Intellectual Property

Prometheus Unbound: The Federal Circuit Responds to *Bilski*

*By David L. Applegate**

Following the U. S. Supreme Court's decision in *Bilski*,[1] the U.S. Court of Appeals for the Federal Circuit wasted little time in responding with a second decision in *Prometheus Laboratories, Inc., v. Mayo Collaborative Services*.[2] On remand from the Supreme Court,[3] the threshold question for the Federal Circuit in *Prometheus* was whether the patents in suit claimed patentable subject matter in view of *Bilski*'s "clarification" of Section 101 jurisprudence. In simple terms, as on initial appeal, the Federal Circuit found that the Prometheus claims were patent eligible.

I. Procedural History

Plaintiff-Appellant Prometheus Laboratories had originally sued Mayo Collaborative Services, d/b/a Mayo Medical Laboratories, and Mayo Clinic Rochester in the Southern District of California for allegedly infringing various method claims of two patents directed to certain medical treatments. On Mayo's motion for summary judgment, the district court found that both patents claimed unpatentable subject matter under 35 U.S.C. § 101, and Prometheus appealed. On initial appeal, the Federal Circuit found that the district court had erred as a matter of law in finding the claims unpatentable under the Federal Circuit's "machine-or-transformation" test announced in *In re Bilski*,[4] and reversed the district court's grant of summary judgment.[5]

After the Supreme Court held in *Bilski v. Kappos* that the "machine-or-transformation" test—although useful and important—was not the sole test for determining the patent eligibility of process claims,[6] the Supreme Court vacated and remanded the Federal Circuit's initial decision.[7] On remand, the Federal Circuit found once again that the patents in suit were directed to patentable subject matter and again reversed the district court.

II. Factual Background

At issue in *Prometheus* were certain method claims of U.S. Patents 6,355,623 and 6,680,302, both directed to determining and administering optimum dosages of certain pharmaceuticals known as thiopurine drugs. Prometheus Laboratories is the sole and exclusive licensee of both patents, which claim improvements in treating autoimmune diseases such as Crohn's disease and ulcerative colitis. Both patents contain method (or "process") claims directed to helping ensure the administration of proper dosages of thiopurine drugs such as 6-MP (6-mercaptopurine) and AZA (azathiopurine, which converts to 6-MP upon administration to a patient). Once in the body, 6-MP breaks down into various metabolites, including 6-MMP (6-methylmercaptopurine) and 6-TG (6-thioguanine) and their nucleotides. Simply put, too high a drug dosage is toxic for the patient, but too low a dosage has no effect. The '623 and '302 patents claim methods for monitoring the proper level of 6-TG and 6-MMP, respectively.

As written, the claimed methods include two steps: (a) "administering" a drug that provides 6-TG to a patient (thus, either 6-MP or AZA) and (b) "determining the level of the drug's metabolites" (6-TG and/or 6-MMP) in the patient.[8] The patents then call for comparing the patient's measured metabolite levels to pre-determined levels in order to "indicate a need" to increase or to decrease the level of the administered drug in order to minimize toxicity and maximize efficacy.[9] (In particular, a 6-TG level above about 400 pmol (picomole) or a 6-MMP level above about 7000 pmol per 800 million red blood cells indicates a downward adjustment,[10] and a 6-TG level below about 230 pmol per 800 million red blood cells indicates the need for an increased dosage for efficacy.[11])

Until 2004, the Mayo defendants had purchased and used thiopurine metabolites tests marketed by Prometheus that used the patented technology. In 2004, Mayo announced that it would begin using and selling to other hospitals its own test for measuring the same metabolites, although using different levels from the Prometheus test to determine toxicity. After Prometheus sued Mayo for infringing certain claims of both patents, Mayo rescinded its announcement and delayed introducing and using its tests. (As of December 2010, when the Federal Circuit issued its second opinion, Mayo still had not yet introduced them.[12]) In November 2005, the district court found on cross-motions for summary judgment that Mayo infringed an independent claim of the '623 patent, and in January 2007 Mayo moved for summary judgment of invalidity under Section 101.

III. District Court Decision

In granting Mayo's motion for summary judgment, the district court found first that both patents claimed only correlations between toxicity and therapeutic efficacy on the one hand and the metabolite levels of certain thiopurine drugs on the other. Second, the district court found that those correlations were natural phenomena rather than patent-eligible inventions.

As part of its reasoning, the district court found that the patents' claims in suit had three essential steps: (1) administering the drugs, (2) determining metabolite levels, and (3) being warned that an adjustment in dosage may be required. The first two steps, the district court reasoned, are merely data-gathering steps and, as construed, the "warning" step is only a mental step because it does not require any actual change in dosage. Rather, the district court found, "it is the metabolite levels themselves that 'warn' the doctor that an adjustment in dosage may be required."[13]

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Based on this understanding, the district court stated that the inventors had not "invented" the claimed correlation but had merely observed the relationship between naturally produced metabolites on the one hand and therapeutic efficacy and toxicity on the other.[14] Because the patents' claims thus covered the correlations themselves, the district court concluded, it followed that the claims "wholly pre-empt" the correlations. This, the district court found, was clear and convincing evidence that the claims in suit were not directed to statutory subject matter under Section 101.[15]

IV. Initial Federal Circuit Decision

On initial appeal, the Federal Circuit disagreed with the district court and found that both "administering" and "determining" were not merely data-gathering steps but instead were "transformative" under the "machine-or-transformation" test that the Federal Circuit had itself adopted in *In re Bilski*.[16] But following that decision, the Supreme Court rejected the Federal Circuit's machine-or-transformation test as the sole test of Section 101 patent eligibility, granted Mayo's petition for certiorari, and vacated and remanded the Federal Circuit's reversal of the district court. On remand, the Federal Circuit requested simultaneous briefing from both parties on the effect of *Bilski* on the Federal Circuit's earlier reversal and, without oral argument, again concluded that the Prometheus method claims recite patent-eligible subject matter.[17]

V. Federal Circuit Decision on Remand

Once again, the Federal Circuit held that the asserted method claims "recite a patent-eligible application of naturally occurring correlations between metabolite levels and efficacy or toxicity" and thus did "not wholly preempt all uses of the recited correlations."[18] In addition, the Federal Circuit found, the patent's claimed treatment methods satisfy the "transformation prong" of the "machine-or-transformation" test because central to the purpose of the claimed process is "the transformation of the human body and of its components following administration of a specific class of drugs."[19]

Beginning with a review of Section 101 jurisprudence, the Federal Circuit observed that the Supreme Court has consistently construed the statutory language of Section 101 broadly, excepting only laws of nature, physical phenomena, and abstract ideas.[20] At the same time, it noted, the Supreme Court has established that "an application of a law of nature or mathematical formula to a known structure or process" may well be patent-eligible, even though a scientific principle can not be made patentable by limiting its use to a particular technological environment or by adding insignificant post-solution activity.[21] As such, the Federal Circuit concluded, patent eligibility in this case depended on whether the asserted claims were drawn to natural phenomena—the patenting of which would entirely pre-empt its use as in *Benson*[22] or *Flook*[23]—or whether the claims in suit were drawn to only a particular application of the phenomena as in *Diehr*.[24] "We conclude," the Federal Circuit said, that "they are drawn to the latter."[25]

A. Continued Relevance of "Machine-or-Transformation" Test

Turning next to the parties' arguments on remand, the Federal Circuit disagreed with Mayo that the Prometheus claims wholly pre-empt all practical uses of naturally-occurring correlations between metabolite levels and drug efficacy. Instead, the court found that the Supreme Court's *Bilski* decision did not undermine its preemption analysis because the Supreme Court rejected "machine-or-transformation" only as an exclusive or "definitive" test.[26] Accordingly, because the machine-or-transformation test remains a "useful and important clue" even post-*Bilski*, as applied to the claims in suit, it leads to the "clear and compelling conclusion" that the Prometheus claims do not encompass laws of nature or preempt natural correlations.[27]

1. The "Administering" Step

As discussed more fully in its opinion, the Federal Circuit found that the asserted claims recite specific treatment steps, not just the correlations, and that those steps involve a "particular application of the natural correlations": treatment of a specific disease by administering specific drugs and measuring specific metabolites.[28] Thus, the inventive nature of the claimed methods stemmed from the application of a natural phenomenon in a series of steps comprising particular methods of treatment, leaving the field open to the administration of other drugs that might also optimize therapeutic efficiency.[29]

Similarly, the Federal Circuit reaffirmed that the claimed methods satisfy the "transformation" prong of the machine-or-transformation test because they transform an article into a "'different state or thing'" that is "'central to the purpose of the claimed process'" in two ways: (1) transforming the human body and its components following administration of a specific class of drugs and (2) causing various chemical and physical changes of the drugs' metabolites that enable their concentrations to be determined.[30] As such, the court found no need to determine separately whether the claims also satisfy the "machine" prong of the test.[31]

Going further, the Federal Circuit enunciated that claims to "methods of treatment" are *always* transformative "when one of a defined group of drugs is administered to the [presumably human] body to ameliorate the effects of an undesired condition."[32] To hammer the point home, the court noted that both the specification and the preambles to the asserted claims made clear the invention's purpose to treat the human body, that when such a drug is administered the human body necessarily undergoes a transformation, and that the transformation that occurs "is the entire purpose of administering these drugs," *viz.,* to provide 6-TG to a subject.[33]

The fact that the administering step *relies* on natural processes, the court found, did not disqualify it from patent eligibility because, simply put, all "[t]ransformations operate by natural principles."[34] But the administering step in the Prometheus patent is not merely data-gathering, the Federal Circuit found; instead, it is a "significant transformative element" sufficiently definite to "'confine the patent monopoly within rather definite bounds.'"[35]

2. The "Determining" Step

Likewise, the Federal Circuit concluded, the "determining" step of the claims in suit is also transformative and central to the patented claims, because determining the levels of 6-TG or 6-MMP in a subject required "some form of manipulation" to extract metabolites from a bodily sample and to determine

their concentration.[36] Unlike in *In re Grams*,[37] therefore, the essence of the Prometheus process is not merely "'an algorithm combined with a data-gathering step'" for the purpose of gathering information;[38] indeed, at the end of the Prometheus process, "'the human blood sample is no longer human blood; human tissue is no longer human tissue'"—clearly a patent-eligible transformation.[39]

B. Not Mere Extra-Solution Activity

In contrast to *Grams*, therefore, neither the administering nor the determining step in Prometheus constitutes mere "insignificant extra-solution activity" in contravention of *Flook*.[40] Likewise, although the "wherein" steps of the Prometheus claims are mental steps and thus not patent-eligible *per se*, the Federal Circuit found that a subsequent mental step does not, by itself, negate the transformative nature of prior steps and thereby "detract from the patentability of the Prometheus's claimed methods as a whole.[41] Consistent with *In re Abele*,[42] therefore, a physician (or presumably, a clinician) who only evaluates the result of the claimed methods without carrying out the administering or determining steps can not infringe any claim that requires those steps.[43]

C. Lab Corp. *Distinguished*

In its only lengthy footnote,[44] the Federal Circuit also dealt with Mayo's argument that the "carefully considered opinion" of three United States Supreme Court Justices "—allegedly cited approvingly by five Justices in *Bilski*—"[45] had rejected the machine-or-transformation arguments for nearly identical claims in *Laboratory Corp. of America Holdings, Inc. v Metabolite Laboratories, Inc.*[46] But those three Justices, the Federal Circuit pointed out, were dissenting from the dismissal of a grant of certiorari in *Lab. Corp*. as having been improvidently granted. "[W]ith respect," the Federal Circuit insisted, "we decline to discuss a dissent; it is not controlling law, and it involved different claims from the ones at issue here."[47]

Continuing, the Federal Circuit noted that even having five Justices cite *Lab. Corp.* with approval in their two *Bilski* concurrences did not transform a dissent into controlling law, and that the concurrence of Justice Stevens in *Bilski* had cited *Lab. Corp.* as support for an argument that "business method" patents should not qualify as patent-eligible processes under Section 101.[48] "But," the Federal Circuit tersely concluded, "this case does not involve business patents."[49]

Conclusion

In sum, the Federal Circuit found the answer to the question "What did the applicant invent?" to be rather simple: "a series of transformative steps that optimizes efficacy and reduces toxicity of a method of treatment for particular diseases using particular drugs."[50] On that basis, it had no problem once again reversing the judgment of the district court and remanding the case with instructions to deny Mayo's motion for summary judgment of invalidity under Section 101, even after the Supreme Court's decision in *Bilski*.[51]

Endnotes

1 Bilski v. Kappos, 130 S. Ct. 3218 (2010).

2 No. 2008-1403 (Fed. Cir. Dec. 17, 2010).

3 Mayo Collaborative Servs. v. Prometheus Labs., Inc., 130 S. Ct. 3543 (2010).

4 545 F.3d 943 (Fed. Cir. 2008).

5 Prometheus Labs., Inc. v. Mayo Collaborative Servs., 581 F.3d 1336 (Fed. Cir. 2009).

6 130 S. Ct. at 3226-27.

7 *Mayo*, 130 S. Ct. 3543 (2010).

8 No. 2008-1403, slip op. at 4 (Fed. Cir. Dec. 17, 2010) (citing, e.g., '623 patent, claim 1).

9 *Id.* (citing, e.g., '623 patent, claim 1).

10 *Id.* at 5 (citing '623 patent, col. 20, ll. 22, 54).

11 *Id.* (citing '623 patent, col. 20, ll. 18-19).

12 *Id.* at 7.

13 Prometheus Labs., Inc. v. Mayo Collaborative Servs., No. 04-CV-1200, 2008 WL 878910 (S.D. Cal. Mar. 28, 2008).

14 *Id.* at *7.

15 *Id.* at *11, *14.

16 Prometheus Labs., Inc. v. Mayo Collaborative Servs., 581 F.3d 1336, 1342, 1345-49 (Fed. Cir. 2009).

17 *Prometheus*, No. 2008-1403, slip op. at 10.

18 *Id.* at 15.

19 *Id.* at 16.

20 *Id.* at 11-12 (citing Bilski v. Kappos, 130 S. Ct. 3218, 3225 (2010); quoting Diamond v. Chakrabarty, 447 U.S. 303, 309 (1980)).

21 *Prometheus*, No. 2008-1403, slip op. at 12 (citing *Bilski*, 130 S.Ct. at 3230; quoting Diamond v. Diehr, 450 U.S. 175, 188, 191-92 (1981)).

22 Gottschalk v. Benson, 409 U.S. 63 (1972). In *Benson*, the application claimed a method for converting binary-coded decimal numerals (BCD) into pure binary numerals using a general purpose digital computer. The Court held that the application was directed to non-patentable subject matter because the allowance of the claim, a method directed to a numerical algorithm, would "wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself." *Id.* at 72.

23 Parker v. Flook, 437 U.S. 584 (1978). In *Flook*, the claims were drawn to a method for computing an alarm limit using a number of different variables. The Court held that the claims were directed to non-patentable subject matter because the application sought to simply protect a mathematical formula for computing the alarm limit. *Id.* at 586.

24 Diamond v. Diehr, 450 U.S. 175 (1981). In *Diehr*, representative claim 1 of the patent application was directed to a method of operating a rubber-molding press for precision molded compounds with the aid of a digital computer. The Court held that the application was directed to patentable subject matter because it involved a physical machine or process making use of a mathematical algorithm, rather than just the abstract algorithm itself. *Id.* at 187.

25 *Prometheus*, No. 2008-1403, slip op. at 13.

26 *Id.* at 14.

27 *Id.* at 15.

28 *Id.*

29 *Id.* at 15-16.

30 *Id.* at 16.

31 *Id.*

32 *Id.* at 17.

33 *Id.*

34 *Id.* at 18.

35 *Id.* (citing Gottschalk v. Benson, 409 U.S. 63, 70 (1972)).

36 *Id.*

37 888 F.2d 835 (Fed. Cir. 1989). In *Grams*, the applicant claimed a process that involved (1) performing a clinical test on individuals and (2) based on the data from that test, determining if an abnormality existed and determining possible causes of any abnormality by using an algorithm. The court held that the process was not drawn to patentable subject matter because "it was merely an algorithm combined with a data-gathering step." *Id.* at 840; *see Prometheus*, No. 2008-1403, slip op. at 20.

38 *Prometheus*, No. 2008-1403, slip op. at 20.

39 *Id.* at 18-19 (quoting Decl. of Dr. Yves Théorêt ¶ 6, Prometheus Labs., Inc., v. Mayo Collaborative Servs., No 04-CV-1200 (S.D. Cal. Mar. 29, 2007) (Dkt. No. 528-3)).

40 *Id.* at 19 (quoting Parker v. Flook, 437 U.S. 584 (1978)).

41 *Id.* at 21.

42 684 F.2d 902 (CCPA 1982). In *Abele*, a method claim called for using X-ray attenuation data, which "necessarily" involved production, detection, and display with a CAT scan; although the method also required use of an algorithm, the claim remained patentable because even without the algorithm all the steps of a CAT scan remained in the claim. *Id.* at 908; *see Prometheus*, No. 2008-1403, slip op. at 21-22.

43 *Prometheus*, No. 2008-1403, slip op. at 21.

44 *Id.* at 16-17 n.2.

45 *Id.* at 14.

46 548 U.S. 124, 138-39 (2006).

47 *Prometheus*, No. 2008-1403, slip op. at 16 n.2.

48 *Id.* at 16-17 n.2.

49 *Id.* at 17 n.2.

50 *Id.* at 23.

51 *Id.*