

Tutorial

# Patenting inventions arising from biological research

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## 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 production of food or medicine. In this article, all of these types of invention are included in the term 'biotechnology'. Some examples are the Polymerase Chain Reaction (PCR) and all of the machines, enzymes, buffers, processes, and computer software to carry out PCR, the 'Harvard Mouse' or 'Onco-Mouse' [1], which can be used to screen for compounds that might trigger the onset of cancer and for drugs to combat the disease, and the breast-cancer predisposition gene *BRCA1* and uses of it. For further details of these inventions and the debates that arose over their patents, see the complete version of this article, online.

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

PCT, Patent Cooperation Treaty.

### Why consider patenting?

Protecting ideas is nowadays a paramount concern, because information about ideas is so valuable and so easy to obtain and use. There is still much debate about the relative merits of legally protecting scientific discoveries and inventions versus their free and unencumbered disclosure and use. Patents provide an incentive for researchers and businesses to undertake scientific inquiry in the hopes of a financial benefit and help to bring new products to the market rapidly. They can, however, result in higher costs for consumers or a delay in advances in a field. Of course, one may always choose to keep an invention secret, but this can backfire 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. Patent protection is also important for academic researchers, as patents can generate prestige and income for the institute and for individual researchers.

An invention is an idea 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. Biotechnology patent applications must satisfy all of the following requirements: novelty, inventiveness and lack of obviousness; adequate description and support for the claimed invention; and utility or industrial applicability. 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. It might not always be advisable to patent an invention, for example if it will be too expensive to bring it to market at an attractive price; and some inventions, such as those relating to public health or gene sequences, are viewed by many in the public as inappropriate for patenting. In general, any invention that is suitable for use by the public, and that does not contravene public morality (ideas of which differ among countries), is patentable. Further details of the advantages and disadvantages of patenting and the differences between countries in ideas of what contravenes public morality are available in the complete version of this article, online.

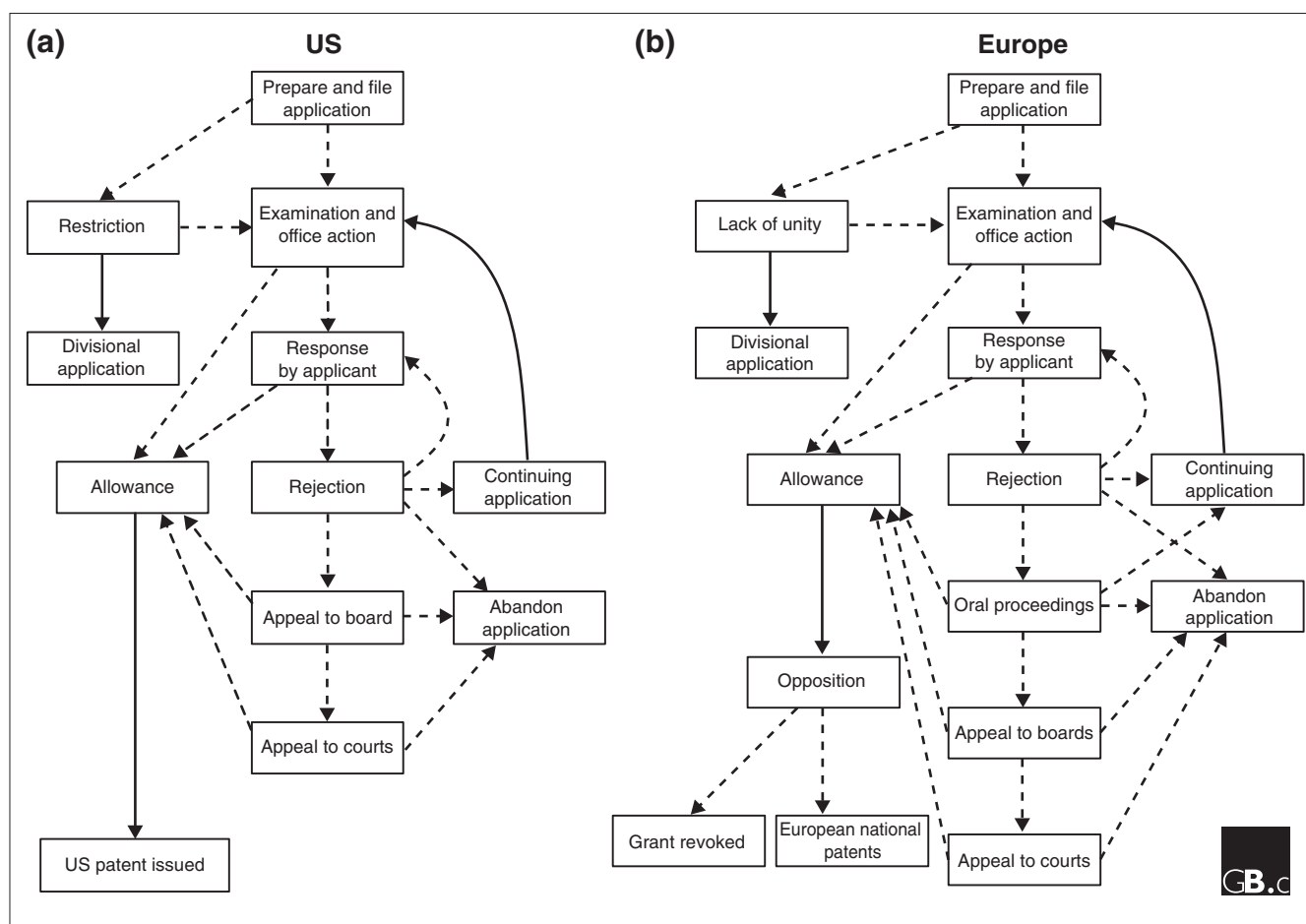
### So you have an invention: how do you patent it?

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 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. Fortunately, most industrialized nations have similar requirements and procedures for obtaining a biotechnology patent [2]. One

major difference is that the US and a few other countries permit public disclosure of an invention up to one year before filing a patent application, whereas the vast majority of countries require absolute novelty.

After a patent application is filed (and often after a delay of up to 18 months [3]), it is examined by an examiner appointed by the patent office, who advises the applicant of any problems or may reject the application for failing to satisfy one or more laws or requirements. The claims of the application, not the disclosure, are what defines the legal right to exclude others from making, using, or selling the invention. The applicant has the opportunity to respond to

any 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. A schematic overview of the patenting process in the US and Europe is depicted in Figure 1, and further details are available with the complete version of this article, online.



**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.

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## 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 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 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.

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]. Further details on what constitutes public disclosure and on the PCT are available with the complete version of this article, online.

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

The single most common reason why a biotechnology patent application is unsuccessful is because of insufficient novelty or inventiveness, almost invariably because a thorough search of patent and scientific databases was not done. A second common pitfall is disclosure of too little information about the claimed invention. Biotechnology patents now typically cover only what is precisely described in the application, and the examiner's judgment of the invention's utility is critically dependent on the amount of information disclosed [8,9]. 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, something that is permitted in certain countries. If an application is prepared in such a way as to satisfy the legal requirements of only the individual country in which it is first filed, its scope in other countries may be limited [10,11].

Prudent applicants now disclose as much relevant data as possible, and it is best to disclose and claim all possible aspects of an invention, not simply the core of the invention. For example, imagine a patent application that covers all antisense molecules that disrupt expression of a gene but provides specific examples of only two antisense molecules. If the applicants cannot 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.

Applicants often find that they have claimed too little, through failing to appreciate fully the true breadth of the invention or to claim the invention in terms that cover its full breadth. Narrowly focused claims are often easy for competitors to avoid. 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. 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. Also, applications that fail to identify specifically the utility of the invention are now frequently 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 data are available that clearly support the utility of the invention. Also, the computer programs used and the parameters used in each analysis should always be disclosed.

Many biotechnology patent applications rely on the sequences of genes and their encoded proteins; these applications can be commercially useless if the nucleotide or amino-acid sequence 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, if biological material is deposited in an internationally recognized depository and identified specifically in the application, this problem can often be avoided. Further discussion of the issues around disclosure in patent applications is available with the complete version of this article, online.

### **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

**reviews**

The complete version of this article, available online at <http://genomebiology.com/2004/6/1/203>, includes the following additional information:

**Further details** of example inventions and the debates that arose over their patents.

**Further discussion** of the advantages and disadvantages of patenting and the differences between countries in ideas of what patents might contravene public morality

**Further details** of the steps involved in the patenting process.

**Further details** on what constitutes public disclosure of an invention and on the Patent Cooperation Treaty

**Further discussion** of the issues around disclosure in patent applications.

**Table 2**, listing databases of patents and scientific publications.

14. **EPO Board of Appeal decision G 001 I/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](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](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.htm](http://ep.espacenet.com/search97cgi/s97_cgi.exe?Action=FormGen&Template=ep/EN/home.htm)]
22. **Japan Patent Office: quick guide** [[http://www.jpo.go.jp/quick\\_e/index\\_search.htm](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/>]

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.

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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](http://www.wipo.int/edocs/prdocs/en/2003/wipo_pr_2003_372.html)]
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11. **Opinion of the enlarged board of appeal G 2/98** [<http://legal.european-patent-office.org/dg3/pdf/g980002ep1.pdf>]
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