Tutorial

Patenting inventions arising from biological research

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Published: 20 December 2004

Genome ***Biology*** 2004, **6:**203

The electronic version of this article is the complete one and can be found online at http://genomebiology.com/2004/6/1/203

Abstract

Patents are the most important way in which researchers can protect the income that might come from ideas or technologies they have developed. This article describes the steps involved and the considerations needed for successful granting of a patent. For instance, inventions must be novel and not obvious, adequately described, and useful, and they should not be disclosed publicly before a patent is applied for.

When a researcher or group of researchers develop a novel technique, tool, material or piece of equipment that may be useful, they may wish to patent it in order to ensure that they or their employer can benefit financially from their work. A patent is defined as property right granted by a national government that gives the patentee the exclusive right to use, manufacture, or sell an invention for a prescribed period of time. For the purposes of this article, an inventor is defined as anyone who is responsible for the idea behind the technique, tool, material or equipment; where several people are involved, they must pursue a patent jointly, even when two or more independent labs are involved. Inventors who are employed by a company typically must transfer their rights with respect to the patent to their employers. In many countries, companies may apply for patents for inventions developed by their employees.

This article briefly explains what kinds of things can be patented, why patents are useful, the steps in the patenting process, the particular requirements for biotechnology inventions and in particular inventions in genomics, bioinformatics and proteomics, and common problems and mistakes encountered during the patenting of biotechnology inventions. Researchers in companies may also be able to get advice from their legal department, and many universities have a 'technology transfer' office that can help researchers with the process. Although this article is not intended as legal advice, some simple ways to maximize the value of biotechnology patents and to avoid the common problems and mistakes are proposed. For a more thorough discussion and explanation of specific issues that might be encountered during the patenting process, readers are advised to contact a registered patent attorney or agent in the country in which they desire patent protection (see below). In addition, good places to start obtaining information on the patenting process can be found in Table 1.

What kinds of biological inventions can be patented?

Inventions arising from biological research can mean nucleic acids, proteins, kits for the manipulation or use of DNA or proteins in the laboratory or in medicine, diagnostic kits, pharmaceuticals, microarrays, pieces of software for bioinformatics analysis, or industrial-scale processes for the production of food or medicine. In this article, all of these types of invention are included in the term 'biotechnology'. For example, biotechnology encompasses the Polymerase Chain Reaction (PCR) and all of the machines, enzymes, buffers, processes, and computer software to carry out PCR. This single, multi-faceted invention has not only spawned numerous patents, but numerous legal battles as well. As some of the original PCR patents draw close to expiration, and after many millions of dollars of expenses for both the patentee (Roche, Basel, Switzerland) and the challengers (Du Pont (Wilmington, USA), Promega (Madison, USA), and others), it appears that the legal battles are subsiding, with Roche maintaining patent coverage for the PCR process in most

Table 1

Online sources of information on patenting

Name	Description	URL	
US Patent and Trademark Office patents	Provides general information on preparing and filing a patent application and obtaining a patent in the US	http://www.uspto.gov/main/patents.htm	[15]
European Patent Office guide to applicants	Provides general information on preparing and filing a patent application and obtaining a patent in Europe	http://www.european-patent-office.org/ap_gd/index.htm	[16]
Japan Patent Office: right obtainment procedures	Provides general information on preparing and filing a patent application and obtaining a patent in Japan	http://www.jpo.go.jp/tetuzuki_e/index.htm	[17]
World Intellectual Property Organization: filing PCT applications	Provides general information on preparing and filing an international (PCT) patent application	http://www.wipo.int/pct/en/access/filing.htm	[18]
IPR Helpdesk	Provides information on issues related to worldwide patenting	http://www.ipr-helpdesk.org/controlador.jsp?cuerpo=cuerpo&seccion=principal&len=en	[19]

PCT, Patent Cooperation Treaty.

countries, including the US and European countries, but losing coverage for enzymes (such as *Taq* polymerase) in some countries, such as the US.

Biotechnology also encompasses inventions for models of diseases and methods of drug discovery, such as the 'Harvard Mouse' or 'OncoMouse' [1]. This invention relates to a mouse that was genetically engineered to develop cancer, and which thus can be used to screen for compounds that might trigger the onset of cancer and, importantly, for drugs to combat the disease. Although most industrialized nations permit patenting of some life-forms, this invention brought to the forefront the issue of whether 'complex' or 'higher' life forms should be patentable. Through numerous court battles brought by groups considering themselves environmentalists or animal rights activists, the Harvard Mouse patents have remained intact in some countries (such as the US), have been restricted in scope in others (such as European countries), and have been denied in others (such as Canada). In view of the various differing outcomes, it appears that the debate regarding the patentability of non-human life forms will continue for the foreseeable future, with questions such as "What defines a 'complex' life form over a 'simple' life form?" and "Are all life forms equal for patent purposes?" being debated.

Furthermore, biotechnology encompasses the diagnosis of diseases, kits for diagnosing diseases, and therapeutic products. The breast-cancer predisposition gene *BRCA1* and uses of it are examples of biotechnology inventions that relate to all of these aspects of biotechnology. Patents for this gene and its uses have been granted in numerous countries throughout the world; recently, however, the European Patent Office revoked the patent directed to methods of detecting mutations in the *BRCA1* gene, concluding that the invention lacked novelty and impeded research. That decision almost certainly will be appealed, and the continuing battle will be closely watched by the biotechnology industry and the law profession for an indication of how much the European Patent Office is willing to look to asserted public policy considerations in determining the patentability of certain inventions.

Why consider patenting?

As the world moves from an economy based on industry to one based on information, protecting ideas becomes increasingly important. This follows from the fact that ideas, when captured and passed on as information, can be transferred from one place to another much more easily and quickly than physical objects. It also follows from the fact that the economic value of information is greatest when it relates to an idea, rather than a fact about a physical object, such as a manufacturing plant or commercial product. Because information about ideas is so valuable and so easy to obtain and use, protecting ideas becomes a paramount concern.

There is still much debate about the relative merits of legally protecting scientific discoveries and inventions versus their free and unencumbered disclosure and use. On the one hand, legally protecting discoveries and inventions through patents provides an incentive for researchers and businesses

to undertake scientific inquiry in the hopes of a financial benefit in return. Likewise, when one inventor patents one solution to a particular problem, it highlights that problem and provides an incentive for competitors to find other solutions, thus bringing new products to the market rapidly. On the other hand, permitting an inventor or company to exclude others from making and using an invention can result in higher costs for consumers or a delay in advances in a field covered by a patent because of a lack of advancement by the patent holder. Of course, regardless of the merits of a patenting system, one may always choose to attempt to maintain an invention secret from the world in order to achieve an advantage in the market. But such a strategy often backfires when the secret is lost and others are able to use it without having to compensate the original inventor. For companies, patenting is by far the more attractive choice because it enables the companies to profit from the ideas of their employees. In these times of tight budgets and financial accountability, pursuing patent protection for scientific discoveries and inventions is also important for academic researchers, as patents can generate prestige and income for the institute and for individual researchers.

The process of patenting always begins with an invention. Various definitions of 'invention' have been used through the ages, with most falling by the wayside for one reason or another. For practical purposes, an invention is an idea in the mind of the inventor of a useful machine, process, article of manufacture, or composition of matter, where the idea is new and is not simply an obvious derivation of something already known. Whether that invention is patentable is a different question altogether, because patentability is defined by statutory requirements. Biotechnology patent applications must satisfy all of the following requirements: novelty, inventiveness and lack of obviousness (one cannot obtain a patent for subject matter that was publicly known or obvious at the time the application was submitted to a patent office or 'filed'); adequate description and support for the claimed invention (one must disclose enough information to permit the public to understand, make, and use the full scope of the claimed invention); and utility or industrial applicability (an invention must have a real-world use). Patentability is based not only on these requirements, though, but also on the description of the invention in the patent document. In biological inventions, it is often also based on the amount of experimental data available to show that the invention actually works as envisioned by the inventor.

Simply because one has an invention, it might not always be advisable to patent it. Many inventions are economically impractical either because they are too expensive to bring to market at an attractive price, or because they appeal to such a small portion of the public that the cost of setting up a production facility would not be recouped. Furthermore, some inventions, such as those relating to public health or gene sequences, are viewed by many in the public as inappropriate for patenting, and applications for these are struck down during appeals brought by parties that protest the patent. In such cases, the inventor or his company will have invested large sums of money to obtain and defend the patent with no legal protection to show for it in the end.

In general, any invention that is suitable for use by the public, and that does not contravene public morality, is patentable. Thus, most biotechnology inventions are suitable for patenting. In view of the differing social mores from country to country, the definition of what constitutes an invention that contravenes public morality can differ among countries. For example, in the US, biotechnology inventions that have no practical use except in killing humans are considered immoral, and thus would not be suitable for patenting. In many other countries, such as countries in Europe, patenting of biotechnology inventions directed to methods of treating humans for diseases is considered against public morality (but they are patentable in the US). Although patents are available in these countries for the drugs and diagnostics used to treat or identify diseases, patents on methods of treating, which could be enforced in such as way as to prohibit doctors from practicing their profession and providing life-saving services, are considered to contravene public morality.

So you have an invention: how do you patent it?

Once you have decided that you have a potentially patentable invention, the next step in the process is to prepare and submit a patent application before publicly disclosing the invention. Details of what needs to be included in the application are outlined below, but the main sections are the claims of an application, statements at the end of the patent document that specifically point out the subject matter that the inventor considers to be his or her patentable invention, and the disclosure itself, which gives details and supporting material. It is important to appreciate that a patent is a national right: there is currently no single patent that provides legal rights throughout the world, so it is therefore necessary to obtain a different patent in each country in which patent protection is desired. Biotechnology inventions generally require a large investment in time, labor, and money and yet, once the invention is completed, it is relatively inexpensive and easy to produce and/or practice the invention. Because patent documents disclose the details of how to make and use the invention, because it is now a simple matter to search for and obtain copies of patents issued in any country throughout the world, and because biotechnology inventions relate to biological systems that are available worldwide, it is important that inventors and their employers obtain patent protection in as many different countries as is practical. Fortunately, most industrialized nations have similar requirements and procedures for obtaining a biotechnology patent. Some similarities and differences between the requirements in the US, Europe, and

Japan can be found at the trilateral website administered jointly by the three patent offices [2]. The similarities permit inventors who are educated in the patenting process of one country to be reasonably educated in the process in other countries, and thus to minimize the cost - in both time and money - of obtaining patents in all countries of interest.

Although the US and a few other countries permit public disclosure of an invention up to one year before filing a patent application, the vast majority of countries require absolute novelty. Thus, inventors who desire patent protection throughout the world must be careful to file a patent application before publicly disclosing the invention. In addition, in all countries except the US, inventors must file a patent application quickly because in these countries the first to file an application (rather than the first to invent) obtains the right to patent the invention.

After a patent application is filed, it typically sits at a patent office in a dormant, pending state for a period of time before substantive examination begins (the period is at least 18 months in the US [3] and is similar in other countries). This dormant period is due to the backlog of applications at the patent offices that have resulted from the tremendous increase in the number of biotechnology patents filed recently; it also reflects the inability of most patent offices to hire and adequately train a sufficient number of examiners to keep pace with the rate of patent filings. Substantive examination begins when the examiner, appointed by the patent office, reviews the application to determine whether it satisfies the requirements for patentability and issues a written communication to advise the applicant of any problems. Patent examiners are employed by the patent offices; they are trained in basic concepts of patent law and also have training in a specialist field, such as molecular biology, bioinformatics, protein biochemistry, or genetics. In the initial communication to the applicant, the examiner may reject the claims of the application for failing to satisfy one or more laws or the requirements mentioned above. The claims of the application, not the disclosure details, comprise the section of the patent application that defines the legal right to exclusively make, use, or sell the invention, or provide the legal right to exclude others from making, using, or selling the invention.

Upon receipt of the written communication from the examiner, the applicant has the opportunity to respond to any objections and rejections. Typically, the applicant makes changes to the claims, cancels or deletes claims that do not appear to be patentable, or submits arguments against the examiner's objections and rejections. If the response by the applicant does not convince the examiner that the application is patentable, the applicant must choose whether to abandon the application, to continue to argue for patentability, or to appeal against the examiner's decision to a supervisory board that has power to overrule the examiner. If the applicant is not satisfied with the decision of the supervisory board, he or she can take the appeal to the national courts, but this is very costly in terms of both money and time. A schematic overview of the patenting process in the US and Europe is depicted in Figure 1.

Why are biotechnology inventions difficult to patent?

Researchers who have biological inventions are often surprised by the difficulties they encounter when trying to patent their inventions, compared with the experience of their counterparts in the fields of electronics and mechanics. These difficulties arise because a higher standard of scrutiny is applied to inventions in biotechnology because they are more complex and unpredictable (see below) [4]. For example, for patents including the sequences of genes or proteins, the current policy of the US Patent and Trademark Office is to require disclosure of "a representative number of examples" of homologs, either from the same organism or from different organisms, of the gene or protein before a patent generically covering it will be issued [5]. Although the European Patent Office does not officially have such a policy, in cases in which the essence of the invention is the achievement of a technical effect, it is often necessary to provide a sufficient number of examples to show that the effect can be achieved in most - if not all - instances of the use of the invention in a particular field. For example, if one wished to patent an antibody for use in detecting all cancer cells, one would probably need to provide examples showing that the antibody could detect a variety of different cancer cells, including solid tumor cells, and lymphoma cells, and leukemia cells.

Patent offices invariably justify their higher standard of scrutiny for biotechnology inventions by asserting that biological systems are complex and unpredictable and that complex and unpredictable technologies should require a greater amount of data and disclosure. Although this assertion might be an inaccurate generalization, one must continually be mindful of the policy before and during the patenting process in order to improve the likelihood of obtaining a patent with commercial value.

How to get the best-value patent

In view of the time and money required to obtain patent protection for a biotechnology invention with the potential for international success, it is important to maximize the value that will be returned on the investment. The following are some key areas on which applicants for biotechnology patents should focus in order to maximize the return on their investment. First and foremost, applicants should not disclose the invention publicly until a patent application has been filed in at least one country. A public disclosure includes absolutely any non-confidential disclosure to any person outside of the

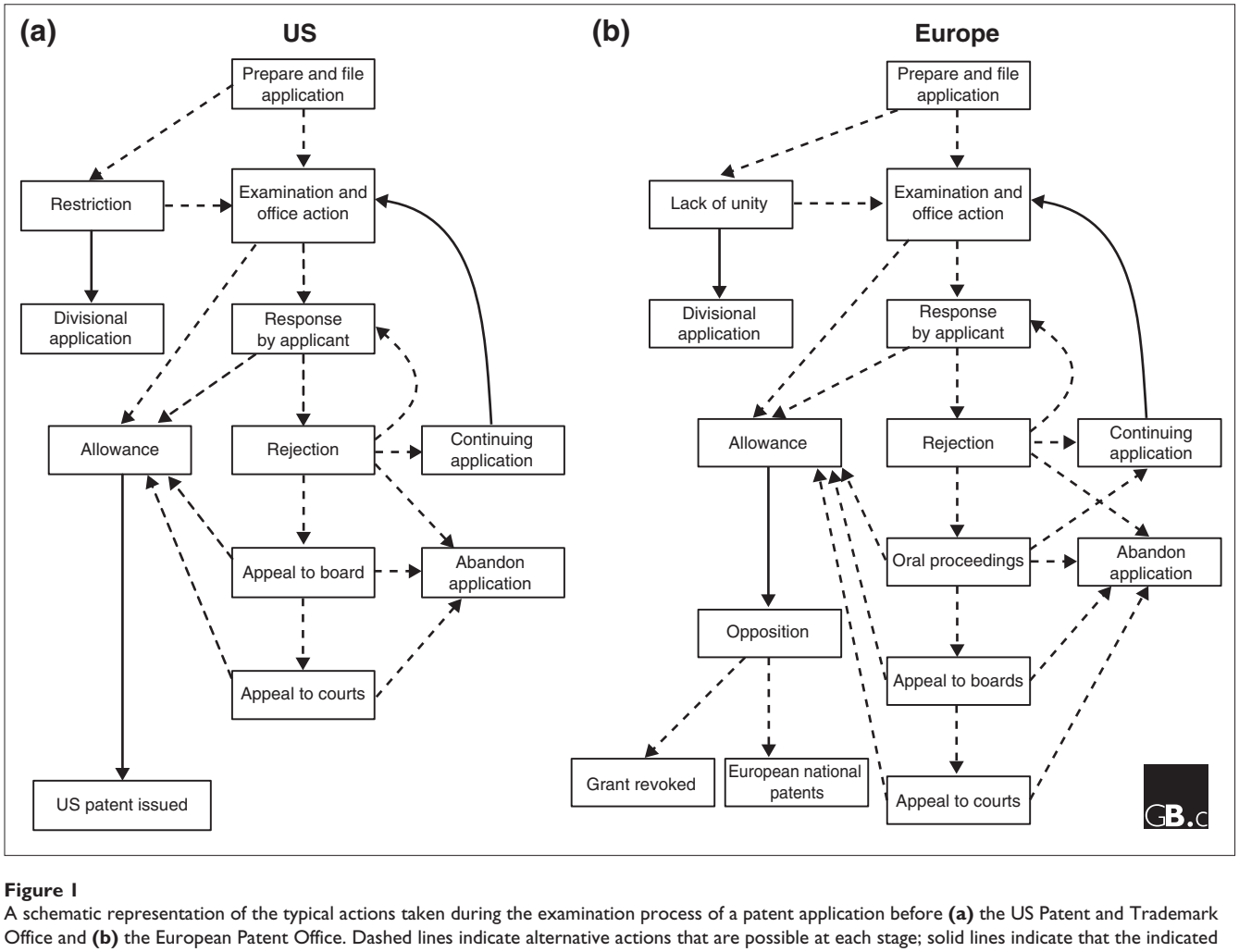

Figure 1

A schematic representation of the typical actions taken during the examination process of a patent application before **(a)** the US Patent and Trademark Office and **(b)** the European Patent Office. Dashed lines indicate alternative actions that are possible at each stage; solid lines indicate that the indicated action necessarily follows the previous one. It can be seen that two steps are available in Europe but not in the US: an optional oral hearing before the patent is allowed, in which applicants may argue orally for the patentability of their inventions before a panel of examiners, and an opposition period after the application is allowed, in which the public may oppose the patent. 'Restriction' and 'Lack of unity' are equivalent procedures through which the patent offices require an applicant to divide a single application into two separate patent applications (an 'original' and a 'divisional'), on the basis of a conclusion that the single original application disclosed and claimed two distinct inventions. An 'office action' is a written report issued by the examiner regarding the patentability of the claimed invention. Upon concluding that an application is patentable, the examiner will 'allow' the application. In the US, the issuing of the patent typically follows allowance after completion of certain simple formalities, whereas in Europe the issuing of a patent does not occur for several months; during this time, members of the public may oppose the patent and the patent applicant must substantively defend the patentability of the invention.

company or organization in which the invention was made, and it can include disclosure by a person other than the inventor. Thus, public disclosure includes publication in a journal (whether print or web-based), presentation of a poster or abstract at a scientific or trade meeting, discussions with others in the field at a meeting or over the telephone, and discussion or mention in an e-mail. The disclosure, however, must be 'enabling'. That is, the information disclosed publicly must be of such a quality and quantity that someone with an ordinary level of skill in the field could make and use the invention. Thus, a mere statement that a company has developed an algorithm to identify and distinguish clinical isolates of a particular pathogen would be unlikely to constitute a patent-defeating public disclosure; more details of the steps in the process would be needed for an ordinary person to arrive at the particular algorithm. Confidential disclosures, such as those between employees of the same company, between an inventor and his or her attorney, or between those covered by a legal agreement, such as a non-disclosure agreement, should not defeat the patentability of an invention. As mentioned above, in most countries, public disclosure of the invention before filing a patent application bars the right to obtain a patent on the invention. In addition, disclosure of improvements or new data relating to the invention could rule out a patent on the new subject matter; care must therefore be taken when discussing any aspect of an

invention in public. As a general rule, to avoid the loss of rights to a patent, any information that could serve as the basis for a patent should be included in a patent application - and filed in a patent office - before that information is made available to the public.

Applicants should also make a thorough search of patent and scientific databases before preparing and filing a patent application, to determine whether the subject matter of the invention has already been disclosed. In searching, one should focus not only on the specific commercial embodiment of the invention, but on broader aspects as well, so as to find out how broad the patent could be. Time and money spent at this stage is well spent, because the results of the search can guide applicants in both preparing the patent application and entering the marketplace with a viable product. Numerous free and commercial public databases are available for searching: a list of some commonly used ones is shown in Table 2.

Applicants should also consider filing the application under the Patent Cooperation Treaty (PCT), which gives applicants access to over 100 countries for a single filing fee and provides at least 30 months in which to decide whether to proceed with the application in one, some, or all of the treaty countries [6]. In addition, under the PCT a single opinion by a patent examiner on other related patents and the patentability of the invention is issued before a decision by an applicant to proceed with the application in commercially important countries must be made [7]. If this opinion uncovers one or more publications that negate the patentability of the invention, the applicant can abandon the application without having incurred the filing fees for the commercially important countries. The 30-month delay also lets the applicant determine whether the invention is commercially feasible before having to pay the filing fees for all commercially important countries.

I had an invention - why didn't I get a patent that is worth anything?

The reasons why a biotechnology patent application might never become a patent or might have limited commercial value fall into two main categories: inadequate research and preparation of the application before filing, and inadequate data to support a commercially valuable patent. The single most common reason for failure is because of insufficient novelty or inventiveness, almost invariably because a thorough search of patent and scientific databases was not done. An applicant in this position must either give up the idea of a patent or spend considerable additional resources attempting to salvage the application. To avoid this common pitfall,

Table 2

Databases of patents and scientific publications

Name	Description	URL	
United States Patent and Trademark Office: patent full-text and full-page image database	For searching and printing US patents and published US applications	http://www.uspto.gov/patft/index.html	[20]
European Patent Office: esp@cenet	For searching and printing worldwide patents and patent publications	http://ep.espacenet.com/search97cgi/s97_cgi.exe?Action=FormGen&Template=ep/EN/home.hts	[21]
Japan Patent Office: quick guide	For searching and printing Japanese patents and patent publications	http://www.jpo.go.jp/quick_e/index_search.htm	[22]
World Intellectual Property Organization: Intellectual Property Digital Library	For searching and printing international (PCT) applications	http://www.wipo.int/ipdl/en/index.jsp	[23]
NCBI PubMed	Database of biomedical research articles	http://www.ncbi.nlm.nih.gov/entrez/query.fcgi	[24]
Thomson Derwent	A collection of databases of biotechnology research articles for fee-based searching and retrieval	http://www.derwent.com/	[25]
Chemical Abstracts Databases	A collection of databases of chemical and pharmaceutical research articles and compounds for fee-based searching and retrieval	http://www.cas.org/casdb.html	[26]
STN	A collection of databases of biotechnology research articles for fee-based searching and retrieval	http://www.cas.org/stn.html	[27]
Google Scholar	A system for searching academic articles and other scholarly publications, and their citations	http://scholar.google.com/	[28]

one should not only perform a thorough search of public databases but also craft the application so as to avoid overlap with similar publications.

A second common pitfall is disclosure of too little information about the claimed invention. Biotechnology patents now typically cover only what is precisely disclosed and described in the application. Likewise, the examiner's judgment of the invention's utility depends critically on the amount of information disclosed. Examiners in the US Patent and Trademark Office rely heavily on strict written guidelines on description and utility when determining whether there is adequate disclosure of information [5,8]. European examiners also rely on guidelines and often also insist that each word in the claims of an application is present in the text of the patent disclosure and is used in precisely the same way as it is used in the claims. Thus, often no generalizations or synonyms are permitted in the claims [9]. More often than not, examiners in most countries look specifically at the examples provided - and any nucleotide and amino-acid sequences disclosed - to determine the breadth of the claims that will be issued in the patent.

The problem of disclosing too little is especially prevalent when an applicant relies on a patent document from another country to provide a 'priority' date for an invention, the date on which the first patent describing it was filed. Certain countries permit applicants to claim priority on the basis of the date that a foreign patent application was filed. This priority date is considered (for the purposes of identifying publications that defeat the novelty or inventiveness of the invention) as the filing date of an application somewhere in the world, even though the actual patent application being examined may have been filed up to twelve months after that date. On the one hand, this mechanism benefits applicants because it allows them to file a single application in one country and wait up to one year to file applications in other countries. On the other hand, it is a trap for the unwary biotechnology applicant who prepares and files a priority application in such a way as to satisfy the legal requirements of only the individual country in which it is first filed. Unfortunately for many applicants, the legal requirements for that first country might not be as stringent as those of other countries, and the scope of the patents in the other countries might be limited accordingly on the basis of an inadequate disclosure. For example, patent applications in some countries, such as some in the Pacific Rim or South Pacific regions, are acceptable if they disclose the general concept of the invention and provide a single specific example of the general concept. In the US, however, such a disclosure, if relating to a biotechnology application, would probably not be sufficient to support a patent covering the general concept. Thus, the US Patent and Trademark Office would probably not recognize the 'priority' date as a valid date for broad claims, and they could limit the breadth of the claims to the specific example if the examiner found a relevant publication that preceded the actual US filing date. Alternatively, if the applicant attempts to add subject matter to the application when it is filed in the other countries, that subject matter will probably not be granted the filing date of the priority document. Information that became publicly available between the dates of filing of the first (priority) application and the second application may be used to defeat the patentability of the second application [10,11].

The cure for this heightened disclosure requirement is obvious, but it is not necessarily simple: one should disclose as much information and data in the first-filed application as is needed to satisfy the requirements of all countries. Prudent applicants now disclose many ranges, data points, and other parameters to support varying claim scopes. For example, applications directed to microarrays often include the use of nucleic acids bound to a solid support, and the number of different sequences present or the number and location of duplicate copies of a single sequence on the solid support is important. In such a situation, it is wise for the applicant to disclose a variety of numbers and locations. The examiner will then be able to differentiate the invention from other relevant publications that might include a general disclosure of the concept, but not the specific data that are important in making the microarray useful.

Prudent applicants will also provide as much relevant data as possible, covering as many chemical compounds or biological species as they can. Because the breadth - and thus the value - of a biotechnology patent now depends essentially on the amount of information presented in an application, it is best to disclose and claim all possible aspects of an invention, not simply the core of the invention. Of course, if an applicant recognizes that the invention is broader than implied by the specific data available at the time of preparing the application, he or she must choose to either support the breadth of the invention with scientific reasoning, and argue to the examiner that the reasoning is sound and sufficient to warrant broad coverage, or forego broad claims and file additional patent applications when data supporting the broader aspects become available. For example, imagine that members of a research group file a patent application that states that the invention covers all antisense molecules that disrupt expression of a gene, but provides specific examples of only two antisense molecules. If they can convince the examiner that the two examples provide enough information for other scientists to create other antisense molecules with the described function, they might obtain a broad patent covering all antisense molecules that disrupt expression of the gene. But if the applicants are unable to convince the examiner that the two specific examples provide enough information to develop other functional antisense molecules, they may have to accept a narrow patent that covers only the two examples. They may then file another application to add further examples of functional antisense molecules and argue that the additional examples, in conjunction with the

original examples, provide enough information for a scientist to create other functional antisense molecules.

In contrast to the problem of disclosing too little, applicants often find that they have claimed too little. This pitfall typically stems from a failure of the inventor to appreciate fully the true scope of the invention, or a failure to claim the invention in terms that cover its full scope. Even when inventors recognize the true breadth of their inventions, they often incorrectly believe that claims to the 'core' of the technology provide coverage for the full scope of all aspects of the invention; unfortunately, narrowly focused claims do not necessarily cover all aspects of an invention. In addition, narrowly focused claims are often easy for the public (or competitors) to avoid - in other words, they can market a product that is very similar but escapes infringement and thus the need to pay royalties by being slightly different. For example, a patent for a microarray containing "5,000 individual oligonucleotides that are specific for an expressed *Escherichia coli* gene" could be designed around by making a microarray containing 6,000 individual oligonucleotides or by a microarray containing 5,000 individual oligonucleotides, one thousand of which bind equally well to *E. coli* and *Salmonella typhimurium* genes and thus are not specific for *E. coli* genes. On the other hand, a broader claim, such as one to a microarray containing "at least 1,000 oligonucleotides that individually either perfectly match, are perfectly complementary, or bind under high stringency conditions to a sequence within at least one expressed *E. coli* gene" would be much more difficult for a competitor to design around and avoid. By failing to consider and claim the broad applicability of their inventions, applicants often obtain patents that cover too little subject matter.

With the increasing emphasis that patent offices are placing on the utility of biotechnology inventions, applicants are now finding that applications that fail to identify specifically the utility of the invention are rejected [12]. For example, applicants typically must now identify the specific function of a cloned gene or its encoded protein and, further, must identify an industrial or 'real world' use for the gene and/or the protein it encodes. Likewise, applicants claiming a therapeutic product or method must typically present data showing that a therapeutic result can be achieved. Prudent applicants now delay filing patent applications until they can identify a specific industrial or other utility for their invention. The most cautious, and most successful, delay filing until data are available to support the utility clearly.

Historically, many biotechnology inventions have been based on gene cloning and the expression of cloned genes, and patents on such inventions necessarily rely on the sequences of the genes and encoded proteins. For various reasons, a significant number of patent applications are filed with incorrect nucleotide or amino-acid sequences. These applications can be commercially useless if the errors are not corrected before a patent is issued. Although it is generally not possible to submit a new, different sequence after an application has been filed, many countries provide a mechanism for correcting sequences or for claiming nucleic acids or proteins as part of a patent without presenting their sequences. To take advantage of this mechanism, it is critical that the applicant ensures that biological material containing the nucleic acid or protein is deposited in an internationally recognized depository and that the biological material is identified specifically in the application. By taking these steps, an applicant may later either correct the sequences or simply claim the deposited biological material as the basis for a patent rather than the published sequences. In the absence of such steps, it is difficult or impossible to correct errors or claim the biological material as containing the invention [13,14].

Another common trap for unwary applicants is failure to disclose the computer software used to analyze sequence data. There are now numerous programs available for this, and they can give differing results from the same sequence information. Accordingly, without information about the programs used to analyze sequence data, it could be difficult, if not impossible, for the public to reproduce the analysis and to determine whether certain activities infringe a patent. This shortcoming can serve as a basis for rejection of the application and thus the computer programs used and the parameters used in each analysis should always be disclosed.

Are genomic, proteomic and bioinformatic patents worth the trouble?

There are some specific issues that should be considered when deciding to patent inventions in genomics, proteomics, and bioinformatics. Firstly, one must always remember that these fields rely, at least to some extent, on both biotechnology and either electronics or physics, and that most patent examiners are not educated in more than one scientific or engineering field. Thus, examination of the patent application can be delayed because the examiner needs to consult with other examiners in a different area of science. Worse yet, an inadequate examination might occur if an examiner lacking the necessary education does not consult with another examiner. In essence, the greatest economic value of inventions in genomics and proteomics is in the information they can provide, such as the genes and proteins involved in diseases and disorders, nucleotide sequences bound by key proteins, and candidates for drug targets. Because patent applications typically do not identify all of these genes, proteins, target sequences, and drugs, they do not cover the greatest economic value of the invention. Likewise, genomics and proteomics inventions typically rely on a large number of individual pieces of data. As discussed above, to ensure that one obtains patents in all of the most economically important regions of the world, an applicant should disclose the primary sequence of all nucleic-acid and protein

components, or at least the specific source and procedure for obtaining each. By disclosing all of this information in the application, however, applicants make it easy for others to 'design around' the patent, that is, to design a product or method that does not infringe by simply adding, deleting, or altering one or a few components. This result is clearly not in the best interest of the applicant. Thus, if it appears that a patent with broad, commercially valuable claims is not obtainable, the applicant might want to consider protecting the invention through other means.

One way to avoid many of the problems that arise in patenting biotechnology inventions is to maintain such inventions as trade secrets. In essence, a trade secret is information that provides economic value to its holder from not being known by other people. Typically, the information provides an advantage in the marketplace for the holder over any competitors. This means that revenue streams can be generated by practicing the inventions in a secure environment, marketing the inventions without disclosing how they are made or how the data provided to customers are generated, or licensing them to others without disclosing the specific sequences, data points, or algorithms. Competitors will therefore find it difficult to produce similar products by making small modifications to the design or 'reverse engineering' (copying of a competitor's technology by disassembling a product and reproducing its individual parts to create an exact copy or functional equivalent), and potentially long-lived, stable revenue streams can be secured without the need for patenting.

In conclusion, patents are important for protecting the right of inventors to profit from their research. The patenting process can be complex and there are numerous traps for the unwary scientist, but a basic understanding of the process can make the important issues clear. Furthermore, although you can never predict a successful outcome, avoiding the common pitfalls can significantly reduce the cost of obtaining patents - and the frustration encountered during the process - and can increase the chances of obtaining a broad, commercially valuable patent.

References

1. Jaffe S: **Ongoing battle over transgenic mice,** *The Scientist* 2004, **18:**46.
2. **Trilateral Patent Office** [http://www.european-patent-office.org/tws/twsindex.htm]
3. **United States Patent and Trademark Office**: **performance and accountability report fiscal year 2003** [http://www.uspto.gov/web/offices/com/annual/2003/040201_patentperform.html]
4. Sampson M: **The evolution of the enablement and written description requirements under 35 U.S.C. § 112 in the area of biotechnology.** *Berkeley Technology Law Journal* 2000, **15:**1233.
5. **Guidelines for examination of patent applications under the 35 U.S.C. 112, paragraph 1, "written description" requirement.** *US Federal Register* 2001, **66:**1099-1111.
6. **United States Patent and Trademark Office: PCT Contracting States** [http://www.uspto.gov/web/offices/pac/dapp/pctstate.pdf]
7. **WIPO Press Release PR/2003/372: PCT reforms kick in on New Year's Day** [http://www.wipo.int/edocs/prdocs/en/2003/wipo_pr_2003_372.html]
8. **Utility examination guidelines.** *US Federal Register* 2001, **66:**1092-1111.
9. **Guidelines for examination in the European Patent Office** [http://www.european-patent-office.org/legal/gui_lines/index.htm]
10. **Title 35 of the United States Code, Section 119 (35 U.S.C. §119)** [http://www.gpoaccess.gov/uscode/index.html]
11. **Opinion of the enlarged board of appeal G 2/98** [http://legal.european-patent-office.org/dg3/pdf/g980002ep1.pdf]
12. **Directive 98/44/EC of the European parliament and of the Council of 6 July 1998 on the legal protection of biotechnological inventions** [http://europa.eu.int/eur-lex/pri/en/oj/dat/1998/l_213/l_21319980730en00130021.pdf]
13. Enzo Biochem, Inc. versus Gen-Probe, Inc.: 296 F.3d 1316 (Fed. Cir. 2002).
14. **EPO Board of Appeal decision G 0011/91** [http://legal.european-patent-office.org/dg3/biblio/g910011ep1.htm]
15. **United States Patent and Trademark Office: patents** [http://www.uspto.gov/main/patents.htm]
16. **The EPO guide for applicants** [http://www.european-patent-office.org/ap_gd/index.htm]
17. **Japan Patent Office: right obtainment procedures** [http://www.jpo.go.jp/tetuzuki_e/index.htm]
18. **World Intellectual Property Organization: filing PCT applications** [http://www.wipo.int/pct/en/access/filing.htm]
19. **IPR helpdesk** [http://www.ipr-helpdesk.org/controlador.jsp?cuerpo=cuerpo&seccion=principal&len=en]
20. **United States Patent and Trademark Office: patent full-text and full-page image databases** [http://www.uspto.gov/patft/index.html]
21. **European Patent Office: esp@cenet** [http://ep.espacenet.com/search97cgi/s97_cgi.exe?Action=FormGen&Template=ep/EN/home.hts]
22. **Japan Patent Office: quick guide** [http://www.jpo.go.jp/quick_e/index_search.htm]
23. **World Intellectual Property Organization: Intellectual Property Digital Library** [http://www.wipo.int/ipdl/en/index.jsp]
24. **PubMed** [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi]
25. **Thomson Derwent** [http://www.derwent.com/]
26. **Chemical Abstracts Databases** [http://www.cas.org/casdb.html]
27. **STN - Your connection to science and technology** [http://www.cas.org/stn.html]
28. **Google Scholar (Beta)** [http://scholar.google.com/]