Enzo Biochem v. Gen-Probe: Complying with the written description requirement under US patent law

Recent court decisions effectively call for researchers and companies to reduce their biotechnology and pharmaceutical inventions to practice before they can apply for patent protection.

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The US patent system is founded upon a *quid pro quo* bargain between the government and the inventor. The inventor fully discloses to the public what he or she claims to have invented and, in exchange, the government grants to the inventor the exclusive right in the United States to exploit the invention for a limited period of time. The issued patent evidences this bargain; it embodies both the inventor's public disclosure of his or her invention, set forth in the patent text known as the specification, and the government's grant of exclusive rights to the invention, set forth in the patent claims.

Through this bargain, the patent system encourages inventors to disclose their inventions so that society as a whole may use and learn from them, instead of guarding them in secrecy so that no one else can benefit. At the same time, the system allows inventors to further develop and exploit their inventions, secure in the knowledge that they have the opportunity to realize a fair return on their R&D investment without the risk of free-riding by others.

Biotechnology and pharmaceutical inventions may represent a dozen or more years and hundreds of millions of dollars of R&D investment. Companies making this sort of investment also take on substantial risks typically associated with the process of developing a viable commercial product or therapy. Given the levels of investment and risk, obtaining broad but strong patent protection for inventions is paramount, and such protection is desirable relatively early in the development process, both to safeguard the interests of owners, investors, and other stakeholders and to preempt competitors who may be working on similar products and therapies.

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The goal of obtaining broad patent protection during the early, rather than later, stages of the development of a biotechnology or pharmaceutical invention creates unique problems when it comes to complying with the government's requirement of full disclosure. Patent law requires a disclosure that describes the components and features of the invention in writing, teaches someone with ordinary skill in the relevant technical field how to make and use the invention, and reveals the "best mode" then known to the inventor for carrying out the invention. Given the complex and unpredictable nature of biological systems, however, an inventor may not fully understand the structure, properties, and mechanisms of his or her invention, or appreciate the different products and therapies that may flow from the invention. As a result, he or she may not be able to provide a disclosure that strictly meets the requirements of the law—at least not during the early stages of the development process.

At the same time, however, the inventor will want to claim as broad rights as possible, lest he or she forfeit them to a competing researcher. Indeed, the embryonic state of many biotechnology and pharmaceutical companies and the inherent difficulty in predicting the direction of their discoveries create enormous pressure to file numerous, broad patent applications aimed at protecting the R&D investment. This pressure to obtain patent protection often drives companies to file patent applications before the significance of their inventions is fully understood. Instead of producing strong patents, this precipitous strategy may produce patents that are vulnerable to challenges of invalidity because their disclosures do not support the broad rights that are being claimed.

The problems described above have come to the forefront through recent decisions from the United States Court of Appeals for the Federal Circuit, the appellate court charged with the primary responsibility for shaping the contours of US patent law and policy. This article discusses the 2002 decision in the *Enzo Biochem v. Gen-Probe* case and the issues that it poses regarding the sufficiency of disclosures of biotechnology and pharmaceutical inventions under US patent law[1]. In *Enzo*, the Federal Circuit resolved a relatively discrete question regarding the so-called "written description" requirement but left unanswered the larger, and more important, question regarding the nature and purpose of this requirement, particularly in the context of biotechnology inventions.

Review of the *Enzo* decision

Enzo involved a US patent claiming nucleic acid probes that preferentially hybridize to the DNA of *Neisseria gonorrhoeae*, which causes gonorrhea, over the DNA of *N. meningitidis*, which causes meningitis. The high degree of homology between the DNA of *N. gonorrhoeae* and that of *N. meningitidis* makes it difficult to detect and distinguish between the two bacterial species unless a probe can target the non-homologous portions of the sequences and thus selectively hybridize to *N. gonorrhoeae* as opposed to *N. meningitidis*. Enzo's inventors succeeded in developing such probes. However, rather than identifying the nucleotide sequences of the probes within the text of the specification, the inventors simply deposited samples, in the form of recombinant DNA within an *Escherichia coli* host, at the American Type Culture Collection (ATCC; Manassas, VA).

Sued for infringement, the defendants argued that Enzo's patent was invalid for failing to comply with the statutory "written description" (WD) requirement, which states: "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."[2]

According to the defendants, Enzo's patent did not provide an adequate written description because its specification describes the probes only in terms of their function—selective hybridization with *N.*

gonorrhoeae—and does not furnish any sequence information. Instead, for WD support, Enzo relied on the text references to the ATCC deposits and their accession numbers. The trial court agreed with the defendants that the patent claims were invalid for this reason.

On appeal, the Federal Circuit initially ruled in favor of the defendants as well[3]. Applying precedent from the 1997 decision in *Regents of the University of California v. Eli Lilly*[4], the appeals court held that a description of the probes by their function was insufficient, absent some known correlation between the described function and a specific structure or other identifying characteristic. The court further held that references in the specification to the ATCC deposits alone did not satisfy the WD requirement. Although the deposits demonstrate that the inventors were in "possession" of the claimed invention—that is, they had in fact created three specific probes—at the time they applied for the patent, "possession" alone does not satisfy the WD requirement. The specification still must contain words, structures, figures, diagrams, or formulae that identify and describe what has been invented and claimed. Enzo's patent specification did not do that, according to the initial Federal Circuit decision, because it did not identify the nucleotide sequences of the probes or provide any other identifying information about their structures and characteristics.

Within the space of three and a half months, the Federal Circuit rethought its analysis and changed its opinion regarding whether the ATCC deposits satisfied the WD requirement. Vacating its earlier ruling, the appeals court held that "reference in the specification to a deposit in a public depository, which makes its contents accessible to the public *when it is not otherwise available in written form,* constitutes an adequate description of the deposited material sufficient to comply with the written description requirement of §112, ¶1."[5] The court agreed that as to the deposited probes, Enzo's reference in the specification to the deposits and their accession numbers constituted an adequate written description. In its analysis the court pointed out that the sequences now could be obtained from the deposits, and that those sequences might not have been "reasonably obtainable and in any event were not known to Enzo when it filed its application in 1986."[6]

In so holding, the Federal Circuit expanded the role of biological deposits beyond the traditional one of satisfying the companion "enablement" requirement under US patent law, which requires that the patent text contain "full, clear, concise, and exact" instructions to "enable" an ordinarily skilled person to "make and use" the invention. As the court explained in *Amgen, Inc. v. Chugai Pharmaceutical Co.*,[7] the practice of depositing samples of biological material originally arose in the field of antibiotics, in which inventors were not always able to explain in words how to obtain a requisite starting material from nature. In lieu of describing a unique biological material, patent law and practice evolved to permit inventors to place a sample of that material in a publicly accessible deposit. By accessing and using the sample, a person with ordinary technical skills would be able to "make and use" the claimed invention, notwithstanding the lack of complete instructions in the patent text. In this manner, the enablement requirement was satisfied.

A patent specification must both adequately describe what the invention is and teach a skilled person how to make and use it. Even if the text satisfies one requirement, it may not have sufficient content to satisfy the other.

Objectives of the written description requirement

Acceptance of the use of biological deposits to satisfy the WD requirement created an issue for the Federal Circuit because this requirement serves very different objectives from the enablement requirement. As recognized in *Eli Lilly* and in the first *Enzo* ruling, the WD requirement has an *independent existence* apart from the enablement requirement. A patent specification must both adequately describe what the invention is *and* teach a skilled person how to make and use it. Even if the text satisfies one requirement, it may not have sufficient content to satisfy the other.

Requiring the inventor to describe his or her invention in writing serves several objectives. First, as the Federal Circuit observed in *Vas-Cath Inc. v. Mahurkar*[8], the WD requirement arose during a historical period when patents were not required to have claims. Consequently, the specification fulfilled "the most basic requirement of the patent law—to adequately identify what one has invented."[9] To prevent his or her perpetrating a fraud on the public, and later claiming exclusive rights to what he or she did not in fact invent, the inventor was required to reduce to words and/or drawings the precise components, features, and operations of his or her invention. Once the inventor had described his or her invention in written and/or graphical form, he or she could not go back and claim rights to something that had not been described.

Even with the introduction of claims, the specification still serves the same historical purpose. Although claims now perform the function of "particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention[,]"[10] they are subject to amendment both during prosecution and after issuance of a patent. By contrast, the specification cannot be amended after the filing of a patent application to add "new matter" and thereby expand the scope of what the inventor can legitimately claim as his or her invention[11]. In other words, whatever is claimed must have been described in the text of the application, as originally filed, and one cannot change that text to add additional details that were not previously present in the application, in order to provide support for a particular claim later presented for consideration and allowance.

In situations where two separate inventors (or sets of inventors) are claiming to have invented the same subject matter in question (known in patent law as a priority contest), the WD requirement helps to establish who was the first to invent. Because each inventor is required to describe his or her invention in a written specification, the application containing that description serves as strong evidence that a given inventor was in "possession" of the claimed subject matter as of its filing date, at the latest. In the absence of any evidence proving an earlier date, the filing date of the application serves as the date of invention.

The judicial bias against claims that are drafted to cover subject matter embodied only in constructive or prophetic examples, as expressed in *Eli Lilly*, *Amgen*, and *Fiers v. Revel*[12], can be best understood in the context of the foregoing objective. Inventors may not patent what they have not yet conceived. From this fundamental premise, it follows that claiming an unknown compound based on a desired and known biological property amounts to "a mere wish or plan" for obtaining any material with that biological property[13]. In this regard, the WD requirement acts as a check to ensure that inventors have in fact conceived, and are in possession of, what they claim as their invention by forcing them to describe the invention in writing. The US patent system thus prevents inventors from "jumping the gun" and filing a patent application for an invention they have not yet conceived, solely to obtain a priority of invention over a competing group of researchers.

The WD requirement serves two other objectives, both of which were mentioned in the first *Enzo* ruling. One objective is to facilitate examination of the patent application by the patent office. The specification, drawings, and the claims serve to communicate to a patent examiner the invention for which a patent is sought. The examiner relies on the written description in performing his or her search of the relevant prior art and in determining whether the invention is patentable.

The other objective is to provide notice to the public regarding what the inventor claims as his or her invention so that the public can resolve any infringement concerns. This objective also arose during the period when patents did not contain any claims. The public therefore had to rely solely on the written description to determine what the inventor was claiming as his or her exclusive property and what actions would or would not constitute infringement of the inventor's rights. Even with the advent of claims, the specification still satisfies the *quid pro quo* disclosure to the public of the inventive subject matter in exchange for the grant of a limited period of exclusivity to the inventor.

In view of the objectives described above, the WD requirement is principally concerned with what details have been set forth in written or graphical form, and not with what missing details can be inferred, deduced, or derived by someone with ordinary skill in the relevant technical field. By contrast, a central premise of the enablement requirement is that the inventor does not have to "reinvent the wheel" when explaining to an ordinarily skilled person how to make and use the invention. The inventor can safely assume that a person who wants to practice the invention will have a basic knowledge and understanding of the relevant technical field, and therefore he or she can focus on describing those details unique or specific to the invention.

Issues posed by the *Enzo* decision

The Federal Circuit's holding in *Enzo* is puzzling because it allows an inventor to dispense with a description of the structure of a chemical compound (the nucleotide sequence of a probe) on the premise that someone with ordinary skill could ascertain the structure for himself or herself by accessing a publicly available sample of the material. This logic conflates the WD requirement with the enablement requirement. As pointed out above, the former requirement focuses on what has been disclosed in the patent, whereas the latter requirement focuses on whether someone reading the patent will be able to understand and use the invention.

In contrast, at the same time that it provides inventors with a shortcut for satisfying the WD requirement, *Enzo* reaffirms the view in *Eli Lilly* that with respect to biotechnology and pharmaceutical inventions, the inventor must obtain a new compound and resolve its structure before he or she is entitled to patent it. In other words, the WD requirement appears to impose an *actual* reduction to practice of a biotechnology or chemical invention before it can be patented. This conflicts with the general rule that constructive reduction to practice of an invention (for example, describing a chemical compound in a patent application without actually isolating or synthesizing it) is sufficient to put an invention in a state "ready for patenting."[14] This application of the WD requirement also elevates a rarely applied doctrine known as "simultaneous conception and reduction to practice"—which recognizes that in certain scientific fields such as chemistry and biology, an inventor may not be able to establish that he or she has conceived of an invention until he or she has reduced it to practice in a successful experiment—into a hard and fast requirement of patentability for DNA sequences[15]. The foregoing concerns no doubt have contributed to one Federal Circuit judge's accusation that *Enzo* and *Eli Lilly* have created an "aberrant form" of the WD requirement that calls for more specific disclosure of the invention than that necessary under the enablement requirement[16].

Living with *Enzo's* written description requirement

Criticisms notwithstanding, *Enzo* and *Eli Lilly* are controlling precedent under US patent law—at least for now. Inventors and companies seeking patent protection for their biotechnology and pharmaceutical inventions therefore must take steps to ensure that their disclosures meet the WD requirement, which can be particularly rigorous. This assessment should be made case by case with the advice of counsel. A few general observations can be made, however.

Descriptions should include information about the structure, the properties, or other identifying characteristics of the compound, molecule, or biologic whenever practicable. A description of function alone probably will not be sufficient. It should be accompanied by an explanation of the relationship between the function described and the structure or properties of the compound, molecule, or biologic. Consequently, it is important to include adequate and real data with the filed patent application to meet the WD requirement. Investors and others involved in evaluating the strength and breadth of a patent portfolio should analyze applications and issued patents with this issue in mind.

Broad claims, such as those drawn to a genus of compounds, will be especially vulnerable to invalidation unless the disclosure identifies characteristics or properties that determine membership in the genus based on the data derived from the species that have been isolated or synthesized. To hedge against this risk, inventors and companies may want to consider filing continuation applications as they accumulate more data from their R&D efforts. Continuation applications can contain claims that better capture the inventive subject matter and its known applications.

An aggressive patent procurement strategy effectively protects a company's R&D investment only if the company takes care to ensure that the disclosure in each patent specification adequately supports the broad rights that are being claimed.

1. *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 296 F.3d 1316, 63 USPQ2d (BNA) 1609 (Fed. Cir. 2002).
2. 35 USC § 112, ¶1.
3. *Enzo Biochem, Inc. v. Gen-Probe Inc.*, 285 F.3d 1013, 62 USPQ2d (BNA) 1289 (Fed. Cir. 2002), *vacated by* 296 F.3d 1316 (Fed. Cir. 2002).
4. *Regents of Univ. of Cal. v. Eli Lilly*, 119 F.3d 1559, 43 USPQ2d (BNA) 1398 (Fed. Cir. 1997), *cert. denied,* 523 US 1089 (1998).
5. *Enzo,* 296 F.3d at 1325 (emphasis added).
6. *Enzo,* 296 F.3d at 1326. Interestingly, this view represents an about-face for the *Enzo* panel from their earlier ruling: "This is not a case in which the inventors could not have provided a description of the nucleotide sequences." 285 F.3d at 1022. "Even if Enzo's expert, Dr. Wetmur, were correct that one of skill in the art could routinely sequence the deposited material and so obtain a description of those deposits, that description is not in the patent." *Id.*
7. *Amgen, Inc. v. Chugai Pharmaceutical Co., Ltd.*, 927 F.2d 1200, 18 USPQ2d (BNA) 1016 (Fed. Cir. 1991). See also *In re Lundak*, 773 F.2d 1216, 227 USPQ (BNA) 90 (Fed. Cir. 1985).
8. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 19 USPQ2d (BNA) 1111 (Fed. Cir. 1991).
9. *Enzo,* 285 F.3d at 1021.
10. 35 USC §112, ¶2.
11. 35 USC §132.
12. *Fiers v. Revel*, 984 F.2d 1164, 25 USPQ2d (BNA) 1601 (Fed. Cir. 1993).
13. *Enzo,* 285 F.3d at 1018; *Fiers,* 984 F.2d at 1171; *Amgen,* 927 F.2d at 1206.
14. *Pfaff v. Wells Elecs., Inc.*, 525 US 55, 67-68 (1998) (holding that readiness for patenting may be satisfied "by proof that prior to the critical date the inventor had prepared drawings or other descriptions of the invention that were sufficiently specific to enable a person skilled in the art to practice the invention"). *Accord Space Sys./Loral, Inc. v. Lockheed Martin Corp.*, 271 F.3d 1076, 1080, 60 USPQ2d (BNA) 1861 (Fed. Cir. 2001).
15. *Mycogen Plant Science, Inc. v. Monsanto Co.*, 243 F.3d 1316, 1330, 58 USPQ2d (BNA) 1030 (Fed. Cir. 2001) ("The doctrine of simultaneous conception and reduction to practice is somewhat rare, but certainly not unknown, especially in the unpredictable arts such as chemistry and biology. …Although *Burroughs Wellcome* specifically notes that the doctrine does not state that an inventor can never conceive of an invention in the unpredictable arts until a reduction to practice has occurred, the doctrine still may apply to cases in such arts.") (citations omitted).
16. *Enzo Biochem. Inc. v. Gen-Probe Inc.*, 42 Fed. Appx. 439, 451 63 USPQ2d (BNA) 1618 (Fed. Cir. 2002) (unpublished) (Rader, J., dissenting).