

Intellectual Property Law

A Primer for Scientists

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Abstract

“Intellectual property” (IP) is a generic legal term for patents, copyrights, and trademarks, which provide legal rights to protect ideas, the expression of ideas, and the inventors and creators of such ideas. A patent provides legal protection for a new invention, an application of a new idea, discovery, or concept that is useful. Copyright provides legal protection from copying for any creative work, as well as business and scientific publications, computer software, and compilations of information. A trademark provides rights to use symbols, particular words, logos, or other markings that indicate the source of a product or service. A further method of benefiting from an invention is simply to keep it secret, rather than to disclose it—a “trade secret.” IP impinges on almost everything scientists do. As scientists are paid to come up with ideas and aspire to patent and/or publish their work, the protection of ideas and of written works especially should be of interest and concern to all.

Index Entries: Intellectual property; patent; copyright; trademark; trade secret.

1. Introduction

“Intellectual property” (IP) is a generic legal term for patents, copyrights, and trademarks, which provide legal rights to protect ideas, the expression of ideas, and names, logos, and marks used to identify a business or product (*I*). IP has many of the characteristics of real property (houses, buildings); IP can be bought and sold (assigned) and rented (licensed). Additionally, the owner of IP can prevent trespass on his or her property by others, though in IP law, a trespass is referred to as infringement.

A patent provides legal protection for a new invention, an application of a new idea, discovery, or concept that is useful. A patent provides the inventor with the right to prevent others from practicing the invention for a period of time.

Copyright provides legal protection from copying for any creative work (e.g., works of art, literature [fiction or nonfiction], music, lyrics, photographs), as well as business and scientific publications, computer software, and compilations of information. Copyright law essentially

gives the author or artist the right to determine whether and how copies of a work are made and distributed.

A trademark provides rights to use symbols, particular words, logos, or other markings that indicate the source of a product or service. Competitors and other businesses are prevented from using similar (and therefore potentially confusing) marks.

A further method of benefiting from an invention is simply to keep it secret, rather than to disclose it. The most famous trade secret of all time is the formula for Coca Cola (*2,3*), a closely guarded secret to this day. Trade secrets have the advantage that they never expire, but special measures are required to ensure continued secrecy, and should it be violated and the secret be disclosed, there is little legal protection for the owner (*2,3*).

IP may seem like a strange topic for an article in *Molecular Biotechnology*, but intellectual property impinges on almost everything scientists do, as the reader will soon realize. Furthermore, as scientists are paid to come up with ideas and aspire to patent and/or publish their work, the pro-

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tection of ideas and of written works especially should be of interest and concern to all.

Write a paper or review (copyright is “created” automatically once your ideas are fixed in a permanent medium; it is not necessary [though it is advisable] to add the copyright sign—©—and the author’s name and date), sign a copyright transfer form when submitting a paper or review to a journal, go to the library to copy a paper from a journal (read the copyright notice in the next journal you copy from, or perhaps the copyright notice attached to the photocopier in the library), open and use a software package (software is protectable under copyright law, and a copyright agreement was probably printed on the envelope from which you removed the disk), or use the PCR process [PCR is covered by US patents (4,5), assigned to Roche (6–9)], and you have entered the lawyer’s realm of IP. In fact, in our knowledge-based, high-tech economy, the subject is difficult to avoid.

Another area where scientists will encounter IP law is in employment contracts. When starting a new position at a pharmaceutical or biotech company, scientists will likely be required to assign all inventions made during their employment to their employer. Under US law, the Court of Appeals for the Federal Circuit has ruled that inventions belong to the employer even without the employee formally assigning them (10). That is not so unreasonable, because, of course, scientists were hired to come up with ideas, and to do so, scientists use their employer’s resources and facilities. US academics will also come across the subject; since the passage of the Bayh–Dole Act of 1980, inventions made in research funded by the US government (e.g., the National Institutes of Health [NIH]) belong to the host university, which is responsible for exploiting such inventions for the public good (11,12). Usually, this means patenting the invention and licensing it to industry, typically with significant payments or royalty streams to the academic inventor(s).

Additionally, the subject of IP has hardly been out of the scientific (or lay) press in the last 20 yr (13–15). From the landmark case of *Chakrabarty*,

where the US Supreme Court held that a genetically altered bacterium could be patented under US law (16–19), the original “Cohen–Boyer” patent, covering many fundamental recombinant DNA techniques (20–22), Genentech’s patent (23), also covering basic recombinant DNA procedures (24), the Pasteur Institute’s battle with the NIH over the patent for the antibody test for HIV (25,26), Wellcome and Genentech’s patent battles over tissue plasminogen activator (t-Pa) (27–32), Hybritech’s battle with Monoclonal Antibodies, Inc. (33–35), the patent for microinjection (to create transgenic animals [36–38]), Amgen’s patent war with Genetics Institute over recombinant erythropoietin (39–45), Centocor and Xoma’s long-running patent battle over their monoclonal antibody products to treat sepsis (46–51), the battle between Wellcome and NIH over the AZT patent (52–58), the battle between DuPont and Cetus over the rights to PCR (59–62), the European and Canadian Patent Offices’ battles with Harvard University over patenting the “Oncomouse” (63–68), Craig Venter and NIH’s attempt to patent cDNA sequences (ESTs, expressed sequence tags) (69–81), Promega’s challenge to the patents on *Taq* polymerase (82–88), Chiron’s dispute over a patent for a hepatitis C test (89), Genentech’s dispute with Chiron over IGF-I (90), the long-running patent war over human growth hormone (hGH) (91–96), the disputes concerning the breast cancer susceptibility gene *BRCA1/2* and tests to assess a patient’s predisposition to breast cancer (97–99), Amgen’s more recent battles with TKT and Aventis over erythropoietin (100), the Kauffman/Ballivet patents on “directed evolution” (101–104), the dispute over AIDS drugs in Africa (105), Elan’s attempt to get a patent on a transgenic mouse model of Alzheimer’s disease (106), the patent battle between Oxford Gene Technology and Affymetrix over microarrays (107), Monsanto’s lawsuit against a Canadian farmer who allegedly infringed its patent on herbicide-resistant canola (108), the debate over the patenting of medical procedures (109–112), Genentech and Chiron’s dispute over the breast cancer drug Herceptin (113), the complex patent

dispute over the lucrative COX-2 inhibitors (114), the patent on Bayer's drug Cipro (115), and the ongoing discussion on patenting genes and genomes (116–128), the scientific press has been loaded with intellectual property news. It is now rare that an edition of *Science* or *Nature* contains nothing on the subject.

Furthermore, as can be seen from the names of the parties in the litigations listed above, patents are extremely important to the pharmaceutical and biotech industries. Armies of lawyers have been kept busy in these litigations. Given the enormous cost of bringing a drug to market, patent protection is essential to obtaining financing for small companies (129,130) and in justifying the vast expenditures necessary to bring a drug to market at larger companies (131).

It is not much of an exaggeration to claim that the world biotechnology industry hangs on two basic techniques, monoclonal antibodies and recombinant DNA. The two technologies have very different and illustrative histories in terms of IP.

It is now part of scientific and legal folklore that neither Köhler and Milstein, nor their employer, the British Medical Research Council (MRC), recognized the commercial significance of their discovery and patented their invention. As a result, neither the inventors nor the MRC made much money out of their seminal work (132–134). Since then, there have been many patents (and disputes about patents) on specific monoclonal antibodies and their uses (33–35,46–49), but the original Köhler and Milstein technique for making monoclonal antibodies was never patented. A new method of producing monoclonal antibodies might be patentable, as might significant improvements on the original method.

Contrast this with the Cohen–Boyer patent (20) on fundamental techniques of recombinant DNA (135) from which Stanford University (Stanley Cohen's employer) and University of California, San Francisco (Herbert Boyer's employer), made tens of millions of dollars before the patent expired in 1997 (136), by selling licenses to the then fledgling biotechnology industry (22,136,137). Also covering basic recombinant DNA techniques

were Genentech's patent (including fusion proteins, the Riggs patent [23,24]) and the Itakura patent (covering plasmid technology [138]), both of which were also widely licensed (14).

2. Patents

2.1. Innovation and Invention

As a society, we greatly value innovation; it is no longer possible—except with regard to the simplest products—to succeed in selling a product solely because it is cheaper. We constantly demand new, better, and more advanced products. No company making a 1980-level car at any price is going to succeed today; we want a 2002 model with fuel injection, airbags, antilock brakes, traction control, CD HiFi stereo system, and so on. Likewise, there is no longer a market for 8086, 80386, or even early Pentium® computers, at any price; you couldn't give them away! Such new and more advanced products are the result of research and development.

Society has long recognized the need to encourage and stimulate inventors to bring new and useful products to the marketplace for the benefit of all. To protect and reward the innovator, it is necessary to protect against cheap copies made by would-be competitors, piggybacking off the expensive and time-consuming research and development efforts.

2.2. What is a Patent?

A patent is a government-given, time-limited right to exclude others from practicing an invention; that is, armed with a patent an inventor can prevent—using the legal force of the state (i.e., courts)—anybody else using the patented technique or making, selling, using, or importing the patented product. In return for this time-limited right to exclude, the inventor is required to describe fully the invention for the benefit of the public and others working in the field. When the patent expires, anyone can use the invention, and during the life or term of the patent, the information in the patent is freely available to all to stimulate related work (which is clearly better for the public as a whole than having the inventor keep the invention

as a trade secret). Consistent with this desire to stimulate related research and despite some ill-informed comments in the press, there is a “research exclusion” under US law. Specifically, a researcher working on a patented matter to improve it for a *noncommercial* (basic, academic research) purpose is exempt from charges of patent infringement (**139**). No patent ever prevented an academic researcher from doing noncommercial, academic research.

Because patents are government-given, an inventor must apply for a patent separately in each country in which protection is sought. Furthermore, because each nation has its own patent system and laws, there are many variations on the basic theme. There are agreements between various groups of nations such that they recognize patent filings in other countries, but there is no “world patent” and it is basically necessary to apply for a patent separately in each country. Whether it is worth doing so in every country depends on the resources of the inventor and the significance and likely commercial value of the patent and resulting product(s).

Under US law, there are three types of patents: utility patents, design patents, and plant patents. A utility patent can cover any invention or discovery of a new and useful (or a new and useful improvement of any) composition of matter (e.g., a new chemical compound or mixture of compounds), process (e.g., an industrial or technical procedure or method), product, or machine. Design patents protect only the appearance of an article. Plant patents cover the “invention” (by cross-breeding) or discovery of new plants, including cultivated mutants, hybrids, and seedlings.

2.3. Requirements for Patentability

To be patentable, an invention must be novel, nonobvious, and useful, to use the US legal terms (**140**). That may sound simple enough, but it is far from always so.

“Novel” or new means simply that the invention must not have been described or disclosed previously. Novel does not mean revolutionary;

indeed, most patented inventions are far from revolutionary. Improvements on existing machines, devices, and processes are often sufficiently different and significant to be patentable in their own right. “Novel” can also include new uses for a known invention. A good example of this is the compound minoxidil (2,4-diamino-6-piperidino-pyrimidine-3-oxide), which was invented, patented, and marketed as an antihypertensive drug (**141–145**) before its hair growth-promoting properties were discovered. While the molecule could not be repatented (it could not be “novel” twice), its new use in treating male pattern baldness (alopecia) could be (**146,147**); minoxidil is the active ingredient in Rogaine® (**147**).

“Nonobvious” means that the invention must be sufficiently different from previously published work (patents, papers, reviews; the so-called “prior art”) that it is not an obvious or trivial next step to one “skilled in the art,” that is, in the scientific or technical discipline to which the invention relates. The hypothetical person “skilled in the art” is not a genius and is not the inventor; the test is not nonobvious to the inventor, but to the hypothetical person. The level of skill required depends on the field, but is typically someone with postgraduate education (not necessarily a PhD) and several years experience in the area.

“Useful” means simply that the invention has some known use. There is a very low threshold for usefulness; almost any use will do, so long as it is functional and not solely aesthetic. In fact, the threshold was considered to be so low, the issue was rarely raised. However, this has been revisited since the various attempts to patent ESTs (expressed sequence tags; small cDNA fragments). What use is an EST, except perhaps as a probe? A probe for what? If you don’t know what the EST encodes, what are you probing for? The full-length sequence from a cDNA library? Should that be patentable—it’s not a complete invention, surely? A more credible use for an EST might be the mapping of the gene from which it was derived in the genome (**149–151**).

2.4. Obtaining a Patent: “Patent Prosecution”

Obtaining a patent is, in concept anyway, fairly straightforward; the whole process is frequently referred to as “patent prosecution.” The inventor invents and carefully documents everything about the invention and all its possible uses. The inventor takes this material to a patent agent or patent attorney who conducts a search of the prior art, that is, all the published literature and all previously granted patents (now greatly facilitated with computer databases). This search enables the inventor and attorney to learn about other related inventions and to begin to analyze whether the invention is patentable over the prior art, that is, whether it is novel and/or a sufficient advance over existing technology. At this stage, it is also advisable to assess the likely utility—commercial and otherwise—of the invention. The inventor then has to “reduce to practice” the invention, if this has not already been done; this means creating a prototype of the invention or showing how it can be carried out in a practical (as opposed to theoretical) way.

A patent application is submitted, detailing the invention and how it can be carried out; the patent office then examines the application for both form and substance. Typically, a patent is not granted immediately, but the application is challenged by the patent office for being insufficient or inadequate in some manner; the inventor responds to this and clarifies or narrows the application and eventually the patent application is rejected or allowed. The claims at the end of the patent are key; it is these that are argued about with the patent office because they define the scope of the invention, that is, what it is that everyone else is excluded from doing, making, selling, or importing during the term of the patent.

Scientists typically live by the mantra “publish or perish”; however, in the world of patents, if work is published before the application is filed, it is the application that may perish. As has been discussed in the medical literature (152,153), scientists, especially those working for corporations or conducting research funded by corporations, have

had publications delayed while patent protection for inventions resulting from the work was sought. This is not just a precaution but a requirement.

Under US patent law, an inventor has a one-year grace period after the first public disclosure or publication to file a patent application; however, in most countries there is no such grace period. Thus, if an invention is published or disclosed publicly (e.g., by speaking about it at a seminar or conference), then the right to a patent for that invention will be forfeited in most countries.

2.5. First-to-File or First-to-Invent

In every nation except the United States and the Philippines, if more than one inventor comes up with the same invention and applies for a patent, the patent goes to the first to file a patent application (the first-to-file system). In the United States and Philippines, it is the first to invent who gets the patent; that is, if two or more inventors come up with the same invention and submit patent applications claiming that invention, they get to prove through their laboratory notebooks and other documentation who first conceived the idea and reduced it to practice.

Clearly, there are arguments for and against each system. The first-to-invent seems more just, but of course causes litigation to settle the issue, whereas the first-to-file system is clean, simple, and efficient, and it is surely not too great an imposition on an inventor to insist that the patent application be filed quickly after the invention.

2.6. The Rights of a Patent Owner (Patentee)

A patent owner has the right to exclude others from making, using, selling, or importing the invention for the duration of the patent term. It is important to remember that a patent does not *necessarily* give the patent owner the right to practice the invention, because by doing so, the inventor may infringe someone else’s patent or violate some other law or regulation. For this reason, it is wrong to think of a patent as providing a “monopoly.” As a simple example, a perfectly valid patent on a

new drug does not permit the inventor to sell the drug; the drug, patented or not, is still subject to the normal drug approval process and all applicable laws. A patent merely permits the inventor to stop someone else doing it.

The patentee may assign (sell, transfer) the patent rights to another (e.g., the PCR patents [4,5], which were assigned to Roche [6–9]) or may retain ownership rights and license them to others, so that they can use the invention without owning it (e.g., the Cohen–Boyer patent [20,22,136]). Once a patent has expired, anyone can make, use, sell, or import the invention without the patentee's authorization. The invention is said to be “in the public domain” at that point; the patent owner has no rights once the patent has expired (e.g., the Cohen–Boyer patent (20), which expired in 1997 [136]).

2.7. Patenting Animals and Plants

An issue that biotechnology has brought to the fore in recent years is the patenting of genetically modified life forms, from microorganisms to higher animals and plants. The patenting of genetically modified microorganisms is now generally accepted throughout the world, whereas the patenting of genetically modified higher animals and plants has been a subject of great controversy.

The United States led the way in this area from the first grant of a patent for a bacterium in 1980, following the Supreme Court's ruling in *Chakrabarty* (16,19). Chakrabarty, a microbiologist, had in the early 1970s genetically engineered a *Pseudomonas* bacterium capable of breaking down oil, and it was hoped that the bacterium could be used in cleaning up oil spills. The Supreme Court held that under US patent law, a modified bacterium was not a product of nature but was man made and was patentable. Indeed, the Supreme Court approvingly quoted language from a Congressional report that “anything under the sun that is made by man” may be patentable under US law (19).

Again taking the lead, in 1988 the US patent office granted a patent on the “Harvard Oncomouse” (154–156), despite opposition (67,157,158). The

Oncomouse is a transgenic mouse carrying an activated mouse oncogene (*myc* plus DNA from the mouse mammary tumor virus [159,160]) and has a greatly increased susceptibility to malignant breast tumors during pregnancy (156). It obviously has potential utility as a cancer model and testing/screening system for anticancer drugs. Harvard to date has been unsuccessful in obtaining a patent in Canada (68). Since then, while not quite routine, US patents have been issued on several other transgenic animals (161). In Europe, there has been much more opposition, both by activists and the European Patent Office (66,67,162–166).

3. Copyright

3.1. Protection for Creative Works

Copyright is created automatically in any creative work (e.g., fiction, nonfiction, photographs, figures, paintings, designs, patterns, sculptures) as soon as it is fixed in a tangible medium (e.g., on paper, film, clay, bronze, canvas, or on a hard or floppy disk) and is essentially a legal right of the author/artist to control copying of the work after it leaves the author/artist's possession. Copyright does not protect the *idea(s)*, only the *form* used to express the *idea(s)*. Thus, someone can take an author's idea, and rewrite it, and there is no copyright violation. Someone else can photograph or paint the same scene and there it no copyright violation.

Copyright law as we currently understand it goes back to 1710 with the Statute of Anne in England and to 1790 in the United States (and there is a copyright clause in the US Constitution [Article I, Section 8]), though the concept that a writer “owned” his work goes back a lot further (167–171). As all scientists aspire to be authors at some stage, this is another important issue. Additionally, we constantly rely on the published work of others, in the form of laboratory manuals and journal articles.

A copyright does not need to be registered, unlike a patent, though it is advisable to do so to gain the fullest protection of the law. Copyright protection is shallower than patent law. Independent creation is a perfect defense to a charge of

copyright infringement, whereas in patent law, the first-to-invent (in the United States or the Philippines) or the first-to-file will get the patent—and the right to exclude others from practicing the invention—even if other inventors independently conceived the same invention.

3.2. Scientific Journals and Books

Journals and book publishers usually ask for the transfer of copyright from the author to the journal or publisher because by having all the copyrights, monitoring and enforcement of rights becomes practical. Alternatively, publishers can—by contract—hire writers to write specific works; such a work is a “work for hire” and the copyright belongs to the publisher.

Very few authors are ever going to scan the world literature constantly looking for copyright infringements, whereas publishers to which copyrights have been assigned and especially groups of publishers can sensibly do so. Likewise, it made sense for journal publishers to band together to form the Copyright Clearance Center (CCC), whereas individual authors could never have sensibly done so. The CCC is a centralized clearing house set up in the United States in 1977 by publishers to sell licenses to institutions and to collect copyright fees from libraries and document services, for copies made of member publishers' works. Canada has a similar scheme, Cancopy (172).

3.3. The Texaco Case

The famous *Texaco* case (173,174) should not go unmentioned. In *Texaco*, the US Court of Appeals for the Second Circuit held that a Texaco researcher violated US copyright law by copying several articles from a journal and distributing them to colleagues at the company (173). The Court's ruling was not as simple or broad as it sounds, and the Court refused to address the situation where an individual copied articles for his or her own use; academics and researchers should not necessarily be quaking in their boots! The ruling was confined to its facts, where Texaco (a large, wealthy corporation) had purchased a

single copy of the journal from the publisher for its library and then systematically made multiple copies of articles for its employees, instead of paying for multiple subscriptions to the journal (173). Additionally, Texaco had not purchased a license from the CCC, as many corporations and institutions had and do. The case was actually settled before the final decision was issued (175); Texaco, without admitting fault, paid a large settlement including retroactive license fees to the CCC (175).

4. Trademarks

4.1. Introduction

A trademark is any symbol, word or series of words, logo, or other marking that indicates the source of a product or service. In the laboratory there are many examples: take your New England Biolabs® restriction enzymes from your StrataCooler® II, purify RNA with the RNeasy® kit, use your Nikon® microscope to inspect your cells, which you obtained from ATCC®, take your references from Reference Manager®, check Current Contents® each week, and it becomes apparent that trademarks are everywhere. Outside the laboratory, the ubiquitous McDonald's golden arches, Prudential's rock, and Coca Cola's name, stylized font, and the distinctive shape of their glass bottles are obvious examples.

4.2. Trademarks and Service Marks

Strictly trademarks apply only to products; service marks indicate services. However, “trademark” is used generically to cover both. If you open an edition of *Science* and look at the advertisements, you will see, for example, Sigma®'s Extract-N-Amp™ kit to extract DNA from blood for PCR. If you open an edition of *Business Week*, you will see, for example, Transamerica's pyramid logo (the shape of the top of their landmark office building in San Francisco), itself a registered trademark, and their slogan “The People in the Pyramid are Working for You™.” Sigma® indicates that Sigma is a registered trademark, as is the Transamerica pyramid logo, Extract-N-Amp™ indicates that Extract-N-Amp is consid-

ered a trademark by Sigma, but that it has not (yet) been registered (with the US Patent & Trademark Office) or that its registration has not (yet) been approved. Transamerica's slogan is a service mark; their service is providing insurance.

Unlike patents and copyrights, which are both based on creative products, a trademark is based on *use*. Unlike patents or copyrights, a trademark can be lost by not using it; there is no such obligation on a patentee who can simply sit back and prevent anyone from using the invention or a copyright owner who can simply decide that nobody can copy a work. Also, unlike copyrights and patents, trademarks can have an indefinite lifespan. Trademarks do not have to be registered; however, if they are, it simplifies some issues should a dispute arise.

4.3. Trademark Litigation

Trademark litigation has attracted much less attention than patent disputes in recent years, but there have been several examples relating to drugs and medical services and the misuse or misappropriation of trademarks or service marks. On several occasions the renowned Mayo Clinic of Rochester, Minnesota, has had to defend its name, literally (176). The Mayo Foundation holds three trademarks; "Mayo," "Mayo Clinic," and the familiar triple-shield logo (176). The Supreme Court of Minnesota held that a man whose first name was Mayo could not sell drugs through his company, "Mayo's Drug and Cosmetic Company," because there was a reasonable likelihood of confusion on the part of the public between Mayo's Drug and the Mayo Clinic and Hospital, with the obvious inference that products sold by Mayo's Drug came with a stamp of approval from the famous and respected institution (177).

4.4. Scientific Trademark Examples

A trademark issue that has been discussed in the scientific press is Bristol-Myers Squibb's claim to the word "Taxol" as the name of its anticancer drug (178–180). The compound in question is the antileukemia drug extracted from the bark of the Pacific yew (181) for which a total synthesis has been reported (182). Bristol-Myers

Squibb does now own the trademark Taxol®, and the compound in question should now be referred to as paclitaxel (178).

Another example of a trademark issue concerns Bayer and aspirin (183,184). Aspirin was synthesized by Felix Hoffmann at Bayer in 1897. Following the expiration of the US patent in 1917, the company sought to protect the drug's name with the trademark Aspirin. The US Patent & Trademark Office canceled Bayer's trademark on aspirin in 1918 (184), though the company maintained the trademark in many other countries. Sterling Drug, Inc. purchased the right to use the name in the US in the 1920s, and in 1994, Bayer's United States affiliate, Miles, Inc., bought Sterling Winthrop's over-the-counter drug business, including the name (183,185), returning it to Bayer.

5. Summary

IP and the protection of ideas and the written expression of ideas should be of concern to all scientists. We constantly use copyrighted journals and laboratory manuals, trademarked products, and patented processes. Additionally as authors, we acquire and then typically transfer copyright in our work to journals and book publishers. Scientists in industry and academia are generally required to transfer all inventions made in the course of their employment to their employer. It is hoped that this brief introduction to IP will heighten awareness and stimulate the reader to delve deeper into the subject.

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