

HEALTH POLICY REPORT

Medical-Process Patents — Monopolizing the Delivery of Health Care

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Patents have helped promote innovation for centuries, but the modern application of patents to the field of medicine raises legal and ethical questions. Patents covering pharmaceutical products and medical research tools are ubiquitous, and many discoveries described by such patents have contributed to the advancement of medical science. At the same time, when patent protection has been too broad, extended beyond the term initially granted, or granted for discoveries that are far from groundbreaking, it has hindered scientific progress and increased costs in the medical marketplace. A wide-ranging debate has emerged over how to balance these competing interests.¹⁻³

This spring, controversy over patent policy resurfaced in a case brought before the Supreme Court, *Laboratory Corporation of America (LabCorp) v. Metabolite Laboratories*. The case centered on a patent for a method of diagnosing a vitamin deficiency on the basis of the levels of homocysteine in blood. The disputed patent exemplifies the growing effort to claim proprietary rights over medical processes, such as making a diagnosis or treating a condition in a particular way.

Medical-process patents threaten to complicate medical practice, increase costs, and restrict access to therapeutic and diagnostic procedures. The American Medical Association (AMA) has declared that this type of patent compromises patients' access to new procedures.⁴ Owing to such concerns, nearly 80 countries refuse to grant patents on medical procedures.^{5,6} U.S. law allows such patents, but in 1996, Congress curtailed the consequences for physicians of certain kinds of medical-process patents.⁷ Despite this provision, the *LabCorp* case highlights ongoing concerns about the effect of process patents on health care.

MEDICAL PROCESSES AS INTELLECTUAL PROPERTY

Patents promote innovation by allowing inventors to control their intellectual property and reap financial rewards without worrying about misappropriation by competitors. To be eligible for patenting, an invention must be novel, be non-obvious, and have some utility. The invention must also involve the proper subject matter, which the Patent Act defines as a "process, machine, manufacture, or composition of matter."⁸

The wide breadth of patentable subject matter was reinforced in the 1980 Supreme Court case of *Diamond v. Chakrabarty*, which involved a microbe into which an inventor had inserted a DNA plasmid.⁹ The Court ruled that the Patent Act covered "anything under the sun made by man," including this single-celled living organism. A year later, in *Diamond v. Diehr*, the Court clarified its earlier ruling by stating that "laws of nature, natural phenomena, and abstract ideas" are not patentable.¹⁰ The invention in that case was an algorithm for determining the proper time and temperature for curing rubber. Although the patent involved natural phenomena (the physical properties of the molecular stability of rubber), the Court upheld the patent because these phenomena were integrated into the inventive process of transforming rubber into another state.

Since the early 1980s, health care–related patents have proliferated, facilitated by changes in the patent review process.¹¹ These patents cover compositions of matter, such as drugs and DNA sequences, and health care–related processes. Process patents have protected intellectual property in research methods, techniques for isolating biologically active compounds and gene sequen-

ces, and medical and surgical techniques. For example, in 2004 a process patent was awarded for a form of rheumatoid arthritis therapy that used two classes of known medications (an antagonist of tumor necrosis factor α and cyclosporine) in doses reduced to a level at which neither would be effective alone.¹²

Controversy over process patents swelled after ophthalmologist Samuel Pallin was awarded a patent in 1992 for a method of performing cataract surgery that did not require stitches. Pallin filed an infringement suit against another ophthalmologist who used his technique¹³ and sought a small licensing fee for each use. The lawsuit attracted national attention, and the AMA issued a policy statement condemning such patents as a violation of physicians' ethical obligation to share their discoveries with their peers.⁴ The AMA stated that process patents raised a more serious danger of inadvertent infringement for physicians than composition-of-matter patents on drugs or devices because the cost of the patent license is integrated into the cost of those products.¹⁴

Congress amended the Patent Act in 1996 to address these concerns. It had considered prohibiting patents on medical and surgical procedures¹⁵ but instead opted to deprive patent holders of remedies against health care practitioners. Under new section 287(c), a court could hold that a physician had infringed a patent but could not order that physician to pay damages or stop using the process.⁷ (This provision does not apply to the *LabCorp* case because the amendment excluded patents filed before its effective date in 1996.)

In the ensuing decade, the limited scope of section 287(c) has become clearer. It applies only to "medical practitioners" who infringe a patent in the course of "medical activity." Medical practitioners are defined as people licensed to perform medical or surgical procedures and the health care entities with which they are affiliated. A researcher using a protected process to develop a drug for commercial purposes is not protected. Nonclinicians can also be held liable for contributing to infringement by others — for example, by disseminating guidelines or educational materials that explain how physicians can perform a process.

Section 287(c) also applies only to "pure" process patents such as Pallin's, which involve a medical or surgical technique. It excludes processes involving patented drugs, devices, or biotechnology products. For example, Myriad Genetics acquired proprietary rights to the *BRCA2* gene itself as well as to the use of the gene in assessing a patient's risk of breast and ovarian cancer. Section 287(c) would not protect a physician using a *BRCA2* gene test supplied by a laboratory that was not certified by the patent holder.

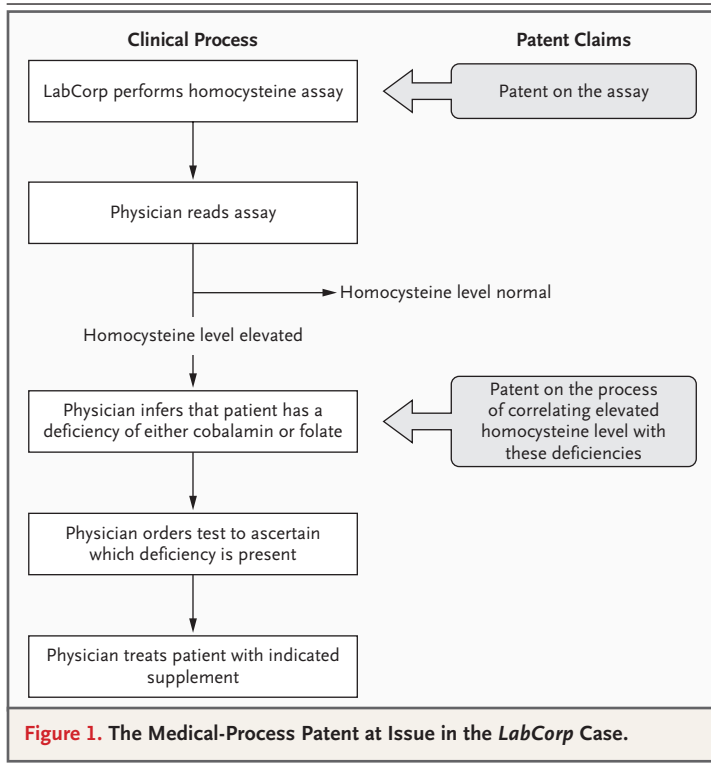
The protection offered by section 287(c) of the Patent Act is thus incomplete. Process patents on medical and surgical procedures can still be enforced, to the detriment of physicians, in a variety of circumstances. Consequently, questions remain about the boundaries of patenting in this area. The most recent battle over these boundaries occurred in the *LabCorp* case, which raised the question of whether basic scientific relationships used in clinical reasoning and diagnosis can be patented.

THE LABCORP CASE

In the 1980s, three medical school professors discovered that elevated levels of homocysteine, a protein known to be involved in inflammation, were associated with a deficiency of either cobalamin (vitamin B₁₂) or folate (folic acid).¹⁶ Their universities patented the discovery and assigned the patent to a licensing company, which licensed it to Metabolite Laboratories.

The patent covered the inventors' novel technique of assaying for homocysteine. In addition, the inventors asserted rights in a process for detecting a vitamin deficiency that consisted of assaying a body fluid for homocysteine and "correlating an elevated level of total homocysteine in said body fluid with a deficiency of cobalamin or folate."¹⁷ This claim (claim 13 of the patent) protected the act of inferring, on the basis of a test result showing elevated homocysteine levels, that a patient had a deficiency of either cobalamin or folate (Fig. 1).

LabCorp sublicensed the patent from Metabolite in 1992, paying a royalty each time a physician ordered the assay. In 1998, LabCorp switched to a faster test developed by a competitor and



stopped paying royalties to Metabolite. Metabolite sued LabCorp for patent infringement. The lawsuit did not claim that the new assay infringed the patent. Rather, it charged that LabCorp intentionally induced infringement of claim 13 by informing physicians that they could detect vitamin deficiency in their patients by using the test results.

In response, LabCorp argued that claim 13 was invalid for a number of reasons: the correlating step was too vague, the claim did not describe the process in enough detail to show practitioners how to perform it, and the process was not novel because it had been described in earlier articles about homocysteine metabolism (or at least was so obvious in light of these articles that it was not worthy of a patent). The trial judge rejected the vagueness argument, and a jury found that claim 13 was valid. The federal circuit court of appeals affirmed the decision, noting that the act of drawing a “simple conclusion that a cobalamin/folate deficiency exists” on the basis of the result constituted infringement.¹⁸

With support from the AMA and the American Heart Association, among others, LabCorp appealed to the Supreme Court, which in 2005

granted certiorari¹⁹ to judge whether the protection of the correlating process in claim 13 constituted a valid monopoly over a “basic scientific relationship” so that “any doctor necessarily infringes the patent merely by thinking about the relationship after looking at a test result.”²⁰ The long-standing rationale for the exemption of natural phenomena or laws of nature from patent protection is that they are “the basic tools of scientific and technological work”²¹ and thus belong in the public domain.

In the 25 years since the Supreme Court last considered the scope of patentable subject matter, numerous judgments by the federal circuit (which hears all patent appeals) have suggested a basis for the validity of claim 13. In particular, the federal circuit upheld a patent on a data-processing system for pooling investment funds because it involved “the transformation of data” through “a practical application” of mathematical formulas and produced a “useful, concrete, and tangible result.”²² Metabolite argued that claim 13 was also valid under this standard, because the correlating step led to the detection of a vitamin deficiency. But a result is inherent to any process. A key question raised by the federal circuit’s jurisprudence is what else, if anything, is required in order for a process to be patentable? What remains of the *Diehr* requirement that a basic scientific relationship may be patented only as part of a transformation of something “into a new state or thing”?

Many have criticized the expansion of patent protection overseen by the federal circuit,²³⁻²⁵ and the *LabCorp* case presented an opportunity for the Supreme Court to restrain that trend. Instead, in June 2006, the Court decided it had erred in agreeing to hear the case.²⁶ Though the Court provided no explanation, the likely reason is that the question presented had not been argued in the lower courts. LabCorp would have to return to the lower courts and, if the patent was upheld there, request certiorari from the Supreme Court anew.

The decision was not unanimous, however. Justice Stephen Breyer (joined by Justices John Paul Stevens and David Souter) dissented, in large part because he perceived an important public interest in “clarifying the law in this area sooner rather than later.”²⁶ While conceding that unpatentable natural phenomena were “not easy to

define,” Breyer believed that claim 13 involved a process that lay well outside the gray zone — it was clearly unpatentable. He opined that this process was one of mere inference, not transformation of matter, and strongly criticized the federal circuit’s suggestion that a “useful, concrete, and tangible result” was enough to make a process patentable. “Claim 13’s process instructs the user to (1) obtain test results and (2) think about them,” he wrote. He argued that it added or changed nothing of significance to the naturally occurring correlation between homocysteine levels and vitamin deficiency.

IMPLICATIONS OF PROCESS PATENTS
FOR CLINICAL MEDICINE

The issues raised by *LabCorp* remind us that medical-process patents continue to have substantial effects on the science and practice of medicine. Breyer worried that upholding claim 13 would subject the medical profession to restrictions that “may inhibit doctors from using their best medical judgment; . . . force doctors to spend unnecessary time and energy to enter into license agreements; . . . divert resources from the medical task of healthcare to the legal task of searching patent files for similar simple correlations; [and] raise the cost of healthcare while inhibiting its effective delivery.”²⁶

Indeed, process patents frequently increase health care costs — for example, a pharmaceutical company can use process patents to extend the effective life of patents on the underlying clinically active molecule.²⁷ AstraZeneca filed a patent application for a method of using its heartburn drug omeprazole (Prilosec) by crushing it and spreading it on applesauce; as a result, the Food and Drug Administration required manufacturers of generic versions of the drug to conduct bioequivalence studies of generic omeprazole administered on applesauce.²⁸ Although the new patent did not preclude generic competition, it raised the cost of market entry. Process patents may also affect medicine by promoting secrecy among physicians who are developing novel therapeutic protocols. A study of life science researchers found that the filing of a patent application constituted a leading reason for withholding data from dissemination in the scientific community for 6 months or more.²⁹

Physicians brush up against three types of process patents in the course of medical practice. The first is the pure process patent, which involves a medical procedure but no patented medical product (e.g., Dr. Pallin’s cataract surgery procedure). Such patents are problematic because, as the AMA has noted, physicians who are uncertain about whether and to what extent a new method of treatment has patent protection may not feel free to adopt the practice; thus, the dissemination of knowledge is inhibited.¹⁴ In *LabCorp*, one of the inventors spelled out the legal catch-22 that currently ensnares physicians: ordering a homocysteine measurement, from LabCorp or any other company, would infringe Metabolute’s intellectual property if the measurement were used to assess a patient for vitamin deficiency, yet “it would be malpractice” for a doctor to receive an assay result showing elevated total homocysteine levels and not consider cobalamin or folate deficiency as a cause.³⁰ Section 287(c) of the Patent Act notwithstanding, such patents expose physicians working in some capacities, as well as nonphysicians such as persons running diagnostic testing companies and providers of continuing professional educational materials, to legal risk. Pure process patents also have implications for epidemiologic research, which relies heavily on the use of existing knowledge about associations between physiological markers or risk factors and health states.³¹

The second category of process patents is that related to patented drugs or devices, such as a method of using a patented drug. Because section 287(c) excludes this type of patent, physicians’ decision making may well be affected in the ways Breyer described. Such patents may also affect medical practice by increasing health care costs. For example, when Pfizer developed sildenafil (Viagra), it claimed proprietary rights over the method of using selective phosphodiesterase inhibitors to treat erectile dysfunction.³² Pfizer later sued to stop competitors from marketing similar drugs based on this mechanism, alleging patent infringement and seeking a license for its broad patent covering the biologic effect of Viagra.³³ The lawsuit was suspended because the U.S. Patent and Trademark Office reexamined Pfizer’s method-of-use claim and invalidated it on technical grounds, although Pfizer has appealed that determination. However, if such cross-

licensing requirements became common, their costs would inevitably get passed on to the public in the form of higher drug prices.

The final category of process patents includes techniques used to isolate compounds or build devices. Numerous patents cover inventive methods such as those used to extract the chemotherapeutic agent paclitaxel from the bark of the yew tree³⁴ or to purify enzymes for biomedical research. (This category includes the homocysteine assay technique described in the Metabolite patent — excluding claim 13.) This third type of process patent is a critical means of promoting innovation, because the search for new, biologically active molecules and health care technologies drives medical progress.

There are a number of avenues for addressing policy concerns about how the first two categories of process patents affect medical practice. In our opinion, the Patent Office and the courts should follow Breyer's lead, applying a more critical eye to process-patent applications and reinvigorating the distinction articulated in *Diehr* between a claim to a process that is truly transformative and a claim that adds only a trivial procedural step to a process involving naturally occurring phenomena.

A legislative solution might involve amending section 287(c) to include processes involving the use of patented drugs and devices, in addition to pure process patents. Alternatively, Congress could refashion section 287(c) to exclude most medical processes from patent protection rather than exempt just one group of infringers from the consequences of infringement. Under such a rule, a novel process for purifying a new pharmaceutical product for human use would be patentable — thereby promoting the discovery of compounds for medical treatment — but the ways in which physicians used the product could not be patented. Although ethically appealing, the abolition of such process patents would represent a sea change in the law. It could be fashioned to apply only to future work, so as not to disrupt business relationships based on thousands of existing patents.

Ever since a Boston dentist obtained a patent on the use of ether as a surgical anesthetic in 1846,³⁵ controversies over medical-process patents have churned in the courts and the medical community. The *LabCorp* case highlights the fissure

that has developed over the years between intellectual property law and medical professionalism. Although certain process patents have undoubtedly helped encourage innovation in medicine, the professional obligation of beneficence and the need to facilitate the rapid dissemination of advances in medical practice point to the need for reflection and restraint in this important area of law.

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