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MEDICAL PATENTS IN THE UNITED STATES

by
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INTRODUCTION

This paper covers five topics of current and unique interest in the prosecution and litigation of medical patents in the United States.

Two of these topics are (i) the experimental use infringement exception and (ii) patent term restoration. These two topics are interrelated, as they were both treated in the Drug Price Competition and Patent Term Restoration Act of 1984. The Act addressed two issues which distorted the standard 17 year patent term in the U.S. These issues related to the need for obtaining permanent regulatory approval for medical products. The other three topics covered are (iii) protection of medical procedures, (iv) claiming of manufactured products of naturally occurring substances, and (v) protection of process patents.

At the outset it should be noted that the medical industry is a very big business in the United States. As reported in the August, 1990

issue of "Biotech Patent News," in 1989 the United States was the origin of 83% of all genetic engineering pharmaceutical or health care-related patents. [insert information on Wednesday from 202-835-3539. Faith Horbat.]

1. EXPERIMENTAL USE INFRINGEMENT EXCEPTION

1. REGULATORY APPROVAL AND THE STATUTE

A first purpose of the Drug Price Competition and Patent Term Restoration Act was to help generic drug manufacturers place their substitutes for patented, brand-name drugs on the market as soon as the patents expire. The law permits generic drug firms to develop and submit information to the Federal Food and Drug Administration ("FDA") and apply to the FDA for approval of their substitutes prior to expiration of the patents. The purpose of the statute was to allow generic drug manufacturers a limited amount of testing so they could establish the bio-equivalency of a generic substitute.

So long as the activity of the generic drug company relates to an application to the FDA, the company's activity is regarded as non-infringing. The company is thus allowed to "make, use or sell a patented invention" prior to the expiration of the patent.

Without this exception the generic drug company had to wait until after expiration of the patent to begin its FDA approval process. This had previously meant in reality that the original patentee had a de facto extension of the 17 year patent term. This law, therefore, was intended to limit that de facto extended period of patent protection for drug companies.

Section 202 of the Act as set out in 35 U.S.C. §271(e), creates a patent infringement exception to the standard for patent infringement contained in 35 U.S.C. § 271(a). Section 271(e)(1) reads:

"It shall not be an act of infringement to make, use, or sell a patented invention ... solely for uses reasonably related to the development and submission of information under a Federal law which regulates the manufacture, use, or sale of drugs."

No injunctive or other relief can be granted.

2. EXPERIMENTAL USE EXCEPTION HISTORICALLY

While an experimental use exception to patent infringement was recognized as early as 1813, the Federal Circuit first considered the experimental use infringement exception in *Roche Products, Inc. v. Bolar Pharmaceutical Co.* In *Roche*, the defendant, a generic drug manufacturer, used a patented drug to conduct bioequivalency tests prior to the expiration of the patent. The data from the tests were to be used to obtain commercial marketing approval of the FDA as soon as possible after the patent expired. The Federal Circuit held that such use of the patented drug constituted infringement because defendant's "intended 'experimental' use is solely for business reasons, and not for amusement, to satisfy idle curiosity, or for strict philosophical inquiry..." The Federal Circuit held that the experimental use exception is "truly narrow". "Infringement is no trifle in its economic effect on the parties even if the quantity used is small. It is no dilettante affair such as Justice Story envisioned." The generic drug manufacturer was found liable for its investigational testing of a patented drug even though, under the Food, Drug and Cosmetic Act, such testing is required to obtain FDA approval to market such drugs.

The holding of *Roche v. Bolar* was overruled by § 271(e). The Congressional Report explicitly stated: "The provisions of Section [271(e)] have the net effect of reversing the holding of the court in *Roche*." The House Judiciary Committee report states that the only activity that will be permitted is "a limited amount of testing so that generic manufacturers can establish the bio- equivalency of a generic substitute." Thus, the type of information which can be developed under § 271(e)(1) is that required to obtain approval of a drug from the FDA. This type of experimentation with a patented drug product will not be a patent infringement.

Despite this legislative history, problems of statutory interpretation have arisen. The statute itself authorizes manufacture, use, or sale of a patented "invention solely for uses reasonably related to the development ... of drugs." Medical devices are not mentioned in the statute, nor are they mentioned in the legislative history. But the reasoning of Congress that no commercial harm occurs to the patentee from experimental use infringements is just as applicable to medical devices as to drugs. Nor is it clear what would be considered as "solely reasonably related" to obtaining regulatory approval. These two issues have been the subject of judicial decisions.

3. USES: SOLELY v. REASONABLY RELATED

Scripps Clinic and Research Foundation v. Genentech, Inc., interpreted §271(e)(1) narrowly. "Solely for uses

reasonably related to development and submission of information" to the FDA covered only the limited testing necessary to establish bioequivalency. The same court later reconsidered the § 271(e)(1) defense. Again it found the § 271(e)(1) exemption to be narrow.

A different court, the Delaware District Court, has however held that the court in *Scripps v. Genentech* interpreted § 271(e)(1) too narrowly. The "reasonably related" language of the statute should control rather than the "solely" language. Thus, there is a split of interpretation in the lower courts regarding this aspect of the statute. This needs to be resolved by the Federal Circuit. Other cases have ruled that where the products are being developed for commercial purposes there is no exception.

6. MEDICAL DEVICES

Does § 271(e) apply to medical devices as well as drugs? Medical devices are not mentioned in either the statute or the legislative history. Nevertheless, the Supreme Court in *Eli Lilly & Co. v. Medtronic, Inc.* held that § 271(e)(1) does apply to medical devices as well as drugs.

Medtronic developed and tested a cardiac pacemaker (medical device) intended to treat cardiac disturbances painlessly with low-energy electrical impulses: Lilly had a patent on a similar device. Medtronic claimed its testing was for the purpose of submitting the information required to obtain FDA approval. The District Court entered a judgment against Medtronics holding that the clear wording of the statute was meant to apply only to drugs and not to medical devices.

The Federal Circuit reversed, holding that Medtronic could proceed with its FDA testing before Lilly's patents had expired. The Federal Circuit held that § 271(e)(1) applied to any type of patented invention if its use is solely for the restricted uses authorized by the statute. The Federal Circuit looked to Congressional intent in overturning *Roche v. Bolar* "in all of its ramifications". Medical devices as well as drugs fall within the ambit of § 271(e)(1).

The Supreme Court upheld the Federal Circuit's holding in June, 1990. Taken as a whole, the statute applies to medical devices as well as drugs. The Court stated that the 1984 Act was intended to remedy two unintended distortions of the 17 year patent term produced by the requirement that certain products must receive premarket regulatory approval:

1. The first distortion to the patent term occurred because the holder of a patent will ordinarily apply for a patent at once. Given the need for FDA approval (which can take many years), the "clock" on certain types of patents (e.g. for drugs) will be running even though the patentee is not yet able to derive any benefit from his invention. The Patent Term Restoration Act was enacted to respond to this inequity. (Patent Term Restoration is discussed later).
2. The second distortion occurred at the end of the patent term. After *Roche v. Bolar*, the manufacture, use or sale of a patented invention could not be commenced by anyone planning to compete with the patentee until after the expiration of the entire patent term. This gave the patentee a de facto monopoly for an often substantially longer period of time than his 17 year patent. There could be no competition until the competitor obtained regulatory approval. The experimental use infringement exception was enacted to address this second inequity. This is the type of distortion with which *Lilly v. Medtronics* was concerned.

The Supreme Court noted that while the experimental use exception does not anywhere mention medical devices, the patent term restoration section does specifically mention such devices. The better statutory construction was to hold that Congress intended that both sections of the Act would apply to medical devices as well as drugs.

7. THE FUTURE Now that we know medical devices fall into the exception, the focus in the future is likely to turn back to the nature of the use. Namely, is it "solely" or "reasonably" related to FDA approval? The purpose for which the "infringer" puts the use could limit the effectiveness of the exception. If the courts ultimately interpret the exception in line with "solely", it is likely to become a very narrow exception to infringement. For instance, use of the data in promotional activities, in association with consultants, in delivery of scientific papers may all still be restricted. Such use would be an infringement as not being "solely" concerned with the FDA.

Conceptually, however, the experimental use infringement exception is a very broad exception. The FDA regulations require the approval and/or testing of products beyond strictly the medical field, for instance, food additives and color additives. Other federal laws govern food, infant formula, cosmetics, pesticides and vitamins. While new infant formula requires approval thus probably triggering the exception, the federal law does not require approval for other products but only sets standards. Accordingly, the exception probably does not apply to such products.

In the medical device field it is possible during pre- approval testing to sell the experimental device. Accordingly an

"infringer" can obtain financial reward during the 17 year patent term of the patent. Since each medical device can be expensive and since there may be only a limited market this pre-expiration use by the "infringer" can effectively permanently negate or distort the market for the patentee. On the other hand, many medical devices may be subject to relatively quick FDA approval, and hence the need to risk pre-expiring patent infringement may not be worthwhile. Some products would include devices such as catheters, needles, stents. The impact of § 271(e) therefore may still be only really felt for pharmaceutical products, and especially for generic drug producers. Also invasive or internal medical devices of a relatively expensive nature, such as prosthetic devices, valves, pacemakers, intraocular lenses should still be effected by this statute.

A broad interpretation of § 271(e)(1) has been favored by some commentators. This would facilitate modern biotechnology and other high technology research. The policy of the patent system, as stated in the U.S. Constitution, is to "promote the progress of... the useful arts". Scientific progress requires access to the improvements of others. Preventing the research use of inventions disclosed in a patent would frustrate this public policy and hamper scientific research. Experimental use should be widely permitted so that competitors can develop improvements without concern for a patent during the research experimental and development phase of a product. Currently, while the U.S. law is restrictive, other countries apparently already provide this breadth of infringement protection.

2. PATENT TERM RESTORATION.

As discussed above, 35 U.S.C. § 156 provides for a patent term extension for a period of time related to the regulatory review period. An extension for up to 5 years can be obtained for a patented product to compensate for the regulatory review period by the FDA. This effectively extends the life of a patent by the amount of time needed to obtain FDA approval. The patentee is thus able to reap financial rewards from an invention for patent term equal to, or approaching, the full 17 year term.

1. **EXTENDIBLE TIME PERIOD** Patents can be extended up to 5 years if the product was "subject to a regulatory review period before its commercial marketing or use." The extension granted to the patent term is related to the amount of time required for the regulatory review. It is limited to only such amount of that time which occurs after the patent is issued.

If the remaining term of the patent is greater than 14 years after regulatory approval for market, no extension shall be granted. If the remaining term is less than 14 years, the remaining patent term and the extension combined cannot exceed 14 years beyond the date of premarket approval.

2. **DILIGENCE**

The patent term extension may be reduced by half if the applicant does not exercise due diligence during the regulatory review period. The term "due diligence" is defined as "that degree of attention, continuous directed effort, and timeliness as may reasonably be expected from, and are ordinarily exercised by, a person during a regulatory review period."

A patent may be extended under § 156 only if the term of the patent has not expired before application is made of the extension, and the patent has never before been extended.

The regulatory review period must be for the "first permitted commercial marketing or use of the product". Accordingly, novel uses of drug products already approved are not covered. In no event shall more than one patent be extended for the same regulatory review period for any product. Also the term "drug product" has been held to be clearly defined.

3. **PRODUCTS**

The statute applies to all food, drug and medical products regulated by the FDA. Products eligible for patent term restoration are defined to include "human drug products". This means "the active ingredient of a new drug, antibiotic drug, or human biological product... including any salt or ester of the active ingredient..." "Any medical device, food additive, or color additive subject to regulation under the Federal Food, Drug, and Cosmetic Act" is also included.

4. **PROCEDURE**

To obtain an extension of the term, the owner of the patent or his agent must submit an application to the Commissioner of Patents. The application must be submitted within the 60 day period immediately following regulatory approval to market the product. It must contain the following:

1. the identity of the approved product and the Federal statute under which regulatory review occurred,
2. the identity of the patent for which an extension is being sought and the identity of each claim of the patent which claims the approved product, use or method,
3. information to enable the Commissioner to make a determination such as the dates of the regulatory review period and date of patent grant.
4. a brief description of the activities undertaken by the applicant during the review period and the dates associated with those activities to determine due diligence. This is brief summary of the most significant aspects of the statute. The statute itself is highly complex and hyper- technical.

3. PROTECTING MEDICAL PROCEDURES.

In the United States, unlike most other countries, patentable subject matter includes medical procedures. By contrast, methods of treatment of the human or animal body by surgery or therapy are expressly excluded from patentability under the EPC.

In fact, only relatively few patents solely directed to a procedure have been sought and granted. The subject is nonetheless discussed because it is at the frontier of the law. It also highlights a different unique perspective of patents in the medical field in the U.S. and gives some insight into the U.S. outlook on patents in medicine.

Patenting of medical procedures involves special problems, not the least of which are ethical dilemmas. First, it is often difficult to specify clearly what a procedure consists of, or determine if it is a new procedure or a mere variation on an existing procedure. Secondly, patenting of medical procedures may interfere with the training of new physicians and patient care, by requiring physicians to seek formal permission or pay royalties when they perform patented procedures. This would create an incentive to use an unpatented procedure rather than a patented one, even if the patented procedure is better for patient care. Further, enforcement of such patents on a wide scale is not feasible from a practical standpoint, and also would likely add to patient costs.

Medical procedure patents that have been obtained are seemingly for procedures that are rarely used, e.g. a method for direct electrical injection of gold ions into bone. A surgical method of fixation of artificial eye lenses has also been patented, when no claim could be obtained for the eye lense itself. Patenting medical processes usually involves procedures on the fringes of surgery, often in connection with specific instruments. Claims for medical treatment are commonly added as one form of claim in an application where there are also claims to apparatus, products, compositions, and methods of composition preparation. A manufacturer or merchant could be sued for contributory infringement or inducement to infringe method of treatment claims. So such claiming technique is not academic.

Arguments for allowing such patents include the ability to attract private investment to finance medical research into new medical procedures if they have a chance to profit from their investment via patenting and licensing. It has also been suggested that control over the procedure is retained so the public is protected from quacks.

Arguments against allowing such patents include the potential conflict of interest regarding physicians reporting their research in an unbiased manner; unlike drugs and devices which require FDA approval, no independent agency has authority to approve, and patenting could restrict independent evaluation by others.

A few years ago a substantial debate was generated in the U.S. on the attempts to patent surrogate embryo transfer. Public policy tilted against allowing patentability of this type of process. It was said that "the government should not be involved in controlling or supervising, directly through police powers, or indirectly through patenting powers, the process of human reproduction. The subject matter does not lend itself to patent infringement enforcement without potentially unbearable privacy violations."

When the plan to patent the medical procedure of embryo transplants was discussed it drew fire from people worrying that monopoly pricing of a medical benefit could price important new discoveries out of the reach of many people. However, it was also stated that if the patent issued, "private capital could find its way into all kinds of medical research if investors can look to high returns from patentable procedure." A legal dispute still exists regarding these patent rights. In response to the complaint that the procedure will not be evaluated by independent experts (like the FDA), the doctor developing the procedure stated that the profit motive provided ample incentive for inventors of procedures to make sure the procedure is effective and safe. Also, if the patent was granted, the information on the procedure would be made available to the public.

There are few U.S. judicial decisions on the patentability of medical procedures. However, one recent interesting case deals with property rights of a patient. It highlights some of the tensions and conflicting issues in the medical field where patentable property rights exist. This case did not deal with the patentability of a medical procedure or a product. Portions of a patient's removed spleen and samples of blood were used to establish a cell line containing T lymphocytes which were

unique in relation to leukemia. A patent on the cell line was obtained, and the doctor negotiated agreements for commercial development of the cell line.

The California Supreme Court found that the doctor had breached a fiduciary duty of not disclosing acts material to the patient's consent or, alternatively, of performing medical procedures without first having obtained the patient's informed consent. While "no law prohibits a physician from conducting research", a physician treating a patient in whom he has a research interest has potentially conflicting loyalties; a physician might, consciously or unconsciously, take a preexisting research interest into account when making procedural recommendations to a patient. Therefore, a physician seeking a patient's consent to a medical procedure has a "fiduciary duty" to obtain the patient's informed consent and to disclose all personal interests. Defendants' unauthorized use of the patient's cells did however, not constitute a conversion. For public policy reasons, conversion liability should not be extended to cover such unauthorized use. The court said that extending such liability to research scientists would be to "impose a tort duty on scientists to investigate the consensual pedigree of each human cell sample used in research" and that such a duty would hinder medical research which is of importance to all of society. There is thus a recognized need for scientists to be able to conduct research free of obligations to a patient. However, there is a duty to inform the patient that there could be a research interest. Accordingly, the law tilts in favor of the science, the patentable property right and against an interfering claim by the patient. As things stand, medical procedures and methods of treatment of the human are patentable subject matter in the U.S.

4. CLAIMING MANUFACTURED PRODUCTS OF NATURALLY OCCURRING SUBSTANCES.

Many of the products which are produced by biotechnology, such as recombinant DNA technology, are products which occur naturally. Obtaining patent protection for such products which exist in nature is difficult because the products may not be novel. Thus the invention does not meet the novelty requirements for patentability.

1. SYNTHETIC PRODUCTS

A manufactured product which differs from one that is naturally occurring only because it is artificially made is not novel and thus is not patentable. However, the process by which it is manufactured may be patentable because it is novel and unobvious. The U.S. Supreme Court spoke on the issue over a century ago:

"Every patent for a product or composition of matter must identify it so that it can be recognized aside from the description of the process for making it, or else nothing can be held to infringe the patent which is not made by that process...While a new process for producing it was patentable, the product itself could not be patented even though it was a product made artificially for the first time in contradiction to being eliminated from the madder root. Calling it artificial did not make it a new composition of matter and patentable as such."

Another case addressing whether a synthetic product is patentable is Funk Bros. Co. v. Kalo Co.. The claimed invention was directed to a naturally occurring strain of bacteria which enable different species of leguminous plants like clover and alfalfa to take nitrogen from the air and fix it to the roots of the plants. No species of bacteria acquired a different use. The Supreme Court held that:

"The qualities of bacteria, like the heat of the sun, electricity, or the qualities of metals, are part of the storehouse of knowledge of all men. They are manifestations of laws of nature, free to all men and reserved exclusively to none. He who discovers a hitherto unknown phenomenon of nature has no claim to a monopoly of it which the law recognizes. If there is to be invention from such a discovery, it must come from the application of the law of nature to a new and useful end. (emphasis added)"

A different result is achieved in the case of genetically altered bacteria where the end product is a bacterium that possesses properties unknown to any other living organism. The bacterium itself would be patentable because it is unique and novel. However, any product produced by the metabolic activity of the bacterium would only be patentable if it too were unique, novel and unobvious. The case establishing the patentability of a human-made, genetically engineered bacterium is Diamond v. Chakrabarty. In 1972, Chakrabarty, a microbiologist working for General Electric, asserted claims for the invention of a bacterium that was capable of breaking down multiple components of crude oil. This property was not possessed by any bacterium known to exist in nature. The significant value of the invention was in the treatment of crude oil spills. This case was distinguished from Funk Bros. because "the patentee produced a new bacterium with markedly different characteristics from any found in nature".

2. PURITY LIMITATIONS

Is a replica of a naturally occurring substance which is of higher purity patentable? This was addressed by the Court of Customs and Patent Appeals in *In re Merz*.

"While appellant may be entitled to a patent on a method for purifying an ultramarine either artificial or natural, he is not entitled to a patent on the article which after being produced has a greater degree of purity than the product produced by former methods. This general rule is a well-settled one, but like all other rules it has an exception. The exception is that if the process produces an article of such purity that it differs not only in degree but in kind it may be patentable."

The exception to the rule was addressed in *Merck & Co. v. Olin Mathieson Chemical Corp.*. The court held that the product claims to a bacterially produced vitamin B12 protein, although known in nature, were patentable because the claims recited a specific purity limitation. The claim stated:

"A vitamin B12 active composition comprising recovered elaboration products of the fermentation of a vitamin B12 activity producing strain of Fungi selected from the class consisting of Schizomycetes, Torula, and Eremothecium, the L.L.D. activity of said composition being at least 440 L.L.D. units per milligram and less than 11 million L.L.D. units per milligram." One decision which is often cited is *In re Bergstrom*.

In *Bergstrom*, claims related to the prostaglandins PGE and PGF, natural substances extracted from sources such as the human prostate gland. The Court held that the pure prostaglandin substance is not naturally occurring and that the applicant had not merely claimed that which had previously existed in nature, albeit was unknown. "Whether the claimed pure materials are novel as compared with the less pure materials of the reference," the Court stated:

"...pure materials necessarily differ from less pure or impure materials and, if the latter are the only ones existing and available as a standard of reference, as seems to be situation here, the "pure" materials are "new" with respect to them."

Similarly, in *In re Bergy*, the C.C.P.A. held that a biologically pure culture of the *Streptomyces* microorganism was not a "product of nature". It was therefore patentable over the microorganism as it existed in nature.

4. RECOMBINANT PRODUCTS

1. Claims to a Purified and Isolated Product

While the U.S. Patent Office often rejects claims for a recombinantly produced product which exists in a natural form, it has become common practice to distinguish the recombinant product from the natural product by stipulating that the new recombinant product exists in a "purified or isolated" form.

Claims to recombinantly produced proteins or DNA sequences have been allowed relying on the levels of purity as the distinguishing feature of the claim. In U.S. Patent Number 4,703,008, the Amgen EPO patent, there is a claim to:

A purified and isolated DNA sequence consisting essentially of a DNA sequence encoding human erythropoietin.

Rejections based on the DNA sequence being a "product of nature" were overcome by the addition of the words "purified and isolated" to the claim.

A Court has stated that this claim was not to the DNA sequence encoding human EPO because that is a "nonpatentable naturally occurring phenomenon 'free to all men and reserved exclusively to no-one'" It was the "purified and isolated" DNA sequence encoding EPO.

Also, in *Scripps v. Genentech*, it was stated:

"There is no dispute over the patentability of a Factor VIII:C preparation. Although Factor VIII:C molecules occur in nature, a purified and concentrated preparation of Factor VIII:C as claimed in the patent constitutes a new form or combination not existing in nature, and hence is patentable under 35 U.S.C. 101.

2. Claims to a Recombinant Product

In *Ex Parte Gray* the Patent Board of Appeals rejected a claim to recombinantly produced nerve growth factor identified by the particular amino acid sequence and being free from other proteins of human origin. The prior art disclosed the material isolated from human placental tissue. The difference between the claimed material and the prior art was primarily that the claimed material was produced by recombinant technology. The Board, however, stated that the applicant needed to establish unexpected properties for the claimed recombinant product over the prior art. The mere presence of a single methionyl moiety on the recombinant protein not present on the natural protein would not in itself render the claim patentable.

This is a new development in patents directed to recombinant products. This means that claims are not allowable merely to recombinantly produced products simply because they are produced by recombinant DNA techniques. Increased purity of biological activity or other property not found in the natural, known product or other properties will need to be shown to overcome an unobviousness rejection.

Thus, the current standard in the United States is that a recombinant product will be patentable if it is in a more highly purified or isolated form than the product can be found in nature. If the purified and isolated natural product is previously known, some other evidence of novelty and nonobviousness is required.

5. PROCESS PATENTS

1. Introduction

Several recent decisions have addressed firstly, the patentability of processes and secondly, the ability to enforce process patents. These two legal issues have clashed recently so that it is now difficult in the U.S. to obtain effective process patent protection for technology not only in the chemical field but also in the biotechnology and medical fields. The issues first discussed are patentability of processes and two recent cases, namely *In re Durden* and *In re Pleuddemann*. Thereafter enforcement of process patents and the *Amgen v. United States International Trade Commission* decision is discussed.

2. Process Patent Claims

1. Durden

Durden concerned patentability of a process for making an insecticide. The end-product insecticide and the insecticide used for the starting material were patentable. However, the process used to make the new insecticide was considered unpatentable as being obvious. The process had been previously described except for the novel starting material and end product. The court held that the patentability of one of the starting reactants in the process did not mean that the process was patentable.

The court said the decision was narrow and refused to establish this holding as a general rule. The *Durden* decision has been severely criticized for lacking logic and consistency. The court stated

"[the] argument... that an otherwise old process with a predictable outcome is unobvious because it is applied to a new material, notwithstanding the new material is similar or analogous to materials identically manipulated or treated before... [makes] little sense."

But if the starting material is "similar or analogous" to materials identically manipulated or treated before, how could the starting material be patentable in and of itself? This decision, in effect, treats part of the patentee's own work as prior art against himself.

Durden-based rejections have proven particularly obstructive to applicants seeking to obtain patent protection for the process of producing a pure protein or other biological product from genetically engineered cells carrying the appropriate genetic information. The problem arises because once the genetic information for the product is obtained as DNA or RNA, the process for generating the product from such genetically engineered cells are frequently well known in the prior art. Under *Durden* the process would not be patentable. However, the genetically engineered cells producing the product can still be considered patentable. In some, but not all, cases, the genetically engineered protein can be sufficiently different from previously isolated or purified proteins that it can also be patented. *Durden* therefore puts an onerous burden in attempting to obtain process protection.

2. Pleuddemann

The August, 1990 decision of *Pleuddemann*, may, however, offer an alternative direction for obtaining process protection that would otherwise be unpatentable under *Durden*.

Pleuddemann's invention for a silane coupling agent to bind polyesters involved both (1) a process for bonding a polymerizable material to a mineral filler, and (2) a method for priming a surface to improve its bonding to certain organic resins. The *Pleuddemann* court held that these were new and unobvious procedures. They further stated:

"The shibboleth which appellant hopes will get the claims at bar into the golden realm of patentability, notwithstanding precedents cited by the PTO, is that they are "method of use" rather than

"method of making" claims... When a new and useful compound or group of compounds is invented or discovered having a particular use it is often the case that what is really a single invention may be viewed legally as having three or more different aspects permitting it to be claimed in different ways, for example: (1) the compounds themselves; (2) the method or process of making the compounds; and (3) the method or process of using the compounds for their intended purposes....The fact that the starting materials and the final product are the subject matter of allowed claims does not indicate that the process employed to make the compounds is patentable."

"We have concluded...that the process-of-use claims are patentable and that it is not necessary to show unexpected utility in order to show unobviousness. We would add, moreover, that in our view it is in the public interest to permit appellant to claim the process of use as well as the product. The result is to encourage a more detailed disclosure of the specific methods of using the novel composition he had invented in order to have support for the process claims. Given this holding, it is not clear whether process inventions now have a way around Durden. Pleuddemann itself, by its terms, is limited to claims directed to a process of using an independently patentable product. However, it suggests that if claims can be obtained to a bacterial cell containing recombinant DNA specific for a particular protein or a hybridoma producing a monoclonal antibody, claims directed to the use of the bacterial cell or hybridoma to produce the protein or monoclonal antibody are patentable. Such process of use claims might nevertheless be subject to rejection under the old doctrine that processes that are only the mere function of a machine are not patentable. The validity of these line of cases, which does not appear to have been followed in recent years, is in some doubt.

3. Practice Note: Claim Practice and Specification Content In the genetic engineering field, a claim drafting technique to be considered is, for instance, the following:

A method of using a purified and isolated RNA/DNA sequence for producing a protein comprising the steps of:

1. incorporating the purified and isolated RNA/DNA sequence into a vector capable of transplanting a bacterial cell;
2. transplanting the bacterial cell with the vector to produce a transfected bacterial cell capable of expressing the protein in recoverable quantities;
3. using the transfected bacterial cell to express the protein; and
4. recovering the expressed protein.

In the monoclonal antibody field the following kind of claim could be used:

A method of using spleen cells producing antibody A to produce a monoclonal antibody directed against X comprising the steps of:

1. fusing the spleen cells with a myeloma fusion partner;
2. selecting fused cells; and
3. culturing fused cells to produce the monoclonal antibody.

The specification itself should contain detailed disclosure of the specific methods of using the novel compositions. This will give support for Pleuddemann type claims. Importantly also to rebut a Durden argument against method of making a product, the specification should point to the unexpected, unpredictable and unforeseeable nature of applying a process to a starting material to generate the end product. The unpredictability of the biological properties of the product and process should be emphasized. Process steps or limitations not found specifically in the prior art should be included.

Whether such drafting technique will actually be allowable in the Patent Office is not yet known. In the U.S. Patent Office, many of the new biotechnology patent examiners may be looking at the predictability of the technology through the eyes of scientists, rather than making determinations based on established patent law tests.

6. Importation

In 1988 the U.S. adopted process patent protection somewhat similar to that existing in other countries. It emphasized liability as an infringer for the importer and the ability to obtain damages with the Patent Statute. The Tariff Act was also amended to give process patent owners the right to bar importation of products produced by a patented process.

Much of the impetus for this improved process protection was founded on the idea that process protection was important in

emerging new technologies such as biotechnology. While this is still true, the Durden effect has knocked much of the impetus out of the new process patent protection. This is illustrated in the renowned patent battle between Amgen and the Genetics Institute over erythropoietin.

Amgen v. United States International Trade Commission, demonstrates the risk for inventors in not having enforceable process patents. This case was decided before *Pleuddemann*. The Amgen case concerns erythropoietin, a hormone which controls the synthesis of red blood cells in bone marrow and which is useful for treating patients suffering from anemia. Recombinant DNA technology is used to produce genetically altered cells (host cells) which in turn produce large amounts of recombinant erythropoietin ("rEPO").

Amgen is the owner of a patent which has claims directed toward the recombinant DNA sequences, vectors and host cells used to produce rEPO. Importantly, there are no claims to the product rEPO, nor to the process for making rEPO. The patent application which matured into Amgen's patent had originally contained claims to the process of producing rEPO. Because the Examiner rejected these claims under Durden, the process claims were canceled prior to issuance of that patent.

Amgen sought to prohibit the importation of rEPO manufactured by Chugai, a Japanese company and licensee of the Genetics Institute. Amgen based its case on 19 U.S.C. § 1337. Amgen argued that the claims to a modified microorganism were really claims on a process carried out by those cells, namely the process of producing the human protein, rEPO.

Amgen's difficulty was in proving that its claims were for a process. Amgen attempted to argue that the rEPO produced and imported by Chugai was made by means of a process even though the patent did not contain, "conventional process claims".

Citing *Chakrabarty*, the Federal Circuit held that the patent claims to the genetically engineered microorganisms were not process claims but merely claims to a composition of matter. The host cell claims covered just the host cells themselves. The host cell could be analogized to a kind of living "machine" since it performs intracellular processes while producing rEPO; however, this did not make the host cell into a process rather than a type of mechanical machine. The court held there is nothing "unique" about Amgen's host cell claims which would transform the claims from traditional product claims into process claims. Since no process was used, Amgen's claim did not come within the scope of § 1337.

The court stated:

"We are of the opinion that in normal parlance among patent lawyers, to whom patent statutes are directed, a patent "covering" a process is a patent containing at least one claim defining a process...§ 337(a) was enacted to prohibit imports made using patented processes, and not to prohibit imports made by a process using patented article."

Thus Amgen's cause of action was denied. Amgen were without recourse against Chugai for lack of a process claim. In the absence of Durden, Amgen would likely have had the process claim and they would have been protected under this statute dealing with unfair foreign trade practices.

With carefully drafted *Pleuddemann*-type claims Amgen may have had a basis to succeed in the importation action against Chugai.

7. Conclusion

In an attempt to correct this problem of biotechnology industry, the "Biotechnology Patent Protection Act of 1990" (H.R. 3957) has been introduced to close these loopholes and widen the scope of protection afforded by patents on biotechnology. This bill legislatively overrules Durden and affords some of the same remedies now available to holders of process patents to holders of patents on recombinant cells producing desirable products.

35 U.S.C. section 103, the section of the patent law dealing with obviousness could be used to state that a process of making a product would not be considered obvious if an essential material used in the process is novel and otherwise not obvious.

Another provision of the bill makes the importation of products that are made, produced, or processed under or by means of the use of a patented biotechnological material an infringement if done without permission of the patentee. The International Trade Commission statute, 19 U.S.C. section 1337, is also amended to allow exclusion of these products.

This proposed legislation has split the biotechnology industry. Some firms favor H.R. 3957 as a matter of fundamental fairness to American companies. Others, however, oppose it as being an expression of American protectionism and interfering with the ability of American companies to do business internationally.

Until these major issues resolve themselves, inventors should continue to prosecute patents in terms of the Practice Note outline above. These positions should be pursued vigorously, and continuation applications and appeals as appropriate should be filed to obtain the best advantages of time delay.

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