for one purchasing decision over another.

Intellectual property is the embodiment of commercial reputation, historical

know how, goodwill and intellectual creativity. For the life scientist the latter is of extreme importance. There is a significant shift towards biotechnology-derived products and there are already in excess of 20 recombinant therapeutic products in use. The globalisation of biotechnology (enhanced by the encumbent power of the pharmaceutical industry) and the importance of advanced technologies to the gross national product of the country has given the biotechnology industry a high profile and a significant political lobby. Thus it is of prime importance that your IP be recognised and protected, both for your own benefit and that of the taxpayer.

For the life scientist, the legal protection of IP primarily involves protection of inventions. This is however, also important for designs, trade marks, artistic and literary items and computer programs. Intellectual property can be treated as any other form of property in that it can be legally mortgaged, licensed or assigned to another party.

Rights and duties

The ownership of IP means that there are various rights and responsibilities that simplistically can be considered to be equal and opposite. A right enables certain privileges, e.g. to use a particular vector or cell line and the corresponding duty is that everyone else should not infringe that right. Importantly, this right exists even if the infringer does not know of the existence of it. There are many compromise situations and exceptions; limitations may include compulsory licences, maximum times for exploitation and a consideration of competition law. With regard to the latter, possession of a patent could result in attempts to unfairly control a market. The monopoly position is open to abuse and both UK and EU law have provisions to control such behaviour.

What are the various forms of IP?

The pre-eminent form of IP protection for the life scientist is the patent (Fig. 2.1). The latter gives a 20 year monopoly right which can be granted for a new invention that is capable of commercial exploitation. The standards are rigorous and therefore the original patent application must be very accurate and precise, particularly with regard to the claims for which protection is sought. Patent rights are an ancient right originally granted by the Crown for certain priveliges, and indeed one of the first can still be seen in Salisbury Cathedral where there are 'letters patent' of Edward III granting one Robert, Bishop of Salisbury, free right of chase in Bishopesbere Wood in Windsor Forest, dated 15 April 1337.

Patents may be assigned or licensed to a person or company, and in order to use the information contained in the patent fees will usually be payable, typically in respect of the extent of likely use. This is embodied in a legal document,

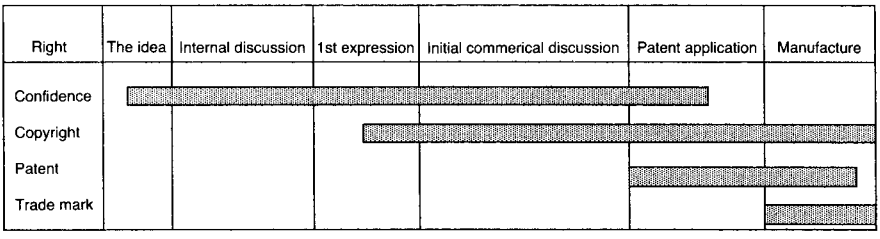

Fig. 2.1. Intellectual property rights.

commonly known as either an **assignment** or **licence**. Usually, patentable inventions are made whilst the inventor is an employee. Depending upon the employment contract, the inventor will always have the right to be identified as such, but the rights to the patent may belong to the employer. However, the inventor need not give up all hope and, if you should patent something that is of outstanding commercial benefit to your employer and there is no revenue sharing arrangement in place, you can apply for an award of compensation. Only you can decide if the internal politics of such a move are wise!

International patent harmonisation is proceeding rapidly, although there are still many inconsistencies across the world stage. In Europe we can expect a community patent to eventually become the dominant vehicle, but at present patents from individual member states are processed through their own offices and if required, the Munich based European Patent Office. For wider protection, there is an International Patent Co-operation Treaty (PCT).

Patents are supposed to be working documents. It is not sufficient to obtain a patent and then not use it, thus preventing others from exploiting the invention. For example, a new technology (e.g. a magic bullet antibody) may supercede an existing therapy (e.g. a drug treatment) that contains a significant element of vested interest (expected profits, etc.). It would not be acceptable for a company to buy the rights to the technology (i.e. be the assignee or a licensee of the patent) and then not use it, in order to protect existing sales. Such behaviour would be anticompetitive and prohibited. Thus, to prevent such abuse compulsory licences may be available three years after grant of the patent, with the terms decided by an independent arbitrator if necessary. In reality, this may be of limited use in biotechnology where the pace of technological advancement is high. Other forms of IP may be of less importance to the biotechnology sector but nevertheless, they will be outlined here to illustrate the range of protection that is available. If a product or idea is not sufficiently novel or inventive to warrant a patent it may be protected with a design right. As the business develops and your product attains market presence, you may consider protecting its image by registering a trade mark, a distinctive symbol or set of words that is identifiable with the product. A set of laws known as 'passing off' governs the misuse of registered and

unregistered trademarks such that misinterpretation of the origin of the product can be reduced. If you have created a literary work, i.e. are an author of an article or a book, then you will always have the right to be identified as the author but the ownership may reside with yourself, your employer or another party. Copyright is not monopolistic and others will be free to create similar product.

For all forms of intellectual property, the law of confidence applies, i.e. it aims to prevent use of information for purposes other than those for which the right was granted. If the information is of an embryonic nature, i.e. pre-patent, then this could be a useful source of protection. However, misuse may be difficult to prove. If you were to give information in confidence on a method to grow a particular cell type, e.g. with a special growth factor cocktail, then it would be a breach of confidence to transfer this information within the receiving company for use on another cell type, unless permission is both sought and granted beforehand.

Having introduced the concept of IP and before discussing how to patent, we must consider the implications of government policy (*Realising Our Potential*, HMSO) upon the protection of IP within UK universities and research institutes.

Fundamental changes in the way we do science

Recent government policy is forcing a change of emphasis upon the UK academic community, towards an increasing involvement of our industrial counterparts. This is an attempt to increase national productivity and to make the UK more competitive with the US, Japan and Europe. It is often said that 'speculative' research is necessary in order to make fundamental break-throughs. However, the notion that more applied research (i.e. that capable of commercial exploitation) does not generate either generic or fundamental results is fallacious. With the appropriate managerial style, there is no reason why the research community should be less productive if there is to be a greater focus upon the applications of the research in question.

There are two major innovations that will become important during the next decade. Their success will determine whether this shift of emphasis to more applied research will, with hindsight, be seen to be a positive step. The first relates to international investment in the UK science base, a delicate balance between the commercial world and academia. This is sometimes referred to as corporate venturing. Whilst this is still in its infancy, there is a definite trend towards these associations. There are four ways in which such investment could be achieved: (a) a direct collaboration; (b) funding posts in a department, e.g. a professional chair; (c) establishing a unit on the university premises; or (d) by establishment of an adjacent research facility. The Department of Trade and Industry favours investment of this nature and we may therefore expect it to increase. For the universities and research institutes there are several advantages to such associations, beyond the obvious influx of funding and an increase in the number of

posts, since it creates a centre of excellence in a particular university. However, at the moment it is very much a case of the 'strong get stronger' and the situation predisposes the style of research, i.e. inevitably there will be a shift towards research with greater applicability. For the company, the advantages are also considerable: (a) close links with the research community, i.e. a source of information; (b) access to human resources, i.e. staff that have been imbued with the corporate ethic; (c) improved options in the intellectual property arena; and (d) a soure of investment that could open a route to those markets which would otherwise be difficult to enter. For example, Japanese or other foreign companies may find this a useful first stepping stone into the UK/European market.

The second relates to the risk/reward argument and the effective development of commercially attractive ideals. There is a big difference between research and development. It is unfortunate, therefore, that they are often linked since there are a different set of skills and resources required for each. Many pharmaceutical companies consider that a competitive edge can be obtained by separating the two departments and concentrating the development resource, i.e. avoiding the inevitable dilution by research goals. Given the speed at which biotechnology is progressing, many pharmaceutical companies have realised that it is almost impossible to keep at the forefront of science at all times and in all areas. This is a major reason for strategic alliances between biotechnology companies and the pharmaceutical industry. The former provide the research leads for the development products of the future, which allied with the large financial resources necessary for both this and the marketing process, makes the alliance conceptually sound. In fact, if one was to extend this situation to its logical conclusion, one could envisage that the major pharmaceutical companies will eventually become 'development' houses that rely upon the research output from smaller specialist research companies. As these companies come and go in any particular subject area, the skilled staff will move from project to project in the search for new research avenues that will challenge their creative spirit. The close relationships that develop between the biotechnology and pharmaceutical sector are already showing in the US markets and indeed, are providing a useful filter for research quality. Unproductive or non-useful research products are not likely to find a customer and will thus be selected out.

The 'development' laboratory will require a very different culture to that of the research laboratory, with both different staff and attitudes. In this laboratory you can set clear targets and milestones. Rather than creative thought, systematic team and project based activities are required, together with cost effective project management. Development is on average nine times more expensive than research since it often includes the clinical studies. In the tough world of competition to put a drug on the market, pharmaceutical companies need to have a significant lead; the chances of a competitor making a mistake cannot be relied upon. So what does all this have to do with commercialising your research? Well, evangelical or prophetic it may be, it is inevitable that there will be a series of

development laboratories set up to reduce the risk and take research projects closer to commercial reality. This will either be on an individual university basis (unlikely except for the largest universities) or perhaps regionalised to support development projects of several universities within a catchment area. When these laboratories are commissioned they will be an integral and efficient part of the mechanism for bringing your research to the market. It will not necessarily involve loss of ownership, but could go a long way towards reducing the risk of your venture, both for you and prospective clients. If non-commerciality is revealed (e.g. your bench top model cannot be scaled up to a useful prototype) then: (a) you will have saved a lot of your own time in the long run; and (b) you will not have compromised a potentially useful industrial contact. If the commercial validity is proven by a development project, then not only does the value (to you) of your product increase, but it becomes considerably easier to sell.

The hope is, of course, that UK universities will eventually augment their existing core competencies with an IP facility, becoming regional technology brokers as they: (a) hold on to a body of IP and judiciously licence; (b) provide facilities for start-up companies where appropriate; and (c) become a clearing house for consultancy services across a wide range of disciplines.

As these commercial relationships develop, so we might expect UK universities to generate revenue through larger, properly managed, contract research agreements and joint ventures, much as exists currently in continental Europe.

Changes in university attitudes to IP

We are undergoing a period of profound and fundamental change in the management of intellectual property in the UK. The days when the British academic community was a soft target for industry will soon be gone and the rethink will require considerable compromise on both sides. The adage of 'he who pays the piper picks the tune' will no longer apply as before, i.e. if industry pays for a piece of work, then it owns all of the resultant IP. The change will involve universities and research institutes holding onto their IP and building a portfolio of IP to justify their existence as centres of excellence. There are a number of conceptual changes, one of which is embodied in the nature of the commercial relationships between industry and academia. From the industrial side, the partner is likely to be somewhat irritated by the 'research grant' mentality of many academics, i.e. the tendency to cost projects on the basis of a research grant rather than on the basis of a commercial proposition. To the defence of the academic, they have probably never known anything else and more to the point, how would they find out about it? Who provides relevant training? The problem is compounded by the often belated and beleaguered attempts of university administrators and technology transfer offices to redress the situation, resulting in an incoherent front being presented to the sponsor. No wonder there is often an air