

No. 09-490

In the Supreme Court of the United States

MAYO COLLABORATIVE SERVICES (D/B/A MAYO
MEDICAL LABORATORIES) AND MAYO CLINIC
ROCHESTER,

Petitioners,

v.

PROMETHEUS LABORATORIES, INC.,

Respondent.

**On Petition for a Writ of Certiorari to the
United States Court of Appeals for the
Federal Circuit**

REPLY BRIEF FOR PETITIONERS

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Prometheus asserts that the Federal Circuit correctly upheld its patents because they describe a “process” that comprises physical steps and includes physical “transformations” that satisfy the Federal Circuit’s “machine or transformation” test. According to Prometheus, embedding the natural scientific principle that there is a correlation between metabolite levels and patient health into this “process” is enough for patentability—even though the *only* step to which Prometheus allegedly made *any* contribution is putting numbers on the biologic correlation, the “transformations” are part of everyday medical practice, and the practical effect of the patent is to preempt *all* uses of the natural correlation in medical research and treatment. That is not the law under this Court’s preemption precedents. Congress never gave Prometheus power to stop Mayo Clinic from disagreeing with Prometheus’s medical judgment and setting forth improved criteria to evaluate patient health. See *Brenner v. Manson*, 383 U.S. 519, 532, 534 (1966) (it was not the “intent of Congress” in Section 101 that “a process claim” should “confer power to block off whole areas of scientific development” by creating a “monopoly of knowledge”).

This case presents issues so important that this Court granted certiorari to consider them five years ago in *LabCorp*—a case indistinguishable from this one in any relevant respect—only to be thwarted by procedural defects that do not exist here. Prometheus’s argument that it now owns a monopoly on a natural correlation that doctors may not even *think* about without paying license fees confirms that this Court’s intervention is urgently needed, as *amici* American College of Medical Genetics and other medical organizations, AARP, and leading medical laboratories all explain.

1. Prometheus is wrong in asserting (Opp. 11) that all its claims cover a “process” comprising the steps of administering certain drugs to a patient, measuring metabolites into which the body naturally converts those drugs, and recognizing that metabolite levels may indicate a need to adjust dosage. Claim 46—quoted in our Petition (at 4-5) but nowhere even mentioned by Prometheus—broadly preempts medical judgments determining the relevance of particular metabolite levels to patient health. The sweeping breadth of that claim—breadth Prometheus successfully argued for below (see Pet. App. 84a-86a)—refutes its contention that “concrete steps” (Opp. 16) narrow its claims.

The additional action Prometheus relies upon in the other claims—providing the patient with a drug—does not narrow those claims. Any physician seeking to understand metabolite levels must administer the drug first. It is impossible to use the correlation without doing so. The “administration” step adds nothing of substance to the claims and does not narrow their scope.

None of Prometheus’s claims requires a physician to do anything in particular with the metabolite determination. See C.A. App. 11041-11043. So Prometheus’s claims monopolize every possible use that a physician could make of the correlations. Although Prometheus now protests that these patents “do not prevent anyone from using [the] correlations in basic research” or “other treatment methods,” the facts found by the district court and left undisturbed by the Federal Circuit show that its claims are that broad. Pet. App. 38a-39a. Indeed, Prometheus asserted them against a

medical researcher, Dr. el-Azhary, who was trying to find a better range for a different disease. Pet. 6-8.

2. The “transformations” Prometheus identifies likewise do nothing to narrow its claims or make them less preemptive of biologic correlation. The first is merely the natural metabolism of the drug in the human body. Indeed, the patients already had been so “transformed” for wholly unrelated purposes when Prometheus found pre-existing information about them in a database. This “transformation” is not part of the invention and should not preempt other researchers from using in different ways natural correlations found in such data.

The second “transformation” is of a patient’s blood sample when it is removed from the body and tested. But that is nothing more than the “observer effect”: everything is transformed when sampled and measured. There is no way for any physician to do research or treat a patient without such a “transformation,” so it does nothing to narrow the preemptive effect of Prometheus’s claims.

As this case demonstrates, the Federal Circuit’s “machine or transformation” test gives far too much significance to physical transformations that have no limiting effect on the scope of a claim and do not prevent it from preempting all uses of a natural phenomenon. Although transformations can be relevant to patentability, they must reflect the underlying preemption standard, not simply replace it. That the Federal Circuit characterized the activity in Prometheus’s claims as patent-eligible “transformations” underscores the inadequacy of its “machine or transformation” test, which permits abuses of the patent system that the rule against preempting natural laws was designed to prevent.

3. Prometheus’s contention that *LabCorp* “presented different issues” from this case centers on these same assertions that its claims embed natural correlations in a “process” involving “transformations.” Opp. 27-28. But this Court granted certiorari in *LabCorp* to decide the validity of claims identical in all legally relevant respects to those involved here.

The steps in *LabCorp* involved using any test to assay a patient’s body fluid to determine the level of an amino acid, then correlating that level with a deficiency in B vitamins “such that any doctor necessarily infringes the patent merely by thinking about the relationship after looking at a test result.” 548 U.S. at 132. The claimant argued that, although any assay might be used and the correlation was a natural phenomenon, the “process” combining these steps amounted to “an inventive diagnostic test.” Oral Arg. Tr., No. 04-607, at 42 (U.S. Mar. 21, 2006). As here, petitioner asked this Court to decide whether patenting this “process” improperly monopolized a basic scientific relationship in the form of a naturally occurring correlation between a substance in the body and patient health. Only procedural defects prevented this Court from deciding that issue. And three Justices nevertheless believed the issue so important to “those who engage in medical research, who practice medicine, and who as patients depend upon proper health care” that an “authoritative answer” was necessary. 548 U.S. at 126.

Differences between the two patents are immaterial. The initial step Prometheus adds to some claims is administration of a drug that Prometheus did not invent (a step absent from claim 46 in any event). That a synthetic drug is administered

and biologically converted into metabolites does not distinguish this case from *LabCorp* (Opp. 28), where the assayed amino acids occurred naturally, because Prometheus has nothing to do with the drug, its administration, the metabolites into which the body naturally converts the drug, or the assay used to measure the metabolites. Each of these steps in the “process” was well understood long before Prometheus’s patent claims. See Pet. 3-4.

To throw into the description of the claim “process steps” that involve nothing new and that center on a natural metabolic reaction is a drafter’s trick. Far from distinguishing *LabCorp*, it implicates the rule cited by Justices Breyer, Stevens, and Souter that describing a natural law “in the abstract patent language of a ‘process’” does not make it less a natural law: “one can reduce any process to a series of steps. The question is what those steps embody.” 548 U.S. at 137-138; see *Diehr*, 450 U.S. at 192 (refusing to “allow a competent draftsman to evade the recognized limitations on the type of subject matter eligible for patent protection”). Likewise, it does not matter to patentability that unpatented steps of the process “involved the transformation of blood” as it was tested, when the focus of the claim was “a simple natural correlation.” *LabCorp*, 548 U.S. at 136-137. Where “qualities are the work of nature,” “packaging” that makes no difference to the way the natural principle operates is “not enough” for patentability. *Funk Bros.*, 333 U.S. at 130-132.

The final step in Prometheus’s claims covers a physician’s mental correlation of the level of metabolites a patient’s body produced with a safe and effective drug dose. See Pet. 5. According to Prometheus, its claims therefore result in “valuable

diagnostic information.” Opp. 28. But the same was true of the claim in *LabCorp*, which likewise sought to exert “control over doctors’ efforts to use [a natural] correlation to diagnose vitamin deficiencies in a patient,” which respondent argued was a “useful, concrete, and tangible result.” 548 U.S. 134, 136. As in *LabCorp*, Prometheus has described in process language “no more than an instruction to read some numbers in light of medical knowledge.” *Id.* at 137; see *LabCorp.*, Oral Arg. Tr., No. 04-607, at 42 (“simply to be aware of that natural phenomenon is all that correlation consists of”) (Scalia, J.). Here and in *LabCorp* the legal principle is the same: observing test results to check for biologic correlations that inform the physician’s diagnosis and treatment may not be monopolized under accepted principles forbidding patents on biological laws or correlations.

4. Prometheus incorrectly contends that this Court has invalidated only patents that themselves *claim* a natural phenomenon. Opp. 21-22. But the prohibition in this Court’s decisions is broader, extending to claims that *effectively preempt* all uses of a natural phenomenon. *Gottschalk v. Benson*, which Prometheus fails to discuss, held that the exception to patentability applies when a claim’s “practical effect” is “a patent on the [natural phenomenon] itself,” because the claim would “wholly pre-empt” all uses of the natural phenomenon. 409 U.S. at 71-72. Thus, where a claim recites a law of nature or mathematical algorithm, a court looks to whether the claim seeks protection for the phenomenon “in the abstract” or instead implements the phenomenon “in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect.”

Diehr, 450 U.S. at 191-192. There is no doubt on which side of this dividing line Prometheus's claims fall. As demonstrated above and in our Petition, Prometheus claims for itself every possible use of a natural correlation between metabolite levels and patient health.

5. This case is like *Benson* and *Parker v. Flook*—decisions Prometheus ignores—and unlike *Diehr*, which Prometheus wrongly claims is analogous. Together, these decisions provide clear guidance here. The claims in *Benson* and *Flook* recited computations without reciting particular activities to be accomplished using the computation, with the result that the claims covered all uses of the computation. For that reason, this Court held the claims to be invalid. In contrast, the *Diehr* claims recited an algorithm, the Arrhenius equation, but also recited specific real-world physical action to be undertaken with the algorithm (opening and closing an injection mold), which left open the possibility that others could make different, non-infringing uses of the computation. Hence in *Diehr* there was no preemption.

The relevant rule of law established by these decisions is the one identified in *Diehr* when it distinguished *Benson* and *Flook*: “respondents here do not seek to patent a mathematical formula” but “a process of curing synthetic rubber” that while it “employs a well-known mathematical equation” does “not seek to pre-empt the use of that equation, * * * only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process.” 450 U.S. at 187.

Contrary to Prometheus's argument (Opp. 11-12), its claims are not analogous to those upheld in

Diehr. Unlike the patentee in *Diehr*, Prometheus did not recite a particular use of the natural correlation to treat patients in a particular way. Instead, like the claimants in *Benson* and *Flook*, Prometheus's claims cover the use of the natural correlation in every manner possible, making its claims invalid under this Court's preemption standard.

6. We do not argue that Prometheus's claims are unpatentable because they include a "mental step" (Opp. 20), but because they preempt all thinking about a natural biologic correlation. The cases Prometheus cites are thus inapt. *Arrhythmia* stressed that the claim there "d[id] not encompass subject matter transcending what Dr. Simson invented." 958 F.2d at 1059. Prometheus's claims *do* prohibit use of the correlation between metabolite levels and patient health, transcending any "discovery" by Prometheus. *Abele* upheld a claim that applied an algorithm to CAT scans. That claim did not prohibit mental steps and the court found unpatentable another claim that preempted all uses of the algorithm. 684 F.2d at 908.

To be sure, the Federal Circuit upheld patents here and in *LabCorp* that, because of their preemptive effect, fail this Court's Section 101 standards. But there is no reason to think—yet—that "literally thousands" of patents preempt medical research and treatment based on well understood and easily detected natural correlations. It is precisely to prevent placing vast areas of scientific thought off-limits to researchers and physicians that this Court's review is urgently needed.

7. Although this Court granted review of the issue presented five years ago in *LabCorp*—where three Justices thought it important to decide the

merits “sooner rather than later” despite procedural defects (548 U.S. at 134)—Prometheus contends that review is “premature.” The question presented is ripe for consideration and delay would obstruct medical progress and harm patient health

Only the Federal Circuit has jurisdiction to address the patentability of natural biologic correlations. Prometheus thus concedes that its ruling here creates “consistent nationwide patent law” concerning the application of Section 101 to such correlations, an issue of “great importance” with “widespread effects.” Opp. 29-30. There is no reason to believe that further percolation in the Federal Circuit will better illuminate the issue presented. Prometheus says the Federal Circuit has only begun to flesh out its machine or transformation test and apply it to medicine (Opp. 28), but its decisions here and in *LabCorp* show clearly, in unanimous opinions reflecting full trial records and extensive amicus participation, how it will apply the “transformation” test to sustain patents that contribute nothing new to medicine yet have broad preclusive effect on research, diagnosis, and treatment.

The cost of delay in addressing the question presented is substantial. The practical consequence of the Federal Circuit’s ruling is that more patent claims turning on natural correlations will be filed and more infringement claims will be made. That will deter medical researchers from trying to improve scientific understanding of those correlations or even, as Dr. el-Azhary’s experience shows, from testing different correlations for use in treating different diseases.

These disincentives to medical progress and optimal treatment are real. It is well documented

that “[t]he notice function [of patents] does not always work,” so that “[c]learance costs” are high. JAMES BESSEN & MICHAEL J. MEURER, PATENT FAILURE 8, 10 (2008). If “mental correlations” may be patented, a physician or researcher would “nee[d] to check a very large number of patents” to be sure that no license is required for a proposed treatment, test, or research, and even then “it would be very difficult to know what [the patents’] boundaries were”—uncertainty that creates “an unavoidable risk of disputes and litigation” that is a powerful disincentive to innovation. *Id.* at 8-9, 27. The threat from “patent trolls”—“patentees who opportunistically take advantage of poor patent notice to assert patents against unsuspecting firms”—magnifies the risk that medical professionals face. *Id.* at 17.

Leading scholars have explained that allowing patents on “abstract ideas,” like taking mental note of natural biologic correlations, leads to claims over ideas “unknown to the inventor” and means “future inventors face reduced incentives because they have to obtain a license” in order to improve upon (or even disprove) the patented correlation. BESSEN & MEURER, *supra*, at 199-200. Rules against patenting “abstract ideas” or “natural rules” are essential to prevent “patents from covering entire concepts,” leaving room for innovators to work out new uses of abstractions and natural phenomena “without fear of patent liability.” DAN L. BURK & MARK A. LEMLEY, THE PATENT CRISIS AND HOW THE COURTS CAN SOLVE IT 123-124 (2009); see *LabCorp*, 548 U.S. at 138 (patents over natural phenomena “inhibit doctors from using their best medical judgment,” force them to enter unnecessary license agreements, “divert resources” from healthcare to “searching patent

files,” and “raise the cost of health care while inhibiting its effective delivery”).

Nothing in 35 U.S.C. § 287(c) suggests that Congress intended courts to adopt a rule with these adverse consequences. Opp. 33. That narrow exemption for certain acts by a physician does not address the scope of Section 101.

Monopolizing knowledge of basic physiological correlations—thereby freezing medical practice and opinion—would be injurious to millions of patients. Such patents place doctors in a position of violating medical ethics rules (Br. of Am. Coll. of Med. Genetics *et al.*, at 9-11) and stifle free speech to the detriment of patient health. Pet. 27. As the AARP and medical associations explain in their briefs, they drive up the cost of care and prevent organizations like the Mayo Clinic from improving testing criteria for the benefit of patient health. Good medical practice and the Nation’s goal of containing medical costs should not be held hostage in this fashion.

8. *Bilski*’s pendency does not lessen the need for plenary review, because *Bilski* will not settle the issue here. It involves the patentability of a method of financial risk management light years removed from the natural correlation of metabolite levels to patient health. And in the patent area, it is well understood that “industry-specific” “judicial tailoring” is necessary to accommodate the “diversity of industry needs and experience.” *LabCorp*, 548 U.S. at 135; BURK & LEMLEY, *supra*, at 104, 108. Indeed, the United States explicitly recognized that *Bilski* is an “unsuitable vehicle” to determine the “patent eligibil[ity]” of “medical diagnostic techniques” because it “doesn’t present * * * any question regarding those technologies.” Oral Arg. Tr., No. 08-964, at

36, 47 (U.S. Nov. 9, 2009); accord U.S. Br. in *Bilski*, No. 08-964, at 40. Patentees and patent defendants alike need certainty in this critical area of medical research and treatment.

CONCLUSION

This Court should grant plenary review, or, at a minimum, grant, vacate, and remand in light of this Court's decision in *Bilski*.

Respectfully submitted.

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