Chapter 12

Intellectual Property Protection

"Ingenuity should receive a liberal encouragement."

Thomas Jefferson

"Congress intended statutory subject matter to include anything under the sun made by man. '

Chief Justice Warren Burger
majority opinion, ***Diamond v. Chakrabarty***

"What has been is what will be, and what has been done is what will be done; and there is nothing new under the sun.'

Ecclesiastes 1:9

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INTRODUCTION

Intellectual property law, which provides a personal property interest in the work of the mind, is of increasing importance to people who use biotechnology to create new inventions. Intellectual property involves several areas of the law: patent, copyright, trademark, trade secret, and plant variety protection. All affect emerging high-technology industries because they provide incentives for individuals and organizations to invest in and carry out research and development (R&D), while adding important technological information and products into commerce.

The 1980s provided a harvest of new biotechnological processes and products as well as incentive for research for future inventions. In industries affected by biotechnology, old law is merging with new biological technology, resulting in novel questions regarding the ownership of intellectual property. For example:

1. Which areas of intellectual property are most relevant to biotechnology?
2. What can be patented?
3. How broad in scope can a patent be?
4. Is U.S. law adequate to protect inventions created through biotechnology?
5. Will inventors receive adequate worldwide protection for their discoveries?

When discussing a nation's competitiveness in industries fostered by the new biology, protection of intellectual property is seen by many as a paramount consideration. This chapter briefly outlines the types of intellectual property protection available in the United States to protect biological inventions, the international agreements that may affect intellectual rights in biotechnology, how U.S. patent law impacts on new inventions created through biotechnology, and emerging issues that affect commercialization of biotechnology-related patents.

U.S. INTELLECTUAL PROPERTY

Intellectual property protection encompasses several areas of statutory and common law: patent, copyright, trademark, trade secret, and plant variety protection. Three categories-patents, trade secrets, and plant variety protection-are particularly important to biotechnology and are the focus of this chapter's discussion.

Patents

United States (U. S.) patent law has its roots in the Constitution, which gives Congress broad powers to "promote the Progress of Science and useful Arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries' (Article I, Section 8). The first patent act was enacted by Congress in 1790 and, though amended several times, has retained its broad scope as to what can be patented.

A patent is a grant issued by the U.S. Government that gives the patent owner the right to exclude all others from making, using, or selling the invention within the United States, its territories, and possessions, during the term of the patent (35 U.S.C. 154). There are three types of patents. The most common type-sometimes referred to as a utility patent—covers processes, machines, manufactures, and compositions of matter. A second category, patents for plants, includes cultivated sports, mutants, hybrids, and newly found seedlings. A third category, patents for designs, is not relevant to biotechnology-related inventions. To qualify for utility patent protection in the United States, an invention must meet several requirements:

. it must be a process, machine, manufacture, or composition of matter (35 U.S.C. 101);
- it must be new, useful, and not obvious (35 U.S.C. 101-103); and
- it must be disclosed in sufficient detail to enable a person skilled in the same or the most clearly related area of technology to construct and operate it (35 U.S.C. 112).

Patents serve two important policy objectives:

- by rewarding successful efforts, a patent provides inventors and their backers with incentive to risk time and money in R&D; and
- by requiring disclosure of the manner and process of making an invention, a patent encourages public disclosure of otherwise se-

cret information, so that others are able to use it.

Although a patent gives the inventor the right to exclude others from making, using, or selling the invention for 17 years, it does not grant the inventor any affirmative right to make or use an invention. Commercial use of a patented invention, just like other products, can be regulated by Federal, State, or local law.

Once obtained, a patent has a term of 17 years, assuming that maintenance fees are paid (35 U.S.C. 154). One exception to this general term of 17 years is relevant to biotechnology: where a patent claims a human drug product, medical device, food, or color additive that has undergone regulatory review prior to approval for commercial marketing or use by the Food and Drug Administration (FDA), the patent may be eligible for an extension of up to 5 years, if certain conditions are satisfied (35 U.S.C. 156).

Plant Breeders' Rights

Intellectual property protection for plant life is based on several statutes (e.g., the Plant Patent Act, Plant Variety Protection Act, and 35 U.S.C. 101), a decision by the U.S. Patent and Trademark Office (PTO) Board of Appeals, and recognized trade secret and contract law. These provide a variety of protection for inventions that constitute plant life (see table 12-1).

Plant Patent Act of 1930

Prior to 1930, no intellectual property rights existed for protecting new plant varieties. Plant breeding and research were conducted primarily by federally funded agricultural experiment stations and, to a limited extent, by amateur breeders. Financial incentives for private breeders were inadequate, since the breeders' sole financial reimbursement was through high sales prices of comparatively few reproductions during the first 2 or 3 years after the variety's initial availability. Once the plant left a breeders' hands, it could be reproduced in unlimited quantity by anyone.

In 1930, Congress passed the Plant Patent Act (PPA) (35 U.S.C. 161-164) to extend patent protection to most new and distinct asexually propagated varieties. The PPA was the first, and to date, only law passed by Congress specifically providing patent protection for living matter. Since then, more than 6,500 plant patents have been issued by PTO covering flowering plants, ornamental and fruit trees, nut trees, grapes, and vegetable crops. Plant patents cannot be obtained for seeds, tubers, biotechnology processes, recombinant DNA (rDNA), or genes (23). On average, more than 225 plant patents are issued each year (34).

Table 12-1—Types of Intellectual Property Protection for Plants

Type	Citation	Subject matter
Plant patent	35 U.S.C. 161-164	Asexually reproduced varieties
Plant variety protection certificate	7 U.S.C. 2321 *et seq.*	Sexually reproduced varieties
Utilitypatent	735 U.S.C. 101 *et seq.*	Process, machine, manufacture, composition of matter
Trade secret	State law	Information used in trade or business that is kept secret

SOURCE: Office of Technology Assessment, 1991.

Plant Variety Protection Act of 1970

Commercial and international developments between 1930 and 1970 influenced deliberations in the United States to protect sexually reproduced plants. Plant breeders had developed new sexually reproducing plants that could replicate "true-to-type' but could not be patented under the PPA. In 1961, several European countries formed the International Union for the Protection of New Varieties of Plants (UPOV) to protect breeders' rights. Unlike breeders in UPOV countries, U.S. breeders had no law protecting their inventions, except for asexually reproduced plants covered by the PPA.

The Plant Variety Protection Act (PVPA) (7 U.S.C. 2321 ***et seq.) was*** enacted by Congress in 1970, to provide patent-like protection for certain types of new, sexually reproduced plant species. It is mainly of interest to breeders and farmers of such sexually reproduced crops as: wheat, alfalfa, soybeans, cotton, corn, lettuce, soybeans, and watermelon (9).

Although PVPA is not a patent statute, the protection it provides to breeders of new plant varieties is similar in concept to patent protection. The act is administered by the U.S. Department of Agriculture (USDA). Upon application to USDA and examination by this agency, a plant variety protection certificate may be issued on any novel

variety of sexually reproduced plant--other than fungi, bacteria, or a frost-generation hybrid. The novel variety must have distinctiveness, uniformity, and stability. Amendments in 1980 (Public Law 96-574) added protection for six vegetable crops and extended coverage to 18 years so the PVPA would be consistent with UPOV provisions.

Under PVPA, the breeder can exclude others from selling, offering for sale, reproducing (sexually or asexually), producing a hybrid from the variety, and importing or exporting the protected variety.

PVPA contains two important exclusions to a certificate holder's protection:

- a research exemption that precludes a breeder from excluding others from using the protected variety to develop new varieties; and
- a farmers' exemption which allows an individual whose primary occupation is growing crops for sale, for other than reproductive purposes, to save protected seed for use on his or her farm or to sell to people whose primary occupation also is growing crops.

From 1970 through 1988, 2,783 applications for plant variety protection certificates were filed with the USDA for some 100 different crops. By December 31, 1988,2,133 certificates had been issued, and 274 applications were pending. Another 376 applications had been abandoned, withdrawn, declared ineligible, or denied (34).

Utility Patents for Plants

In addition to specified plant patent and plant variety protection, U.S. inventors may also seek utility patent protection for plants. In 1985, the PTO Board of Appeals and Interferences ruled, in Ex ***parte Hibberd (16),*** that a corn plant containing an increased level of tryptophan, an amino acid, was patentable subject matter under 35 U.S.C. 101. Since the ***Hibberd ruling,*** utility patents have been granted on plants.

Trade Secrets

Trade secrets extend protection to information used in one's trade or business, that is maintained in secret by its owner and provides a competitive business advantage over those not having the information. A plan, process, tool, mechanism, recipe, chemical compound, customer list, or formula, all are examples of information that can be maintained as trade secrets.

Table 12-2—International Intellectual Property Agreements

Agreement	Entered into force	Number of signatories
Paris Union Convention	July 1884	100
Union for the Protection New Varieties of Plants	August 1968	19
European Patent Convention . . .	October 1977	14
Patent Cooperation Treaty	January 1978	45
Budapest Treaty	August 1980	23

SOURCE: Office of Technology Assessment, 1991.

Unlike patents (which are governed exclusively by Federal law), trade secrets are the subject of State law. The theft of a trade secret is a tort, and action lies against the thief for misappropriation. Trade secret law promotes two beneficial ends: it encourages commercial morality and fair dealing, and it encourages research and innovation. Unlike patent law, however, trade secret law does not encourage public disclosure of technical information.

If a trade secret is disclosed in a nonconfidential reamer, it is lost forever. Trade secret rights require that a trade secret be disclosed in confidence only to those having a reasonable need to know (e.g., employees). Measures must be taken to prevent disclosure of the trade secret to the public or to competitors (e.g., expressly identifying the information as a trade secret and prohibiting its disclosure).

INTERNATIONAL INTELLECTUAL PROPERTY PROTECTION

The need for protection of intellectual property is well accepted inmost nations. Formal patent statutes were first enacted by England in the 1600s; the United States and France adopted laws in the late 1700s. With the development of international trade, patent protection was formally adopted by other nations, and mechanisms were adopted to harmonize intellectual property rights among-trading nations.

Several international agreements are relevant to protecting biological inventions (see table 12-2). These agreements provide comity, in the area of patents, plant breeders' rights, and deposit of biological materials.

Table 12-3--Member Countries, Paris Union Convention

Algeria	Finland	Lesotho	Senegal
Argentina	France	Libya	South Africa
Australia	Gabon	Liechtenstein	Soviet Union
Austria	Germany	Luxembourg	Spain
Bahamas	Ghana	Madagascar	Sri Lanka
Bangladesh	Greece	Malawi	Sudan
Barbados	Guinea	Malaysia	Suriname
Belgium	Guinea-Bissau	Mali	Sweden
Benin	Haiti	Malta	Switzerland
Brazil	Holy See	Mauritania	Syria
Bulgaria	Hungary	Mauritius	Togo
Burkina Faso	Iceland	Mexico	Trinidad and Tobago
Burundi	Indonesia	Monaco	Tunisia
Cameroon	Iran	Mongolia	Turkey
Canada	Iraq	Morocco	Uganda
Central African Republic	Ireland	The Netherlands	United Kingdom
Chad	Israel	New Zealand	United Republic of Tanzania
China	Italy	Niger	United States
Congo	Ivory Coast	Nigeria	Uruguay
Cuba	Japan	Norway	Viet Nam
Cyprus	Jordan	Philippines	Yugoslavia
Czech and Slovak Federal Republic	Kenya	Poland	Zaire
Denmark	Korea, Democratic People's Republic of	Portugal	Zambia
Dominican Republic	Korea, Republic of	Romania	Zimbabwe
Egypt	Lebanon	Rwanda	
		San Marino	

SOURCE: Office of Technology Assessment, 1991.

Paris Convention

The Paris Convention for the Protection of Industrial Property, first adopted in 1883, is the major international agreement providing basic rights for protecting industrial property. It covers patents, industrial designs, service marks, trade names, indications of source, and unfair competition. The United States ratified this treaty in 1903, and many other nations have adopted it (see table 12-3).

The treaty provides two fundamental rights:

- The principle of national treatment provides that nationals of any signatory nation shall enjoy in all other countries of the union the advantages that each nation's laws grant to its own nationals. The purpose is to eliminate discrimination against foreigners, who, in turn, must observe the conditions and formalities imposed on nationals of the member country in which protection is sought.
- The right of priority enables any resident or national of a member country to, frost, file a patent application in any member country and, thereafter, to file a patent application for the same invention in any of the other member countries within 12 months of the original filing and receive benefit of the original filing date. The effect is to give subsequently filed applications the right of priority established by the first filing date.

The convention permits member nations to enter into separate agreements for the protection of industrial property-as long as the agreements do not contravene the provisions of the convention. This provision has permitted the ratification of other bilateral and multilateral agreements, between nations, addressing specific areas of intellectual property protection.

Patent Cooperation Treaty

The Patent Cooperation Treaty (PCT) is a worldwide convention, open to the members of any Paris Convention country. It entered into force in 1978, and has been ratified or acceded by 45 countries (see table 12-4). Unlike the Paris Convention, which addresses substantive intellectual property rights, the PCT addresses procedural requirements, aiming to simplify the filing, searching, and publication of international patent applications.

After an application is filed with the patent office of a member nation (usually the national patent office of the country in which the applicant is a resident or national), the application is transmitted to the international bureau of the World Intellectua1 Property Organization (WIPO) in Geneva. An inter-

Table 12-4-Member Countries, Patent Cooperation Treaty

Australia	Korea, Democratic People's Republic of
Austria	Korea, Republic of
Barbados	Liechtenstein
Belgium	Luxembourg
Benin	Madagascar
Brazil	Malawi
Bulgaria	Mali
Burkina Faso	Mauritania
Cameroon	Monaco
Canada	The Netherlands
Central African Republic	Norway
Chad	Romania
Congo	Senegal
Denmark	Soviet Union
Finland	Spain
France	Sri Lanka
Gabon	Sudan
Germany	Sweden
Great Britain	Switzerland
Greece	Togo
Hungary	United Kingdom
Italy	United States
Japan	

SOURCE: Office of Technology Assessment, 1991.

national search is conducted by an appropriate international searching authority (ISA). In the case of U.S.-initiated applications, the ISA is the U.S. Patent and Trademark Office or the European Patent Office. Following the international search, the application and the search report are published by WIPO, and copies are provided to each of the designated offices in the countries where protection is sought. These countries then subject the application to their own national procedures.

Budapest Treaty

United States patent law requires applicants to file a specification (i.e., a writing, specifying in clear, concise terms how to make and use the invention and the best mode contemplated by the applicant for carrying out the invention). The patenting of living organisms presents a unique administrative problem, because it is the only known art where-in some instances-this requirement cannot be satisfied with words alone. In these instances, it is necessary to deposit micro-organisms and plants for patent purposes. This practice has become commonplace internationally, leading to the need to harmonize deposit requirements worldwide.

The Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure is a vehicle harmonizing such requirements. It entered into force in 1980,

Table 12-5-Member Countries, Budapest Treaty on the International Recognition of Micro-organisms for the Purposes of Patent Procedure

Australia	Japan
Austria	Korea, Republic of
Belgium	Liechtenstein
Bulgaria	The Netherlands
Czech and Slovak Federal Republic	Norway
Denmark	Philippines
Finland	Soviet Union
France	Spain
Germany	Sweden
Hungary	Switzerland
Italy	United Kingdom
	United States

SOURCE: Office of Technology Assessment, 1991.

and provides that member states recognize a deposit of a micro-organism strain made in another country for their own patent procedures. Currently, 23 nations are members of the Budapest Treaty (see table 12-5).

The key element of the treaty is the establishment of a series of approved International Depositary Authorities (IDAs). These depositories are recognized by all member countries for deposit purposes. Once a viable deposit is made in an IDA, two facts are recognized: the deposit was made on the indicated date, and any sample furnished by the IDA is a sample of the organism or other replicable material deposited on that date. As of January 1990, a total of 20 depository institutions had acquired IDA status; three are located in the United States (see table 12-6).

International Union for the Protection of New Varieties of Plants

With the development of plant sciences came the realization that the rights of plant breeders were entirely overlooked in many countries. The patent laws of many countries, for example, specifically excluded the patenting of any type of lifeform. An international conference in 1957, led to the drafting of the International Union for the Protection of New Varieties of Plants (UPOV); it was signed by several nations in 1961, and entered into force in 1968. Currently, 19 nations are members of UPOV (see table 12-7).

The International Union for the Protection of New Varieties of Plants was designed "to recognize and to ensure the breeder of a new plant variety. . . the right to a special title of protection or of a patent. " The goal was to provide a model for the adoption of

Table 12-6--U.S. Depositories Recognized Under the Budapest Treaty

American Type Culture Collection
12301 **Parklawn Drive**
Rockville, MD 20852
A private, nonprofit institution organized in 1925 for the purposes of acquiring, preserving, and distributing cultures of micro-organisms to scientists. Currently holds an estimated 8,000 deposits for patent purposes.
Northern Regional Research Laboratory
1815 N. **University Street**
Peoria, IL 61604
Established in 1940 as part of the U.S. Department of Agriculture for the study of micro-organisms of agricultural and industrial importance. currently has approximately 3,000 cultures on deposit.
In Vitro International, Inc. (IVI)
611 **(P) Hammonds Ferry Road**
Linthicum, MD 21090
Incorporated in 1983 as a for-profit company for the purpose of accepting cultures for patent purposes. Approximately 100 cultures are on deposit.

SOURCE: Office of Technology Assessment, 1991.

breeders' rights statutes in individual countries and to assure reciprocity between countries in the convention.

To obtain protection in each member country, it is currently necessary to file a separate application in each country. There is no central filing system, and international protection is not available by filing in only one member country. While both sexually and asexually reproduced plants can be protected, the UPOV convention requires that each protected variety have a specific, unique name for registration purposes. In all member nations except the United States, new varieties are subject to official inspection establishing that conditions for protection are satisfied.

The UPOV Convention is presently under consideration for revision. A recent diplomatic conference, held in March 1991, may lead to revision of Article 2, which currently does not allow both patent and breeders' rights for the same botanical species or genus (35).

European Patent Convention

The European Patent Convention (EPC) is an agreement between European nations to centralize and standardize patent law and procedure. To date, 14 countries are members of the EPC, which took effect in 1977 (see table 12-8).

Because the patchwork of traditional national patent systems in Europe was recognized as creating a potential conflict with the need for free trade, EPC established the so-called "European patent," a single, supranational patent obtained by filing one application with the European Patent Office in Munich. Once granted, the patent matures into a bundle of individual patents-one in each member country. The ultimate goal is for each member country to adopt, in its national law, the same substantive and procedural law of patents established by the EPC agreement.

EPC streamlines procedural requirements for applicants seeking a European patent. It avoids duplicate filing, searching, and examination costs; minimizes the number of translations that must be made; and economizes on the use of professional time, both on the part of the applicant's domestic patent representative and representatives in countries where protection is sought (3).

Table 12-7—Member Countries, Union for the Protection of New Varieties of Plants

Australia	The Netherlands
Belgium	New Zealand
Denmark	Poland
France	South Africa
Germany	Spain
Hungary	Sweden
Ireland	Switzerland
Israel	United Kingdom
Italy	United States
Japan	

SOURCE: Office of Technology Assessment, 1991.

Table 12-8-Member Countries, European Patent Convention

Austria	Italy
Belgium	Liechtenstein
France	Luxembourg
Denmark	The Netherlands
Germany	Spain
Great Britain	Sweden
Greece	Switzerland

SOURCE: Office of Technology Assessment, 1991.

INTELLECTUAL PROPERTY RIGHTS IN BIOTECHNOLOGY

The merging of intellectual property law and biotechnology represents the joining of old law with new technology. In theory, statutes designed to facilitate creation of unforeseen technologies and reward inventors for their creativity should blend easily with the inventions of biotechnology. Although intellectual property laws have fostered

R&D in biotechnology, novel legal and social questions have also arisen.

During the 1980s, events in the United States shaped the application of intellectual property law to biotechnology. First, the Supreme Court was called on to determine whether a living organism could be patented. Second, Congress and the executive branch took actions making it easier for federally funded inventions to become commercialized. These actions ignited a flood of biotechnology patent activity. By 1989, an examining unit specifically for biotechnology was established at the PTO.

The Chakrabarty Decision

The development of rDNA technology in the 1970's led to debate regarding what constitutes a patentable invention. Although patents on biotechnological processes had been issued since the 1800's, PTO did not permit patents on living products created by the technology, on the grounds that such matter were ''products of nature" and not statutory subject matter as defined by 35 U.S.C. 101 (see box 12-A).

Although proposed patent claims were rejected if directed to living organisms per se, patent protection was granted for many compositions containing living things (e.g., sterility test devices containing living microbial spores, food yeast compositions, vaccines containing attenuated bacteria, milky spore insecticides, and various dairy products) (29).

The issue of whether a genetically engineered organism could be patented was addressed by the Supreme Court in 1980, ***in Diamond v. Chakrabarty*** (10). In this case, the patent applicant had developed a genetically engineered, but not recombinant, bacterium capable of breaking down multiple components of crude oil. Because no naturally occurring bacterium possessed this property, Chakrabarty's bacterium was thought to have significant value for the cleanup of oil spills.

Chakrabarty filed a patent application with 36 claims. Process claims for the method of producing the bacteria were allowed by the PTO; but claims for the bacterium, itself, were rejected on two grounds: 1) micro-organisms are 'products of nature,' and 2) as living things, micro-organisms are not patentable subject matter under 35 U.S.C. 101. The case was eventually heard by the Supreme Court; the justices, in a 5-4 ruling, held that a live, human-made micro-organism is patentable subject matter under section 101 as a "manufacture" or "composition of matter.

Box 12-A—What Can Be Patented?

One section of the U.S. patent law, 35 U.S.C. 101, was part of the first U.S. patent law enacted by Congress in 1790, It defines what constitutes a patentable invention:

> Whoever invents or disoovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

This section of the patent Code has changed little, and its broad language has made possible the issuance of more than 5 million U.S. patents.

SOURCE: Mice of Technology **Assessment,** 1991.

The ***Chakrabarty*** decision provided a judicial framework for subsequent PTO decisions to issue patents under 35 U.S.C. 101 for plants and nonhuman animals. The decision also provided great stimulus for the economic development of biotechnology processes and products in the 1980's.

Federal Patent Policy

Other revisions in Federal patent policy encouraged increased patent activity from federally funded research. Prior to 1980, no single patent policy existed for such research, resulting in the development of 26 separate patent policies by various government agencies (33).

To promote efforts to develop a uniform patent policy that would encourage cooperative relationships and to commercialize government-funded inventions, Congress passed the Patent and Trademark Amendments of 1980 (Public Law 96-517) and amendments in 1984 (Public Law 98-260). The law allows nonprofit institutions (including universities) and small businesses to retain title to patents arising out of federally funded research, with the Federal agency retaining a nonexclusive, worldwide license. Universities are required to share royalties with the inventor and to use any net income for research and education (35 U.S.C. 202).

The law, which gave statutory preference to small businesses and nonprofit organizations, was extended by executive order to larger businesses (with

some exceptions) in 1983 (24). The Technology Transfer Act of 1986 (Public Law 99-502) granted Federal authority to form consortia with private concerns. Executive order 12591, issued in 1987, further encouraged technology-transfer programs, including the transfer of patent rights to government grantees.

ELEMENTS AFFECTING INTERNATIONAL PATENT RIGHTS IN BIOTECHNOLOGY

A number of differences exist among nations, regarding intellectual property protection for biotechnological inventions. International agreements have set norms for substantive intellectual property protection (e.g., national treatment under the Paris Convention) and for procedures for obtaining patents (e.g., simplified searching and filing under the Patent Cooperation Treaty and deposits under the Budapest Treaty), but further harmonization of intellectual property law is seen by many as necessary for improved trade and effective protection of intellectual property in a global marketplace.

Biotechnology is a particularly good example of technology where patent questions are raised by rapid scientific and technological change. The major international agreements governing intellectual property were ratified prior to the development of new biotechnological inventions (25). As legal issues are developed and dealt with in various nations, a primary consideration arises: what impact do these issues have on the development of an international marketplace for inventions developed by biotechnological means?

Intellectual property is an important component of U.S. competitiveness in fields relying on biotechnology. Without adequate international protection, this valuable asset is seriously tarnished and diminished in value, and future investment is discouraged. American competitiveness in this area focuses largely on securing patents, both in the United States and abroad, while understanding and operating smoothly within the procedural requirements for obtaining substantive patent rights.

This section focuses on six elements that affect U.S. competitiveness based on international intellectual property rights for biotechnology:

1. the patent application backlog,
2. patentable subject matter,
3. procedural distinctions,
4. process patent protection,
5. deposit issues, and
6. patent infringement litigation.

Patent Application Backlog

The Process

When a patent application is received by the PTO, it is assigned to 1 of 16 examining groups in the agency. Each examining group includes a number of art units, each responsible for a specific area of technology. Examiners in the art units review patent applications to decide whether the invention claimed in the application is entitled to patent protection. The examination process includes a search through U.S. patents, available foreign patent documents, and relevant nonpatent literature.

After the examiner decides whether to grant a patent, the PTO, through a procedure called an action, notifies the applicant of the examiner's decision, or any objection or requirement, and provides information that may assist the applicant in judging whether to pursue the application. If the invention is not considered patentable subject matter, the claims will be rejected. Some or all of the claims may be rejected on the first action by the examiner; relatively few applications result in patents as originally filed (31).

If an application is rejected or objected to, the applicant can either abandon the application or request a reconsideration, responding in writing to every rejection raised by the PTO. The PTO then issues a second action, which is normally final. Following a second action rejection, the applicant is normally limited to administrative review (either through the PTO Board of Patent Appeals and Interferences or Federal court action) or to filing a continuing application.

Continuing applications are an alternative to appealing the rejected application. If the application is filed within an allotted period of time and refers to an earlier application, the applicant is entitled to the date of the earliest filed application for subject matter common to both applications (35 U.S.C. 120). The ability to maintain the earliest filing date is an important benefit to the applicant, since the earlier priority date determines patent rights.

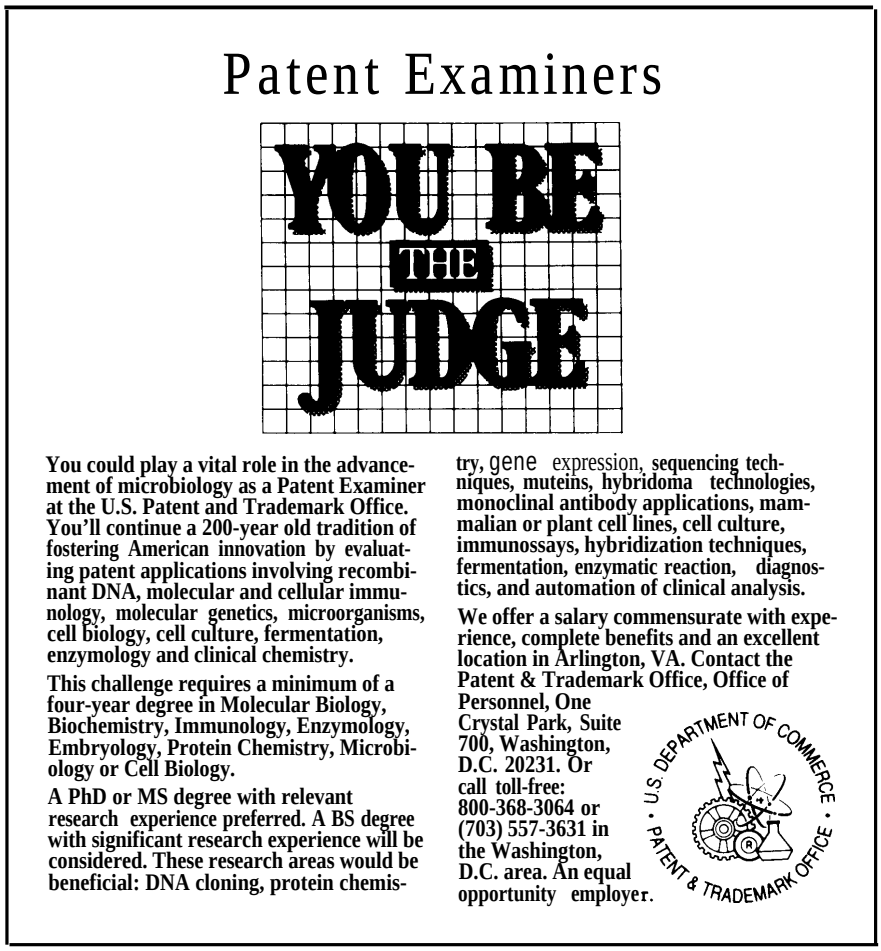

Photo credit: Patent and Trademark Office

PTO add for patent examiners.

The Problem

The abnormally long patent application review and action by PTO is frequently cited as the primary impediment to commercialization of biotechnology-related processes and products. Recent congressional reports reveal the pendency period for biotechnology patent applications is longer than that of any other technology (average pendency is 36.1 months from the date of application to the date of issue, compared to 21.0 months for all patents issued (30). Several reasons have been cited:

. due to the nature of the technology, its newness, and its rapid development, the level of technical scrutiny required to process an application for a biotechnology patent exceeds that required to process patent applications in most other areas of technology (30);
- high turnover among patent examiners, lured to the private sector by higher pay (8);
- failure to retain senior staff, well-trained in biotechnology patent prosecution, results in a lack of continuity, increased examination time per application, and inconsistent examination; and
- the pressure on examiners to meet certain efficiency quotas results in increased pressure and job disenchantment, further causing depletion of personnel.

Two key elements play a part in the patent application backlog: 1) the number of applications received by PTO and 2) the amount of time it takes for an application to be acted on. The number of biotechnology applications filed has grown at a significantly higher average rate--20 percent-than

that for all patent applications-2.9 percent—from 1983 through 1988 (30). On the other hand, the amount of time between filing and first action declined-from 14.5 months in 1989 to 13.1 months in 1990 (30,31). Despite the improved performance by PTO in reaching first actions, total pendancy appears to be increasing.

The effect of delays in obtaining patents varies between different subgroups in the biotechnology examining area. Although the average pendency of a biotechnology patent application is 36.1 months, the average time is shorter for applications related to plants and animals (24.9 months) and longer for applications related to genetic engineering (47.4 months) (see table 12-9). The actual time required to process inventions disclosed in patent applications is longer than the pendancy reported by the PTO, because they measure pendancy of applications, not inventions. A patent granted on an invention may be the result of a chain of replacement applications, or continuing applications. For example, during 1989, about one-third of all backlogged patent applications resulted from a chain of continuing applications. Factoring in the chain of continuing applications adds 9 months to PTO's reported average patent pendance of 26.3 months (31).

While there is clearly a difference between the average pendancy in biotechnology, as compared to an average pendancy for all technologies in the PTO, patents, even in biotechnology, are granted faster in the United States than in any major examining office in the world—and faster by a significant amount of time (35). In Japan and Europe, for example, pendancy time does not normally include the 18 months prior to publication of the application. In Japan, publication often leads to oppositions being filed against the application—nearly 30 such oppositions were filed against the patent for human tissue plasminogen activator (tPA) in Japan—further delaying the issuance of the patent (35).

Effect on Commercialization

Because patents are one of the most important assets of a startup, high-technology company, failure to procure timely patent protection can adversely affect a company's ability to secure the financing needed to develop processes and products. From the viewpoint of an individual inventor or assignee of a patent, several problems are apparent.

Table 12-9—Average Waiting Period, Application to Issue, for Biotechnology Patents, 1989

Art unit/description	Total patents issued	Average months
181/equipment	723	37.2
182/immunology	417	44.1
183/biochemicals	665	36.7
184/plants & animals	754	24.9
185/genetic engineering	307	47.4
186/biochemicals	268	37.7
187/equipment and immunology	1	33.4
188/microbiology	0	0.0
Biotechnology total	3,135	36.1

SOURCE: General Accounting Office, *Biotechnology: Processing Delays Continue for Growing Backlog of Patent Applications, 1990.*

First, the delay in getting a patent can slow down efforts to commercialize the invention. A second problem involves filing for protection in foreign countries. Under the Paris Convention, an applicant filing in the United States has 1 year to file in foreign countries and obtain the benefit of the U.S. filing date. As a practical matter, this decision is typically postponed until close to the end of the frost year, because of the considerable expense of foreign filing. Thus, it is desirable to have the U.S. patent examiner decide on patentability prior to the close of the 1 year period, so that the applicant has the benefit of the initial PTO search and examiner reaction before deciding whether foreign filing costs are justified. Without the PTO action, the decision is much more difficult and sometimes involves committing substantial funds, even when patent protection is not likely (7).

A third problem relates to the fact that pending U.S. patent applications are secret (35 U.S.C. 122). When an inventor makes a preliminary search, to determine whether the invention is novel, access to information is limited only to the available prior art (i.e., printed scientific and trade publications, foreign published applications, and issued patents). The backlog of patent applications creates a large body of hidden knowledge that may later become prior art. As a result, an inventor may file an application, only to learn years later that the application will be rejected, because a previously filed application made the same claims or claims broad enough to encompass the claims made in the, later application. If the backlog could be shortened, the amount of potentially hidden prior art would be reduced proportionately.

The delay to an inventor caused by the patent application backlog results in increased costs for

processing the application. Inmost fields, the cost of receiving a U.S. patent runs between $3,000 and $6,000. Biotechnology patents generally cost between $8,000 and $15,000. This difference is primarily due to attorney fees and the time involved responding to patent examiners who are not sufficiently skilled in biotechnology patent prosecution (18).

Proposed Solutions

In an attempt to reduce the backlog of biotechnology patent applications, the PTO instituted a 13-point, catch up plan (see box 12-B). The plan has not succeeded in its goal of reducing the backlog of patent applications. During calendar year 1989 and the frost half of 1990, the inventory of unexamined biotechnology patent applications increased by approximately 33 percent (from about 6,200 to about 8,200) (31).

The most immediate way for an applicant to avoid the current backlog is to request accelerated examination. This is done with a written petition describing the applicant's preliminary search and description of the prior art. The additional fee of $72, to request accelerated examination, is worthwhile for applicants needing to establish a definitive patent position for investors or licensees. Of approximately 5,000 biotechnology-related applications received by the PTO in 1987, only 17 were petitions requesting accelerated examination (30). Legal and business considerations may explain the limited use of accelerated examination. From a legal standpoint, the PTO practice requires that an applicant seeking an accelerated examination provide a complete search report of literature and prior art relevant to the application. Failure to do so can result in a rejected application. (35) From a business perspective, there may be little incentive to have the 17-year patent term begin to run until a product is ready for market. From this perspective, a company wants their patents to issue more slowly than those patents belonging to a competitor (12).

Suggestions for reducing the backlog include:

- increased pay, benefits, and training for PTO personnel to enhance job satisfaction and performance.
- cutting down on the excessive volume of paper that an applicant sometimes provides an examiner to support the application (5) .

Box 12-B—PTO Plan To Reduce Biotechnology Patent Backlog

In 1988, the Patent and Trademark Office initiated a 13-point plan to process biotechnology patent applications more expeditiously:

1, Creating a new examining group to deal exclusively with the field of biotechnology. Called "Group 180," this examining unit consolidated units and examiners from preexisting examining groups.
2. Adjusting examiner complexity factors.
3. Obtaining greater hiring authority from the Office of Personnel Management.
4. Obtaining special engineering pay rates for new examiners.
5. Hiring as many new biotechnology examiners as can be trained by senior examiner staff.
6. Increasing overtime for several years to the maximum level sustainable.
7. Liberalizing and publicizing, as necessary, the procedure for requesting accelerated examination.
8. Identifying examiners in other groups who can be transferred and retained to examine biotechnology applications in a reasonable period of time.
9. Improving communication about Patent Office goals and reeds and improving morale in the new biotechnology examining group.
10. Examining search tools-especially for searching DNA, RNA, and protein sequences.
11. Enhancing technical and legal update training for all examiners.
12. Stimulating higher productivity in the new biotechnology examining group.
13. Hiring and initially training new examiners for the biotechnology group in other examining groups.

SOURCE: General Accounting Office, *Biotechnology: Backlog of Patent Applications,* 1989.

. adoption of a selective examination scheme, whereby applicants select cases for priority treatment and defer less important applications for later examination.

. adoption of the 18-month publication system found in many other countries, whereby all applications are published within a certain time period, thus decreasing the amount of potential hidden prior art; and

- Adoption of a payback system, similar to Federal medical training grants, whereby, in exchange for educational assistance, Ph.D-level graduates would pay back the Federal Government's investment by serving a specified term as an examiner.

As PTO attempts to reduce the patent application backlog, some applicants complain that the quality of patent examination has decreased. Procedural mistakes and a general lack of understanding of the law occasionally results in erroneous actions by patent examiners (e.g., the issuance of overly broad patents, or erroneous rejections). Such errors increase the cost of the patent application process, either through lost opportunities or through refiling and appeal costs.

Others, however, claim that the patent application backlog is not detrimental to U.S. capability in biotechnology for two reasons:

- Despite the U.S. backlog, it takes significantly longer to obtain a biotechnology patent in other countries (35).
- For products that have a long regulatory approval time, the delay in obtaining a patent extends the period of intellectual property protection, since the 17-year term does not begin until the patent is actually issued (1 1).

Patentable Subject Matter

Under U.S. Patent law, four broad areas constitute the core of patentable subject matter: processes, machines, manufactures, and compositions of matter (101). As the Supreme Court noted in ***Chakrabarty,*** Congress plainly contemplated that the patent laws would be given wide scope and 'intended statutory subject matter to include anything under the sun made by man. '

After ***Chakrabarty, the*** patenting of microorganisms became commonplace in the United States. In 1985, the PTO's Board of Patent Appeals and Interferences relied on ***Chakrabarty*** to rule in Ex ***parte Hibberd (16)*** that corn plants, seeds, and plant tissue culture containing an increased level of the amino acid, tryptophan, were patentable subject matter under 35 U.S.C. 101, even though such plants could be protected under the PVPA. Today, a variety of protections—plant patents, plant variety protection certificates, utility patents, and trade secrets—exist for inventions that constitute plant life.

In April 1987, the PTO Board of Appeals and Interferences ruled that polyploid oysters were patentable subject matter (15). Subsequently, PTO announced that it would, henceforth, consider nonnaturally occurring, nonhuman, multicellular organisms (including animals) to be patentable subject matter. In April 1988, the first patent on a nonhuman animal was issued to Harvard University for mammals genetically engineered to contain a cancer-causing gene (U.S. 4,736,866). Although 120 animal patent applications are pending, no additional patents on animals have issued (35). The PTO policy and the issuance of the sole animal patent initiated a broad public debate and the introduction of legislation in Congress (see box 12-C).

Europe

European subject matter law is noteworthy in that 1) a convention exists whereby a number of nations subscribe to one law regarding subject matter patentability; 2) because of a developed science base, the issue of subject matter patentability has arisen in the context of biotechnology; and 3) issues addressed by the European Patent Office highlight similarities and differences with U.S. law.

Article 52(1) of the E.P.C. defines patentable subject matter as inventions that are susceptible to industrial application, are new, and involve an inventive step. In this respect, European and U.S. law both have expansive language defining what can be patented. Unlike U.S. law, which identifies classifications that are patentable (i.e., process, machine, manufacture, and composition of matter), the European provision does not provide a definitive, positive definition of classes of patentable inventions. Instead, Article 52(2) narrows the broad language of Article 52(1) by explicitly excluding from the term "inventions'

- discoveries, scientific theories, and mathematical methods-including naturally occurring products;
- aesthetic creations;
- schemes, rules, and methods for performing mental acts, playing games, or doing business;
- programs for computers; and
- presentations of information.

Article 53(b) stipulates that European patents not be issued for plant or animal varieties and essentially biological processes for the production of plants and animals (with the exception of microbiological

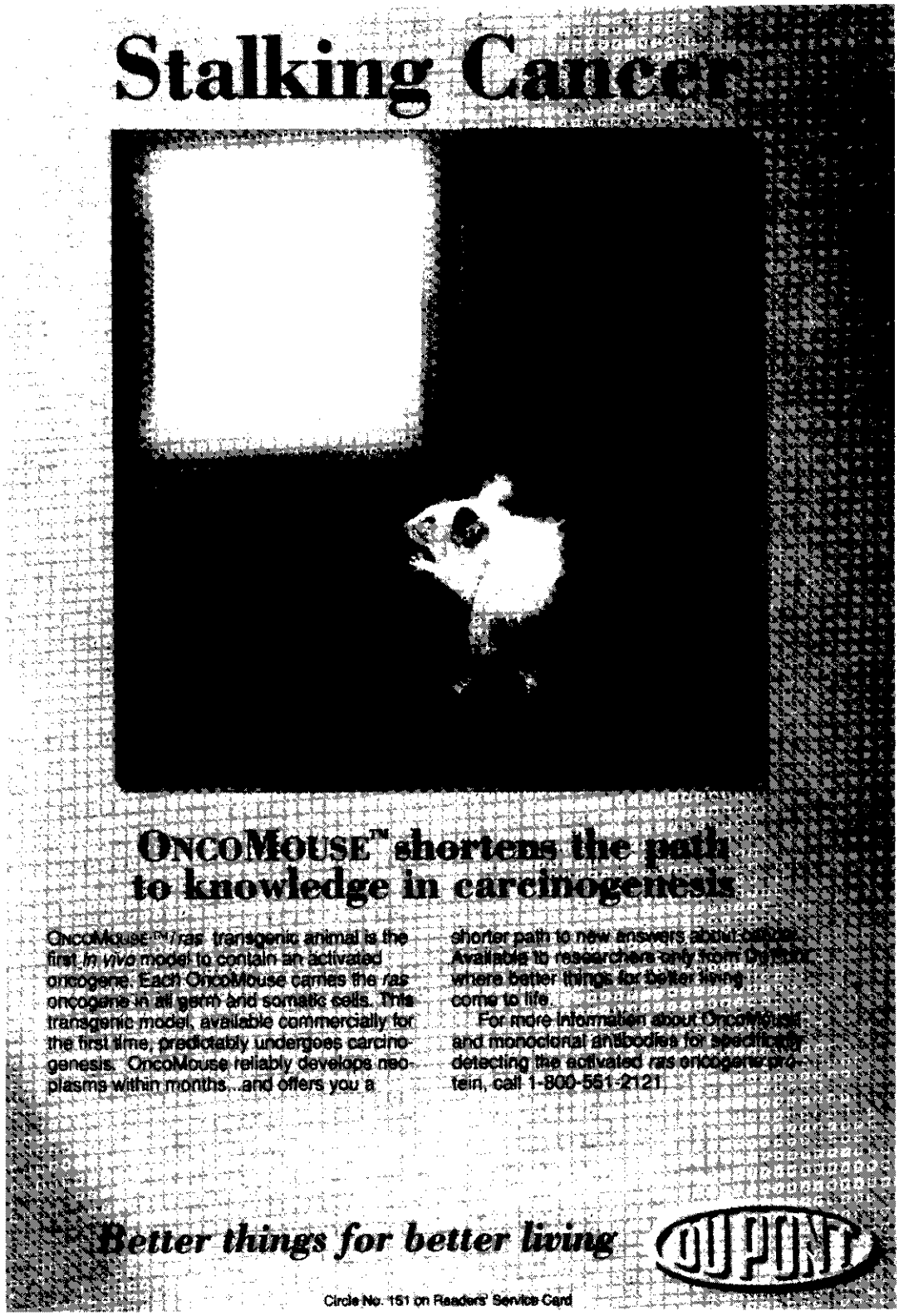

Photo credit: DuPont

Advertisement for OncoMouse, the subject of the first U.S. patent on a transgenic animal.

Box 12-C—Patenting of Animals: The Legislative Response

Several pieces of legislation were introduced in the 100th and 101st sessions of Congress addressing the patentability of animals. The following actions occurred during the 100th Congress (in session during 1987 and 1988):

. An amendment to a supplemental appropriations bill (Senate Amendment 245 to H.R. 1827) to prohibit the use of appropriated funds for the patenting of genetically altered or modified animals. The amendment was adopted by the Senate by voice vote but not adopted by the conference committee.
. H.R. 3119 to establish a 2-year moratorium on the patenting of animals and to revoke previously granted patents.
. S. 2111 to prohibit animal patents and revoke previously granted patents.
• H.R. 4970, the Transgenic Animal Patent Reform Act, to provide that exemptions from infringement for: 1) making or using a patented animal solely for research or experimentation without any commercial intent; or 2) for a person whose occupation is farming, to reproduce through breeding, the use, or to sell a patented transgenic farm animal under certain circumstances; 3) to permit the Patenting and Trademark Office to accept a deposit of biological material; and 4) to declare that human beings are not patentable. The bill was adopted by the House of Representatives, but no action was taken by the Senate.

The following legislation was introduced in the 101st Congress (in session during 1989 and 1990):

• H.R. 1556, similar to H.R. 4970 (see above), later incorporated into H.R. 5598 (a bill addressing several patent-related issues).
• H.R. 3247, to impose a 2-year moratorium on the granting of patents on genetically altered animals, except for animals whose commercialization is subject to a Federal regulatory process that imposes environmental, health and safety, and biomedical ethical standards.
. S. 2169, similar to H.R. 3247 (see above).

SOURCE: Office of Technology Assessment, 1991.

processes or the products thereof). There are two reasons for this approach, adopted in 1973. First, granting patents in this area would create legal and administrative difficulties. Second, plant variety protection enacted in several European nations is the only system applicable to that category of inventions (1).

The question of whether a process is essentially biological depends on the extent of technical human intervention in the process. If such intervention plays a significant part in determining or controlling the desired result, the process is not excluded. According to the EPC, essentially biological processes and specific plant varieties, regardless of whether they were produced by breeding or genetic engineering, are not patentable.

Despite the exclusions in the EPC, patents have issued on microbiological inventions. Plant variety protection statutes generally offer more limited protection than that provided by U.S. law, since protection generally extends only to those varieties specifically set forth in varietal lists compiled by each country.

Comparison of Subject Matter Laws

The principle of patenting micro-organisms is now widely accepted by many nations (25, 34). Plant protection generally falls into the domain of national plant variety rights statutes, which usually apply to plant products obtained by traditional breeding methods-that could not be patented. United States law offers a plant breeder the most generous menu of choices for intellectual property protection of inventions that constitute plant life.

To date, the United States is the only country to both state a patent policy regarding animals and to issue a patent for a transgenic animal. The subject matter of the sole U.S. patent is currently pending at the European Patent Office (see box 12-D). The patent offices of Japan and Australia may per-r-nit animal patents, because their statutes lack subject matter restrictions analogous to EPC's Article 53(b).

United States patent law is also noteworthy because it is, generally, neutral about any potential use of patented inventions. Such social considerations are left, instead, to Federal, State, and local laws that regulate the development and use of

Box 12-D—The Harvard Mouse Goes to Europe

On April 8,1988, the first U.S. patent on an animal was issued to Harvard University for transgenic nonhuman mammals genetically engineered to contain a cancer-causing gene (U.S. Patent No. 4,736,866).

The so-called "Harvard Mouse Patent" was filed with the European Patent Office on June 24, 1985. In examining the application, two substantial issues were raised by the patent examiner:

. Article 53(b) of the European Patent Convention (EPC) does not permit claims to animals, per se.
Article 83 of the EPC, which relates to sufficiency, is satisfied only if any embodiment of the invention, as defined in the broadest claim, is substantially capable of being realized on the basis of the disclosure. The application in this case "unduly extrapolated to transgenic non-human eukaryotic animals from what has actually been carried out, namely transgenic mice.

In response to these concerns, the applicant reformulated the application in order to emphasize the microbiological nature of the invention and to request that "eukaryotic animals" be restricted to "nonhuman mammalian animals.

Despite these reformulations, the EPO patent examiner rejected the application in July 1989. The decision stated that Article 53(b), which bars the patenting of animal varieties, was conceived in 1962, when "the question of patenting transgenic animals was scarcely conceivable. " Although the EPO Board of Appeals had interpreted plant varieties, which are also excluded under 53(b) as "excluding from patentability only plants in the genetically fixed form of a plant variety,' this interpretation is based, in part, on a desire not to permit double protection under patenting and plant variety protection. Because no similar situation exists for animal varieties, "the idea behind this exclusion was that animal varieties are not appropriate subject matter for patent protection. "

In finding the application objectionable under Article 83, the decision said:

"The **Applicant has carried out his experiments with *one* oncogene, the mouse mycgene, by using a mouse as the nunhuman mammalian animal. The invention as disclosed in its broadest concept, however, relates to *any*** oncogene and ***any*** conceivable mammalian animal. . . The claims [refer not only to mice] but to any kind of mammals such as anthropoid apes or elephants, all of which have a highly different number of genes and a differently developed immune system. . . the success with the transgenic mouse cannot be reasonably extrapolated to ***all mammals."***

The examiner's decision was later reversed on appeal, and the application was remanded to the examining unit for further examination. As of August 1991, the application was still pending at EPO.

SOURCE: European Patent Office, ***In re President and Fellows of Harvard College, Decision to Refuse a European Patent Application,*** **European Patent Application No. 85304490.7, Refusal Under Art. 97(1) EPC, 1989; European Patent Office, Boards of Appeal, Case T 19/90-3.3.2, Decision, Oct. 3, 1990.**

commercial products. In contrast, Article 53(a) of the EPC states, that patents shall not be granted if the exploitation of the patent would be contrary to public order or morality.

Absent congressional action restricting subject matter patentability, U.S. law is more generous from an inventor's perspective than the law of any other nation. The concept of patenting animals has, however, resulted in broad public debate, and calls for both a moratorium or prohibition of animal patents and passage of legislation by the House of Representatives (H.R. 4970, 100th Congress) that would specifically preclude the patenting of human beings.

Procedural Distinctions

The patent statutes of most nations are similar in many respects. This similarity extends to the procedural aspects of obtaining a patent. In some respects, however, U.S. law differs from that of other nations. These differences can affect competitive advantage and, thus, have become topics of discussion as nations look for ways to harmonize patent statutes and practices. All these procedural differences affect all areas of inventive inquiry. In some ways biotechnology-related inventions are more vitally affected, due to the novelty of the sciences involved, the number of applications being filed, and the lack of experience in many patent offices for dealing with this art.

The United States has been involved in two sets of negotiations-one under the auspices of the World Intellectual Property Organization (WIPO) and the other as part of the General Agreement on Tariffs and Trade (GATT)-----to discuss harmonization of patent statutes in countries around the world.

Issues raised in these forums have included priority date, grace period, and patent application publication.

Priority Date

In all Paris Convention countries, the first practical step for gaining worldwide protection for a patentable invention is to be the first-to-file a patent application in the home country patent office. This basic rule, which appears to create a level playing field for all competitors, becomes muddled when two factors—1) first-to-invent v. first-to-file and 2) filing procedures-are considered.

United States law awards patent priority to the frost inventor to conceive, diligently reduce to practice, and claim the invention. The United States and the Philippines are the only nations that grant priority on this first-to-invent basis. The primary advantage of the first-to-invent system is that it permits a patent applicant to determine some of the scientific implications of an observation before rushing to the PTO, for fear that someone else will frost file a patent application for the same invention. Japan (a first-to-file country), for example, receives in excess of 500,000 patent application-type disclosures each year, almost 40 percent of which do not become the subject of a request for examination (35). If the United States were to adopt a first-to-file system, the number of patent applications would likely increase dramatically.

All other nations provide priority on a frost-to-file basis. Some argue that a patent applicant in a first-to-file nation has an advantage because the key requirement is simply to file a registration or application that can be perfected, as needed, at a later time. Thus, the result, it is argued, is a far lower cost to the inventor per patent application and a speedier filing of each application when compared to U.S. practice (37). However, a first-to-file system can cause disadvantages for foreign applicants if other onerous administrative requirements are present (see box 12-E).

Grace Period

The United States gives the inventor who publishes patentable information before filing a patent application or who commercially uses the invention a l-year grace period to file the patent application. Other nations either have no grace period or grace periods of varying and more limited duration. Japan, for example, has a grace period of 6 months for limited public disclosure (i.e., disclosure at a technical meeting in Japan) (4) while Europe has no grace period.

The grace period in U.S. law can aid inventors of biotechnological processes and products, especially smaller companies and individual scientists who feel the need to publish research findings immediately. However, lack of grace periods in other industrialized countries can mean that publication (a de facto professional requirement for many U.S. scientists) can result in forfeiture of patent rights in other countries.

Box 12-E—The Race to the Home Patent Office

Three competitors--one in Germany, one in Japan, and one in the United States-are working on the same area of polypeptide chemistry. Each works independently of the other, and has completed work on anew polypeptide at about the same time. Which of the three inventors gets worldwide patent protection?

The answer depends on whether the inventor files in a "first-to-file" or "first-to-invent" country. In Japan and Germany (first-to-file), the winner is the inventor who wins the race to a member country's patent office. Even if the American and the German inventors have made their polypeptide before the Japanese inventor, if the Japanese inventor files a patent application in Japan before the German and U.S. inventors file applications in their respective countries, then, under the Paris Convention, the Japanese inventor has worldwide priority before either competitor.

A different result could occur in the United States. If the American inventor made the polypeptide before the Japanese inventor, even if the Japanese inventor was the first to file a patent application, the Japanese inventor would obtain certain procedural advantages in an interference proceeding in the United States but would not be granted a patent if the American inventor was able to show that the invention was made by the American before the Japanese filing date. Under 35 U.S.C. 104, any applicant foreign to the United States is precluded from relying on dates of activities in a foreign country before the filing date of a patent application in a foreign country in order to establish priority of invention. Consequently, the Japanese inventor is not likely to prevail in the United States, in this instance.

SOURCE: Office of Technology Assessment, 1991.

Publication of Patent Applications

In the United States, patent applications are, by law, confidential (35 U.S.C. 122). In other countries, a patent application is published 18 months after the initial filing date. Proponents of secrecy point out that publication can give competitors the information necessary to reverse-engineer the invention (i.e., take the idea and, through experimentation, repeat the invention) (13). On the other hand, the secrecy provision in U.S. law makes it difficult to determine whether the invention is being claimed by another inventor waiting approval of a patent application. Either way, in determiningg whether to file for patent protection outside of the United States, the inventor must determine whether it is commercially acceptable to have the application published prior to the grant of a patent.

Process Patent Protection

A major concern of U.S. biotechnology companies is the adequacy of U.S. law to protect against patent piracy. Process patents constitute the majority of patents issued in the biotechnology area. Such patents can be vital, especially if they cover a new process for making a known product. Purified human insulin, for example, has been produced before and thus, is unpatentable. New processes for making insulin, however, are patentable (22). Concern has mounted that processes patented in the United States are being used abroad and the resulting products then exported to the United States. Congress enacted legislation in 1988, to address concerns regarding process patent protection. Debate, however, continues as to whether additional protection is needed.

Process Patent Amendments Act

Until recently, the import, sale, and use in the United States of a product made abroad according to a process patented in the United States was not considered to be an act of patent infringement. The patent owner had no recourse in a U.S. court of law but could only request an investigation by the International Trade Commission (ITC). The ITC could issue an import exclusion order if it was shown that the responding party had used abroad a process patented in the United States and imported the product into the United States, since such action, by law, was considered to be an unfair method of competition. However, this alternative was seen by some as inadequate; no monetary damages could be obtained, and the U.S. manufacturer had to show injury to an established domestic industry.

In an attempt to correct this problem, Congress in 1988 enacted the Omnibus Trade and Competitiveness Act (Public Law 100-418). The new law holds that whoever without authority imports into the United States or sells or uses within the United States a product made by a process patented in the United States shall be liable as an infringer if the import, sale, or use of the product occurs during the term of such process patent. This provided the U.S. patent holder with access to Federal courts as a means of enforcement action in addition to any ITC action. The legislation noted two limitations: a product made by a patented process will no longer be so considered after 1) it is materially changed by subsequent processes, or 2) it becomes a trivial and nonessential component of another product (35 U.S.C. 271(g)).

The legislative record indicates that it will be difficult for an alleged infringer to rely on these two exceptions:

> In the biotechnology field it is well known that all living organisms contain within them particular genetic sequences composed of unique structural characteristics. The patented process may be for the process of preparing a DNA molecule comprising a specific genetic sequence. A foreign manufacturer uses the patented process to prepare the DNA molecule which is part of the patented process. The foreign manufacturer inserts the DNA molecule into a plasmid or other vector and the plasmid or other vector containing the DNA molecule is, in turn, inserted into a host organism; for example, a bacterium. The plasmid-containing host organism still containing the specific genetic sequence expresses that sequence to produce the desired polypeptide. Even if a different organism was created by this biotech procedure, it would not have been possible or commercially viable to make the different organism and product expressed therefrom but for the patent process, the product will be considered to have been made by the patented process (32).

Despite the Federal legislation, issues surrounding the scope and use of process patents will continue to arise. In 1988, the ITC instituted an investigation into whether the import of certain recombinant erythropoietin (EPO) constituted an unfair act under the Tariff Act (see box 12-F).

Despite unresolved problems in this area, the Omnibus Trade and Competitiveness Act of 1988,

Box 12-F—Litigation, 1990-91

Moore v. Regents of the University of California

The California Supreme Court, in 1990, ruled that a patient does not have a property right to his body tissues after they were used by researchers to develop a commercially important cell line.

Xoma v. ***Centocor***

On the same day, in May 1990, that the University of California received a U.S. patent covering the therapeutic use of certain monoclinal antibodies for treatment of septic shock, Xoma (Berkeley, CA) (the exclusive licensee of the patent) sued Centecor (Malvern, PA), which had filed its patent application 7 years ago.

Upjohn v. Syntro

In August 1990, plaintiff and defendant settled their patent dispute over rights to a genetically engineered veterinary product, a vaccine used against pseudorabies disease of swine. Under the terms of the agreement, Synto (San Diego, CA) will take a license under the Upjohn (Kalamazoo, MI) patent and pay a royalty to Upjohn.

Genentech v. Genetics Institute and Wellcome Foundation

A Federal District Court found that the defendants infringed three Genentech tPA patents.

Cetus v. ***DuPont***

In February 1991, a Federal court jury upheld two Cetus patents for polymerase chain reaction. Cetus had charged DuPont with patent infringement. DuPont claimed that it should not be liable under Cetus' patents, on the grounds that work done in the early 1970s at the Massachusetts Institute of Technology anticipated PCR technology.

Amgen v. Genetics Institute and Chugai Pharmaceuticals

In a dispute concerning patent and marketing rights to Erythropoietin (EPO), a naturally occurring glycoprotein produced by the kidneys, Amgen (Thousand Oaks, CA) filed four patent applications and was issued a patent claiming rights to genetic materials and host cells used in the recombinant production of EPO. Genetics Institute (GI) (Cambridge, MA) later filed an application with the Patent and Trademark Office. The GI application claimed a purified and isolated sequence for EPO, the vectors used, and the transected host cells. The PT0 declared two interferences between GI's and Amgen's patent in May 1989. The interference proceeding, which allows the PTO to investigate and determine which company was actually the first to invent, is still pending and is expected to take several years to decide.

Both companies established marketing agreements with other companies to market EPO. Amgen has a joint venture with Kirin Brewery Ltd. of Japan (known as Kirin/Amgen) and GI entered an exclusive licensing agreement with Chugai Pharmaceutical Co., Ltd. of Japan. As a result of these agreements, other subsidiaries and licensing agreements were established.

In January 1988, Amgen filed a complaint before the International Trade Commission (ITC) to prevent the import of EPO by Chugai U.S.A. into the United States for clinical trials. The ITC, in 1989, decided that the importation of EPO into the United States did not violate Section 337 of the Tariff Act of 1930. The ITC investigation marks the first time that a trade law has been used to challenge a product developed through biotechnology and is indicative of the problems of process protection for biotechnology in the United States.

Amgen received FDA approval in June 1989, for the treatment of anemia associated with chronic renal failure, which includes both dialysis and predialysis patients. Genetics Institute has yet to receive approval for its EPO in the United States.

In April 1991, the U.S. Court of Appeals for the Federal Circuit held that Amgen's patents were valid, enforceable, and infringed by GI. The ruling blocks GI from selling its version of EPO in the United States. Following the ruling, Amgen's stock increased by 12 percent, and GI's stock dropped 35 percent.

SOURCE: Office of Technology Assessment, 1991

altered the the rules of patent-based Section 337 actions. The requirement that the plaintiff show injury to a domestic industry was eliminated. Instead, the patent owner need only establish the existence of a domestic industry relating to the patented invention. Activities such as substantial investment in exploiting the patent. including engineering, research, development, or licensing, is sufficient to establish the existence of a domestic industry (9).

The *In re Durden* Dilemma

Another controversy in the area of process patent protection is the so-called Durden Doctrine, named after a 1985 case of increasing importance to

biotechnology patent applicants (19). ***Durden in***volved a challenge to the denial of a patent for a process to make a novel chemical. The process to make the chemical, although similar to that of a previously issued patent, used a novel though related starting material and produced a novel, though related, end-product. Although PTO denied a patent for the process, it did grant a patent for the novel starting materials and the novel end-product. The court, in ***Durden,*** concluded that a chemical process, otherwise obvious, is not patentable--even if the specific starting material employed or the product obtained are novel and nonobvious.

Although the technology in ***Durden was*** not biotechnology, the ***Durden*** decision has been a source of frustration to biotechnology-related patent applicants; examiners are increasingly using the doctrine to deny certain process patents on the basis that a patent should not be issued when the process is old and predictable (38).

Opponents of the application of ***Durden*** to biotechnology cases argue that the case applies to chemicals, and its application to biotechnology cases is not warranted. As one commentator notes, expressing a gene in a cell is not always easy or obvious and thus, in certain cases should be patentable (36). Another critic of the doctrine argues, that ***Durden*** is in direct conflict with another case (20) in which it was held that a new microbe could not be treated as prior art in determining the patentability of a method of using the microbe to produce an antibiotic, therefrom, by an otherwise standard process. In essence, novelty and unobviousness of the microbe imparted patentability to a method of using it (2). A third commentator questions, why a conventional process using a novel starting material is not patentable, yet a pharmaceutical compound comprising a novel ingredient and a conventional carrier is patentable (4).

Despite widespread dissatisfaction with the ***Durden*** doctrine, efforts to legislate a solution have met resistance from some companies and patent attorneys involved in biotechnology R&D. Some argue, that overruling ***Durden*** by legislative action would lead to the issuance of excessive numbers of process patents, thus diluting the obviousness requirement. Another argument is, any legislative action will result in additional uncertainty and additional patent infringement suits. Proponents of legislative change note that until the alleged loophole is closed,

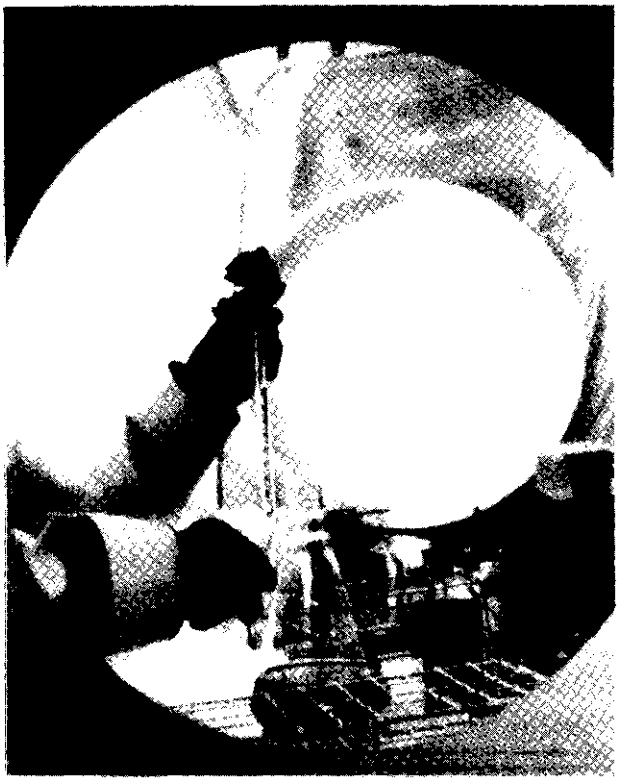

Photo credit: American Type Culture Collection

Glove box for handling deposited cultures.

processes using novel and patentable starting materials will be produced outside of the United States and then imported back to the United States. This approach, would deny to product patent holders royalties that would have been required had the product been produced in the United States. The controversy has resulted in public debate among patent practitioners and various companies (17,36).

Deposit Issues

United States patent law requires a patent application to include a specification-a written description of the invention in such clear, concise, and exact terms that any person skilled in the art to which it pertains can make and use the invention. This requirement, called enablement, presents a unique procedural issue when words alone cannot fully describe the invention.

In 1949, PTO began recommending that patent applications for inventions involving microorganisms include the deposit of the pertinent micro-organism with a culture collection. Although not a formal requirement, patent examiners advised

applicants that, in cases where words alone were not sufficient to describe the invention adequately, a deposit was advisable. PTO first published guidelines on the deposit of micro-organisms in 1971. In 1977, the Budapest Treaty instituted a system of International Depositary Authorities, making deposits a normal part of international patent practice.

Three issues of deposit practice raise international questions. When is a deposit required? When should a deposit be released to the public? What is the scope of the so-called "research exemption'

When is a Deposit Required?

All Budapest Treaty nations require deposits when it is not possible to reproduce a claimed invention without reference to deposit. The requirement for a deposit is determined on a case-by-case determination in all countries. When a patent applicant is able to disclose how to re-create the invention with mere words alone, then a deposit is not required (21).

Uniquely, however, the United States requires that the application disclose the best mode for practicing the invention, and thus, the "best" sample may sometimes be required for compliance, if that best sample cannot be recreated from the words of the patent application alone. The best mode requirement is essentially a requirement against concealment. As a result, U.S. patentees are encouraged to err on the safe side; and on issuance of a U.S. patent, deposit their best biotechnology samples, which on patent issuance are then easily available to others, including those who would take such samples outside of the jurisdiction of the United States.

Public Access to Deposits

The role of the depository is to retain and be a convenient source of an inventor's deposit. The depository is an objective entity-independent of the patent applicant and the PTO. The availability of samples from U.S. depositories for cultures involved in the patenting process is straightforward. If the depository number and the U.S. patent number are known, the culture may be requested and is routinely made available on payment of a minimal fee. There is no record of a U.S. depository ever denying access to someone eligible to receive a culture (34).

Some patent owners contend that free access to a deposit amounts to super-disclosure (giving away the invention itself in addition to the written recipe). Some owners of hybridoma patents, for example, contend that open access to a hybridoma deposit amounts to giving away their invention plus all the know-how the inventors might have been able to sell separately. This claim of loss may be exaggerated, however, since knowledge of how to produce and maintain hybridoma cells in culture does not generally permit large-scale operation. The latter methods must either be reverse-engineered, or the knowledge must be purchased separately (34). Nevertheless, it is generally easier to reproduce a deposited micro-organism than to create it from a written description.

To some patent owners, another issue is the timing of public accessibility to the deposit. For patenting outside of the United States, if a deposit is needed to teach the invention, that deposit must be made before the first priority filing date. In the United States, where patent applications are maintained in secrecy up until the grant of the patent (often several years from the filing date), deposits must be made prior to issuance of the patent. In Europe, however, patent applications are published 18 months from the filing date, which limits any secrecy (both in terms of the contents of the patent application and any enabling deposit) to a specific time-frame. For those desiring a longer period of secrecy, this limited timeframe is seen as inadequate, because biotechnology-related applications take far longer than 18 months for processing. The result is ***de facto*** release of the intellectual property before the inventor knows whether a patent will issue. Another potential problem for patent owners involves the export of an accessed deposit to countries where there is no patent protection. This could result in a major loss of property rights (6).

The Research Exemption

Once a sample that relates to a patented invention is released, there is controversy over the degree to which that sample can be used in the United States and other nations.

Generally, use of a deposited culture that is the enablement of an invention constitutes patent infringement. The United States, Japan, and Europe, however, all have research exemptions that permit various uses of a patented invention for experimental inquiry.

Japan and Europe have statutory exemptions that freely permit the use of a patented invention in the laboratory to create new inventions. Thus, a depos-

ited sample of a hybridoma may be used without patent infringement to create new technology. Whether the new technology can be commercialized without patent infringement depends on whether or not the claims of the patent cover the new product.

In the United States, the experimental-use defense to patent infringement is a court-created doctrine, holding that an experiment with a patented invention for the sole purpose of gratifying true scientific inquiry or philosophical curiosity does not attack the right of a patentee and thus, does not constitute infringement. In 1984, the Court of Appeals for the Federal Circuit ruled that "the limited use of a patented drug for testing and investigation strictly related to FDA drug approval requirements during the . . . term of the patent" did not fall within the experimental-use exemption and thus constituted infringement (26).

In the wake of this case, Congress amended the patent code (Public Law 98-417), which now provides:

> It shall not be an act of infringement to make, use, or sell a patented invention (other than a new animal drug or veterinary biological product (as those terms are defined in the Federal Food, Drug, and Cosmetic Act . . .) which is primarily manufactured using recombinant DNA, recombinant RNA, hybridoma technology, or other processes involving site specific genetic manipulation techniques) solely for the purposes reasonably related to the development and submission of information under a Federal Law which regulates the manufacture, use, or sale of drugs (35 U.S.C. 271(e)(l).

To date, the courts have been divided on what activities are permissible under 271(e)(l) (14,27, 28).

Patent Infringement Litigation

The emergence of biotechnology as an important field in patents has resulted in a surge of litigation, as companies seek to enforce their rights against infringement and defend the patent grant in opposition or revocation proceedings. Such litigation is not surprising, given the web of partially overlapping patent claims, the high-value products, the problem of prior publication, and the fact that many companies are interested in the same products (see box 12-F).

Because biotechnology is a new area in patent law, litigation is not something that Congress can readily alleviate. By its nature, infringement is an area that can only be addressed by Congress in general terms, leaving to the courts the jurisdiction for settling property disputes between companies.

How the courts interpret biotechnology patent claims, and how well U.S. companies protect patent rights abroad will be issues facing biotechnology companies during the years ahead. Uncertainty over patent rights will be costly and will affect the way many biotechnology-related companies structure R&D strategies. Until precedents are set in court rulings, predicting the outcome of patent litigation will be extremely difficult.

SUMMARY

Intellectual property law, which provides a personal property interest in the work of the mind, is of increasing importance to people who use biotechnology to create new inventions. Three areas of intellectual property law—patents, plant variety protection, and trade secrets-are particularly important to biotechnology.

Broad patent protection exists for all types of biotechnology-related products and processes in the United States. The Supreme Court holding in ***Diamond v. Chakrabarty*** that a living organism was patentable along with action by Congress and the executive branch to change Federal policy to increase patent activity from federally funded research have spurred biotechnology-related patent activity. Internationally, several agreements (e.g., the Paris Union Convention, the Patent Cooperation Treaty, the Budapest Treaty, the Union for the Protection of New Varieties of Plants, and European Patent Convention) provide substantive and procedural protection for inventions created through the use of biotechnology.

Despite a generally favorable international climate, a number of elements affect U.S. competitiveness in protecting intellectual property. The patent application backlog at PTO, uncertainties in the United States and internationally regarding what constitutes patentable subject matter, procedural distinctions in U.S. law (e.g., first-to-invent v. frost-to-file, grace period, secrecy of patent applications, and deposit considerations), uncertainties in interpreting process patent protection, and the spate of patent infringement litigation all constitute unsettled areas that could affect incentives for developing new inventions.

Congress has considered legislation addressing concerns, such as patentable subject matter and process patent protection. Other problems, particularly scope of patent protection and infringement, will be litigated in the courts as stakeholders in new biological technologies attempt to assert their property rights.

International forums, such as World Intellectual Property organization, General Agreement on Tariffs and Trade, and bilateral and multilateral trade negotiations, can serve as arenas for discussions relating to harmonization of intellectual property issues.

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