Patenting Life: Issues and Controversies

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(Prepared for the Washington State Bar Association Animal Law Section Newletter, Vol. 1, No. 3, Fall 2003)

Introduction

Recombinant DNA technology makes it possible to selectively modify the genetic material of higher organisms. Genes can be transferred between different species of organisms and between organisms that are not even closely related, for example, bacteria and mice. Existing genes can be cut and spliced to form new gene combinations with new and improved functions.

By comparison with selective breeding methods, the ability to combine genetic material from different organisms by recombinant DNA technology provides a more rapid and reliable way to produce organisms with desired traits. The "transgenic" animals[1] that are produced are used in medical research, in pharming[2] and as farm animals with improved nutritional value, reproductive efficiency, growth rate and disease resistance. Transgenic technology can also potentially be used to preserve animal species.

The ability to produce and patent transgenic animals has led many to question whether the creation and patenting of inventions that are alive should be permitted.

This article focuses on the history of patenting higher organisms, and some of the resulting issues and controversies.

Patents

Patents are property rights that reward innovation and promote the disclosure of inventions to the public. In return for this disclosure, the patent holder is given the right for a limited time period, to prevent others from making, using, selling, offering to sell or importing the patented invention, thereby affording protection from exploitation by free-riding competitors. This time-limited monopoly provides incentives to investors to assume the financial risks of supporting research and development of new products and processes, and gives them the opportunity to collect royalties on the invention through licensing.

Patent rights are exclusionary rights of the patent holder against all others. The patent holder and his licensees may themselves be unable to freely use the patented invention, however, either because of existing regulations or because of conflicting rights of other patent holders.

Patent laws are national and territorial in scope. Patents may only be enforced in countries and territories where the patents are in effect.

In order to qualify for patent protection, an invention must meet statutory requirements for patentability. While differences exist, most of the developed countries have patentability requirements that are similar to those in the U.S. An invention must fit

[1] "Transgenic" animals are animals whose DNA or hereditary material has been modified by genetic material that has been transferred from a different animal or a human, and has been incorporated into the animal's genome.

[2] "Pharming" refers to the production of pharmaceuticals and other valuable products that are not naturally produced by the animal. The production (and secretion) of human antibodies in the milk of a lactating mammal is an example.

into a patentable subject matter category[3], and must be novel[4], non-obvious[5], and useful[6]. The applicant must provide a written description of the invention in clear and complete terms, giving the best mode of the invention known to the inventor. The applicant must also describe how to make and use the invention, and provide claims that inform the public of what the invention includes.

Intellectual property has become a commodity in global trade, and there are ongoing efforts towards international harmonization of intellectual property regimes. Patent law and patent enforcement varies from country to country, and countries differ in their views about what should and should not be patented. In attempting to reconcile these differences, multilateral agreements such as NAFTA and TRIPs[7] allow contracting states to exclude certain inventions from patentability that are contrary to *ordre public* or morality[8]. Under these agreements, contracting states are allowed to exclude from patentability plants and animals other than microorganisms, and biological processes for producing these plants and animals.

A short history of patenting life

Patenting life forms is not a recent phenomenon. Lewis Pasteur was awarded a U.S. patent in 1873 for an isolated yeast preparation that was germ-free and could be used in fermentation processes. The first legislative act to explicitly provide patent protection for living organisms was the Plant Patent Act of 1930 (35 USC §§161-164). Patent protection was limited to new and distinct varieties of plants that could be reproduced asexually. The requirements for patenting a new variety were not as rigorous as those for regular "utility" patents, and the scope of protection was limited to the whole plant, not its parts. At the time, however, plants were ineligible for regular patent protection and this Act provided at least some level of protection and incentive for breeders to develop new plant varieties.[9]

The Plant Variety Protection Act of 1970 (7 USC §§ 2321-2582) provided intellectual property rights to breeders of novel varieties of sexually reproduced plants. The exclusive rights granted for plant varieties do not include research uses, or a farmer's right to save and use seed of protected varieties for growing crops.

The development of recombinant DNA technology in the 1970s made it possible to cut and splice genetic material from any organism to create new genes which could then be transferred into different organisms. This technology, with its far-reaching consequences, forced the courts to interpret the broad language of the Patent Act to determine whether new and improved life forms could be patented. The issue was

[3] The Patent Act specifies in broad terms what is meant by "patentable subject matter", namely, "any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof".
[4] i.e., not previously known or used publicly
[5] i.e., non-obvious to those skilled in the technology; a technical advance
[6] i.e., be of practical use
[7] North American Free Trade Agreement Between the Government of Canada, the government of the United Mexican States and the Government of the United States of America (1992); Agreement on Trade-Related Aspects of Intellectual Property Rights (1994)
[8] e.g., inventions that may adversely affect public health and safety, the environment, and animal welfare.
[9] Plants and plant parts first became eligible subject matter for utility patents in 1985 (Ex parte Hibberd, 227 USPQ 473 (PTO Board of Patent Appeals and Interferences, 1985).

presented in Diamond v. Chakrabarty, which is described below. The prior caselaw had made it clear that in order to be patentable, an invention must be a non-naturally occurring product of human ingenuity, rather than an undiscovered natural phenomenon, law of nature, or abstract idea. [10]

The Chakrabarty case involved an application for a patent on a bacterial organism that was genetically modified to degrade multiple ingredients in crude oil. This property was not possessed by any bacterium found in nature, and could be used for cleaning up oil spills. The patent application claimed a method of producing the modified bacterial organism, an inoculum comprising a carrier material containing the bacteria, and the bacterial organism itself. Claims to the process of making the bacteria and the inoculum were allowed, but the claim to the organism was denied on the grounds that bacteria were products of nature, and living things could not be patented. Several appeals were brought, and the case was finally heard by the U.S. Supreme Court. In a 5-4 decision, the Court held that Congress intended the statutory definition of patentable subject matter to be broadly interpreted to include organisms that were made with human intervention, whether living or not. In essence, "anything under the sun that is made by man" was potentially patentable[11]. Amicus briefs that were filed with the Court warned of potentially hazardous effects of genetically engineered organisms on the environment, and ethical issues that would be raised if patenting of living organisms was allowed, but the Court declined to consider these arguments. The Court believed that the grant or denial of patents on microorganisms was not likely to put an end to genetic research or its attendant risks.[12] Furthermore, the Court believed that its role was to interpret the language of the statute, not to make political judgments about competing values and interests. It was up to Congress to amend the Patent Act to exclude genetically engineered organisms from patent protection, or to enact new legislation that would specifically apply to living organisms.

The Chakrabarty decision, bolstered by Federal policy relating to technology transfer of federally-funded research, promoted increased patenting in all technology areas, and provided the incentives that were necessary to finance the growth of the U.S. biotechnology industry. The timing of Federal policy-making in relation to advances in biotechnology is shown in the Table which is appended to this article.

According to statistics compiled by BIO, the Biotechnology Industry Organization[13], more than 370 biotech drug products and vaccines targeting more than 200 diseases are in clinical trials. As of 2001, there were 1457 biotechnology companies in the US. These companies spent in the aggregate more than 15.7 billion dollars per year, had sales amounting to 20.7 billion dollars, and revenues of 28.5 billion dollars. The number of U.S. patents granted annually for biotechnology inventions grew from approximately 1000 in 1983 to almost 8000 in 2003, and these numbers do not include

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[10] Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980)

[11] 447 U.S. at 309, citing Congressional hearings at the time of the 1952 recodification of the patent laws.

[12] As the Court stated: "The large amount of research that has already occurred when no researcher had sure knowledge that patent protection would be available suggests that legislative or judicial fiat as to patentability will not deter the scientific mind from probing into the unknown any more than Canute could command the tides. Whether respondent's claims are patentable may determine whether research efforts are ccelerated by the hope of reward or slowed by want of incentives, but that is all."

[13] These statistics and other information can be found on the BIO website at www.bio.org

patents that were granted by other countries. The growth of U.S. patents on biotechnology inventions is shown below in Figure 1.

Patenting Multicellular Organisms

Seven years after the Chakrabarty decision, the U.S. Patent and Trademark Office (PTO) announced that claims to non-naturally occurring nonhuman multicellular plants and animals would no longer be rejected as unpatentable subject matter [14].

In 1984, Harvard University had filed a U.S. patent application for a transgenic nonhuman mammal, specifically, a mouse that was genetically altered to increase its susceptibility to cancer by incorporating a cancer-promoting "oncogene" into each of its cells. The mouse could be used for carcinogenicity testing and for testing new drugs for the prevention and treatment of cancer. The Harvard "Oncomouse" patent, U.S. Patent No. 4,736,866, issued in 1988 with broad claims to a transgenic nonhuman mammal containing a recombinant activated oncogene sequence that was introduced into the mammal, or an ancestor of the mammal, at an embryonic stage.

The "Oncomouse" application was also filed in Australia, Japan, Europe and Canada. The application was initially rejected in Europe on the basis of patent law provisions in the European Patent Convention (EPC).[15] The rejection was overturned on appeal, and the European Patent Office (EPO) granted the patent in 1992 with claims to transgenic mice. This outcome was particularly significant because European patent law contains an exclusion from patentability of inventions that are contrary to *ordre public* or morality, and the EPO could have invoked this exclusion if it wished. Instead, the EPO balanced the public's interest in alleviating "widespread and dangerous diseases", against the potential for releasing unwanted undesirable genes into the environment and the potential for increased suffering of animals, and concluded that the benefits to mankind justified granting the patent. In its decision, the EPO stated its view that appropriate legislation could be enacted by the legislature if it wished to restrict the uses of patented inventions. Several years later, the European Parliament issued a Directive on Biotechnological Inventions[16]. The Directive explicitly excluded certain inventions from patentability as contrary to *ordre public* or morality, such as processes for cloning humans, processes for modifying genetic information in the human germ line[17], uses of human embryos for industrial or commercial purposes, and processes for modifying the genetic identity of animals which are likely to cause them suffering without substantial medical benefit to man or animal. The human body and human germ cells were also excluded from patenting.

The Directive also explicitly provided for patenting of certain biotechnological inventions that had previously been excluded under the EPC, such as plants and animals

[14] Claims to a multicellular organism must include the term "nonhuman". The grant of a limited but exclusive property right in a human being is considered as slavery, which is prohibited by the 13th Amendment to the U.S. Constitution.

[15] Article 53(b) of the European Patent Convention excludes plant or animal varieties or biological processes for the production of plants or animals , except for microbiological processes or their products. In addition, the Examiner believed that the application lacked support for claims to transgenic mammals other than mice.

[16] Directive 98/44/EC of the European Parliament and the Council of 6 July 1995 on the legal protection of biotechnological invention. The Directive was adopted by the EPO on September 1, 1999.

[17] For example, by inserting genes into a fertilized egg or an early embryonic cell.

other than particular plant or animal varieties, and processes for their production; and sequences or partial sequences of a gene or element of the human body isolated from or produced by a technical process, if the gene or element had industrial applicability.

At the present time, the patenting of higher life forms is allowed in the U.S., Japan, Australia, New Zealand and Europe. The "Oncomouse" has been patented in many countries. The sole exception is Canada. In December of 2002, the Supreme Court of Canada decided that the definition of "invention" under the Canadian Patent Act excludes the patenting of mammals[18]. The decision leaves open the possibility that other multicellular organisms, such as plants and invertebrates, may be patentable. Single cell organisms and cell cultures are patentable, as are claims to modified genes, vectors for transferring genes into cells, cells containing the genes, methods of modifying genes, methods of using genes, cells and life forms, and methods of using cultured cells (including mammalian cells).

It should be pointed out that many of the objections that were made against granting the Oncomouse patent in Canada had little to do with patent policy issues. Some of these objections were directed to animal welfare and animal rights. In particular, opponents of patenting argued that: patents on transgenic animals would lead to the unregulated treatment and uses of animals; the transfer of genes between unrelated species would produce unpredictable results and increase animal suffering; the production and cloning of transgenic animals would reduce the genetic diversity of animal species; genetically-modified animals might escape into the environment with potentially disastrous consequences; and the categorization of animals as "compositions of matter" or "articles of manufacture" for patent purposes would encourage their commoditization and discourage their humane treatment.

Summary and Perspectives

The legal issue of whether higher life forms are patentable has been decided in most patent jurisdictions. With the exception of Canada, most countries agree that there is no reason why genetically modified plants and animals should be treated differently from other inventions that qualify as patentable subject matter. Nevertheless, the debate about the economic, environmental and ethical consequences of patenting living organisms is likely to continue. Clearly, there is a need for a balancing of interests on both sides of this debate in a way that will benefit society as a whole. Creative legislative solutions will be needed to address the issues that arise from future advances in biotechnology. The patent system is ill-equipped to deal with these issues and was never intended to be used for this purpose.

It is generally believed that patents are an important catalyst for biotechnology research and product development. Biotechnology uses living organisms or parts of organisms to create products and processes that are useful to society. The contributions of biotechnology are already visible in agriculture, food technology, law enforcement and medicine. Ultimately, the marketplace will decide which types of biotechnology inventions are commercially valuable, and which are not.

[18] Commissioner of Patents v. President and Fellows of Harvard College, 2002 SCC 76. File No.: 28155

Figure 1

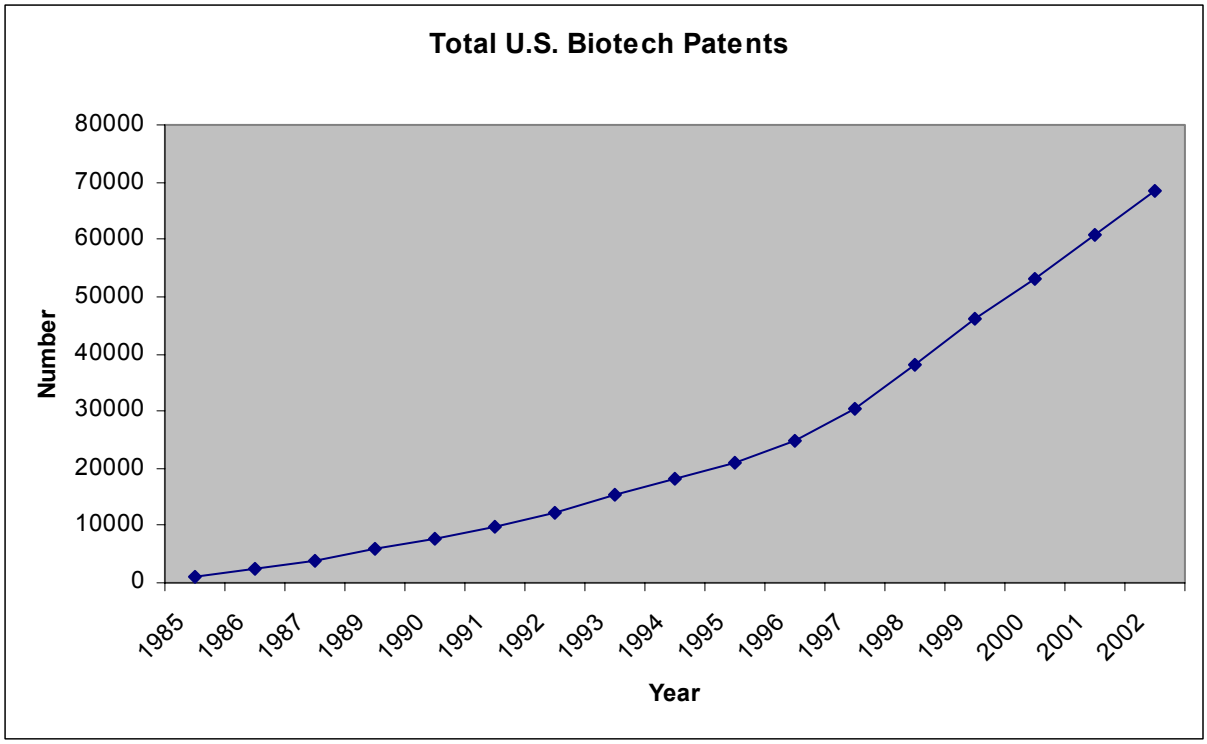
Total U.S. Biotech Patents
Number
80000
70000
60000
50000
40000
30000
20000
10000
0
1985
1986
1987
1989
1990
1991
1992
1993
1994
1995
1996
1997
1998
1999
2000
2001
2002
Year

Table 1

	FEDERAL POLICY	BIOTECHNOLOGY
1873		Louis Pasteur obtains patent on yeast
1928		Discovery of transformation in bacteria (Griffith)
1930	Plant Patent Act	
1944		DNA is the transforming factor (Avery et al.)
1946		Genetic recombination produced in viruses
1947		Discovery of "jumping genes" in corn (McClintock)
1953		DNA is a double helix (Watson and Crick)
1956		DNA polymerase (Kornberg)
1960		DNA-RNA hybridization; discovery of messenger RNA
1966		Discovery of genetic code
1970	Plant Variety Protection Act	Discovery of restriction enzymes for cutting and splicing genes
1975	Asilomar Conference on recombinant DNA guidelines	Monoclonal antibodies
1977		Human gene is expressed in bacteria
1978		recombinant human insulin
1980	Bayh-Dole Act - promotes use of federally funded inventions by small businesses and nonprofits	Cohen-Boyer patent on recombinant DNA technology (gene splicing); Genentech goes public
1980	Stevenson-Wydler Technology Innovation Act-promotes cooperative research between government and industry(CRADAS)	First Nobel Prize for recombinant DNA
1981		Production of transgenic mice
1983 1983	Federal Guidelines for Recombinant DNA	Invention of PCR method
1983	US Govt Principles for the Care and Use of Vertebrate Animals in Research (50 FR 20864)	Genetic transformation of plants; artificial chromosomes; plants regenerated from single cells, and others
	Health Research Extension Act recognizes PHS Policy on Human Care and Use of Laboratory Animals	
1985	Plants are patentable subject matter	
1985	NIH Guidelines for human gene-therapy	

1986	**Public Health Service Policy on Humane Care and Use of Laboratory Animals (regulates use of vertebrate animals by most Federal agencies)**	**recombinant hepatitis B vaccine; recombinant interferon**
1986	**Federal Technology Transfer Act-rewards inventor employees of federal agencies**	
1987	**Executive Order extends Bayh-Dole provisions to large businesses**	
1987	**Multicellular animals are patentable subject matter**	
1987	**Senate moratorium on animal patents is adopted, then dropped.** **House resolution to prohibit patents on genetically modified animals is introduced, then dropped.**	
1988	**Senate bill to prohibit patents on genetically modified animals is introduced, then dropped.**	
1988	**Oncomouse patent issues**	
1988	**House passes Transgenic Animal Patent Reform Act.**	
1990		**Human Genome Project begins; transgenic dairy cow; Bt corn;**
1992	**American Technology Preeminence Act of 1991-commission to analyze and improve federal policies on technology development.**	
1995	**National Technology Transfer and Advancement Act of 1995-IP rights under CRADAS**	
1997		**Dolly, is cloned; rhesus monkeys cloned.**
1998		**mice cloned; calves cloned.**
2000-present		**The human genome, plant genomes, and genomes of several other organisms are mapped.**