

Janice M. Mueller, *Patent-Ineligible Methods of Treatment*, in *MUELLER ON PATENT LAW, VOL. I (PATENTABILITY AND VALIDITY)* (Wolters Kluwer Law & Business 2012), last revised October 2015

Chapter 3. Patent-Eligible Subject Matter

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[E] Methods of Treatment

[1] Overview

Less than two weeks after the Federal Circuit's decision in *Research Corp. v. Microsoft Corp.*, analyzed in the previous subsection,¹⁷⁸ the Circuit in December 2010 sustained the §101 eligibility of medical treatment claims in *Prometheus Laboratories Inc. v. Mayo Collaborative Services*.¹⁷⁹ The Supreme Court had remanded *Prometheus* to the Federal Circuit for reconsideration post-*Bilski v. Kappos*.¹³⁷ The Federal Circuit's decision to uphold the §101 validity of the claims in *Prometheus* (for the second time)¹⁸⁰ suggested that the appellate court viewed method of medical treatment claims as fundamentally different and inherently more

¹⁷⁸ See *supra* §3.02[D][4][e] (“Federal Circuit Decisions Applying ‘Abstract Idea’ Exception to Process Patent Eligibility”).

¹⁷⁹ 628 F.3d 1347 (Fed. Cir. 2010).

¹³⁷ See *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 561 U.S. 1040, 130 S. Ct. 3543 (2010) (granting certiorari in *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, 581 F.3d 1336 (Fed. Cir. 2009), vacating Federal Circuit’s judgment in *Prometheus*, and remanding *Prometheus* to Federal Circuit “for further consideration in light of *Bilski v. Kappos*, 561 U.S. —, 130 S.Ct. 3218, — L.Ed.2d — (2010)”).

¹⁸⁰ *Prometheus Labs., Inc. v. Mayo Collaborative Services*, 628 F.3d 1347 (Fed. Cir. 2010). As noted, the cited 2010 case was the Federal Circuit's second decision in *Prometheus v. Mayo*. The Federal Circuit had first confronted the case in *Prometheus Labs. Inc. v. Mayo Collaborative Services*, 581 F.3d 1336 (Fed. Cir. 2009). In its 2009 decision, the Federal Circuit held that a district court had erred as a matter of law in finding that Prometheus's asserted medical treatment claims were not patent-eligible under §101 and in granting summary judgment of invalidity to the accused infringer. In reaching its judgment of invalidity, the district court had applied the Federal Circuit's then-controlling MORT test.

After the Supreme Court's 2010 decision in *Bilski v. Kappos* holding that the Federal Circuit's MORT test was merely a useful and important clue but not a dispositive test for §101 process eligibility, *see* 130 S. Ct. at 3226–3227, the Court vacated and remanded the Federal Circuit's 2009 *Prometheus* decision. In December 2010, the Federal Circuit on remand held for a second time that Prometheus's asserted method claims were drawn to statutory subject matter. Hence the Federal Circuit again reversed the district court's grant of summary judgment of invalidity under §101.

likely to fit comfortably within §101 than business method claims of the type at issue in *Bilski*.¹³⁸ The Supreme Court did not agree, however, reversing the Federal Circuit as described below.¹³⁹

[2] Patent-Ineligible “Laws of Nature”

[a] *Prometheus v. Mayo* (Fed. Cir. 2010)

Prometheus's patents in suit claimed methods for calibrating the proper dosage of a drug for treating autoimmune diseases such as Crohn's disease and ulcerative colitis.¹⁴⁰ The goal of the methods was to determine a therapeutically optimal drug dosage while minimizing toxic side effects to the patients taking the drug. More particularly, certain of the claimed methods involved the steps of (1) administering to a patient a drug that, in the patient's body, would metabolize to 6-thioguanine (“6-TG”); then (2) determining the level of 6-TG metabolite in a blood sample taken from the patient; and finally (3) comparing the level determined from the sample against particular predetermined levels, to warn or indicate a need to adjust the drug dosage administered thereafter to the patient. A representative claim recited:

1. A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:

administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and

determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,

wherein the level of 6-thioguanine less than about 230 pmol per 8×10^8 red blood cells *indicates a need* to increase the amount of said drug subsequently administered to said subject and

wherein the level of 6-thioguanine greater than about 400 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.¹⁴¹

A district court held that Prometheus's claims were not patentable under §101 because the claims were drawn to correlations between metabolite levels and therapeutic efficacy and toxicity. According to the district court, such correlations were unpatentable natural phenomena resulting from a natural body process and hence outside of §101.

The Federal Circuit reversed. The appellate court interpreted Prometheus's patent claims as

¹³⁸See *Prometheus*, 628 F.3d at 1356 n.2 (pointing out that “this case does not involve business method patents”).

¹³⁹See *Mayo Collaborative Serv. v. Prometheus Labs.*, 132 S. Ct. 1289 (2012). *Mayo* is analyzed *infra* §3.02[E][2][b].

¹⁴⁰See U.S. Pat. Nos. 6,355,623 and 6,680,302.

¹⁴¹*Prometheus*, 628 F.3d at 1350 (quoting '623 patent claim 1) (emphases added by Federal Circuit).

directed not to a natural phenomenon, but rather to a particular *application* of that phenomenon. Allowing patents on the former would admittedly and entirely preempt the use of the correlation, which would contravene the Supreme Court's teachings in *Gottschalk v. Benson*¹⁴² and *Parker v. Flook*.¹⁴³ In the case at bar, however, the claims passed muster under the Supreme Court's preemption test because the correlation was put to practical use in a method of medical treatment. According to the Federal Circuit, such particular applications of natural phenomenon are patentable in accordance with the Supreme Court's decision in *Diamond v. Diehr*.¹⁴⁴

Prometheus's claimed methods of medical treatment were also patent-eligible under §101 because they satisfied the “transformation” prong of the Federal Circuit's MORT test. Although the Supreme Court in *Bilski v. Kappos* held that the MORT test was not a dispositive inquiry for §101 eligibility, the Supreme Court nevertheless described the MORT test as a “useful and important clue, an investigative tool” for determining whether some claimed inventions are processes under §101.¹⁴⁵ Relying on the continued vitality of the MORT test (at least as an “important clue”), the Federal Circuit in *Prometheus* reaffirmed that the claimed treatment methods transform a human body.¹⁴⁶ In particular, “[t]he asserted claims are in effect claims to methods of treatment, which are *always* transformative when one of a defined group of drugs is administered to the body to ameliorate the effects of an undesired condition.”¹⁴⁷ That the claimed methods treated the human body was made clear by the patents' disclosure as well as the preambles of the asserted claims. These claims recited, for example, a method of optimizing therapeutic efficacy to treat certain gastrointestinal disorders and a method of reducing the toxicity associated with such treatment.

Contrary to validity challenger Mayo's arguments, the “administering” and “determining” steps of Prometheus's claimed methods did not merely involve data gathering for use in the recited correlations. Although these first two steps did gather data, they were part of a larger treatment protocol. The “administering” step provided a drug for treating a disease, and the “determining” step measured the drug's metabolite levels to assess the drug's dosage level during the course of treatment.

The Federal Circuit in *Prometheus* conceded that, as the district court had ruled, the final “wherein” clauses of the asserted claims were merely “mental steps.” These claim clauses required a comparison of the level of 6-TG determined from sampling the patient against a pre-determined level of 6-TG, so as to provide an indication or warning that the drug dosage thereafter administered would need to be adjusted up or down. Such a mental step, *in isolation*, would not be patent-eligible under §101. But Prometheus's claimed invention was the *entire* recited method, comprising the administering and determining steps as well as the final indicating step. “[W]hen viewed in the proper context, the final step of providing a warning

¹⁴²409 U.S. 63 (1972), discussed further in §3.02[D][4][b], *supra*.

¹⁴³437 U.S. 584 (1978), discussed further in §3.02[D][4][b], *supra*.

¹⁴⁴*See Prometheus*, 628 F.3d at 1354, 1355 (citing *Diehr*, 450 U.S. 175 (1981), discussed further in §3.02[D][4][b], *supra*).

¹⁴⁵*Prometheus*, 628 F.3d at 1352–1353.

¹⁴⁶*Prometheus*, 628 F.3d at 1355.

¹⁴⁷*Prometheus*, 628 F.3d at 1356 (emphasis added).

based on the results of the prior steps does not detract from the patentability of Prometheus's claimed methods as a whole.”¹⁴⁸ Although the claimed methods did not require a physician to make any adjustment in a patient's drug dosage, the administering and determining steps provided useful information for such adjustments using particular drugs for a particular patient/subject. Hence, the Federal Circuit concluded, the claims satisfied the transformation prong of the MORT test, as well as the Supreme Court's *Bilski* preemption test.¹⁴⁹

[b] *Mayo v. Prometheus* (U.S. 2012)

In a unanimous decision with potentially vast ramifications for patent-ineligibility,¹⁸¹ the Supreme Court in March 2012 roundly rejected the Federal Circuit's reasoning in *Prometheus* and reversed the appellate court's judgment.¹⁵⁰ In the Supreme Court's view, Prometheus's claims did not recite patentable subject matter under 35 U.S.C. §101 because they expressed

¹⁴⁸*Prometheus*, 628 F.3d at 1358. Because all asserted claims required all three steps, and contrary to defendant Mayo's assertion, “a physician who only evaluates the result of the claimed methods, without carrying out the administering and/or determining steps that are present in all the claims, cannot infringe any claim that requires such steps.” *Id.*

In the author's view, this statement by the *Prometheus* court would seem to ignore the possibility of inducing infringement liability on the part of the physician, as well as the possibility of “joint” infringement by the physician and other actors who are under the common control of a single “mastermind” entity. *See infra* §14.02[A][2].

¹⁴⁹*Prometheus*, 628 F.3d at 1359.

¹⁸¹ *Cf. Alice Corp. Pty. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014) (observing that “[i]n *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 566 U.S. —, 132 S.Ct. 1289, 182 L.Ed.2d 321 (2012), we set forth a framework for distinguishing patents that claim laws of nature, natural phenomena, and abstract ideas from those that claim patent-eligible applications of those concepts”). Thus, the *Mayo* framework applies across the board to all categories of potentially patent-ineligible subject matter.

As elaborated in the discussion of *Alice Corp.*, *supra* §3.01[D] (“Exceptions to §101”), step one of the *Mayo* framework asks “whether the claims at issue are directed to one of those patent-ineligible concepts.” *Alice Corp.*, 134 S. Ct. at 2355 (citing *Mayo*, 132 S. Ct. at 1296-1297). If the answer is yes, then step two of the *Mayo* framework asks “[w]hat else is there in the claims before us?” *Alice Corp.*, 134 S. Ct. at 2355 (quoting *Mayo*, 132 S. Ct. at 1297). To answer the second *Mayo* question, courts should “consider the elements of each claim both individually and ‘as an ordered combination’ to determine whether the additional elements ‘transform the nature of the claim’ into a patent-eligible application.” *Alice Corp.*, 134 S. Ct. at 2355 (quoting *Mayo*, 132 S. Ct. at 1298, 1297). The second step of the *Mayo* framework can be described as “a search for an ‘inventive concept’—i.e., an element or combination of elements that is ‘sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.’” *Alice Corp.*, 134 S. Ct. at 2355 (quoting *Mayo*, 132 S. Ct. at 1294).

In the view of this author, the sweeping language used by the Supreme Court to define step two of the *Mayo* framework has already resulted in unintended negative consequences. *See infra* §3.02[E][2][c], discussing the Federal Circuit's invalidation of a ground-breaking prenatal testing patent in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*, Nos. 2014-1139, 2014-1144, 2015 WL 3634649 (Fed. Cir. June 12, 2015).

¹⁵⁰*Mayo Collaborative Servs. v. Prometheus Labs., Inc.*, 132 S. Ct. 1289 (2012).

unpatentable “laws of nature” accompanied merely by “additional steps consist[ing] of well-understood, routine, conventional activity already engaged in by the scientific community.”¹⁵¹ The additional steps “add[ed] nothing significant beyond the sum of their parts taken separately” and were “not sufficient to transform unpatentable natural correlations into patentable applications of those regularities.”¹⁵²

The Court in *Mayo* initially observed that §101 contains “an important implicit exception” providing that “[l]aws of nature, natural phenomena, and abstract ideas’ are not patentable.”¹⁵³ In the case at bar, the first of these categories—“laws of nature”—encompassed Prometheus’s newly discovered “precise correlations” between metabolite levels in a patient’s blood¹⁵⁴ and the “likelihood that a particular dosage of a thiopurine drug could cause harm or prove ineffective.”¹⁵⁵ The correlations (recited in the “wherein” clauses of representative claim 1 quoted above¹⁵⁶) were “relationships” which, although triggered by human action in the administration of a thiopurine drug, nevertheless “exist[ed] in principle apart from any human action.”¹⁵⁷ The correlation or relation was a “consequence of the ways in which [the drugs] are metabolized by the body—entirely natural processes.”¹⁵⁸ A patent such as Prometheus’s that “simply describes that relation sets forth a natural law,”¹⁵⁹ the Court concluded, even though the “laws of nature” at issue were admittedly “narrow” and likely had “limited applications.”¹⁶⁰

The additional recitation of the “administering” and “determining” steps in Prometheus’s method claims was not enough to “transform an unpatentable law of nature into a patent-eligible *application* of such a law.”¹⁶¹ The Court decreed that

[i]f a law of nature is not patentable, then neither is a process reciting a law of nature, unless that process has additional features that provide practical assurance that the process is more than a drafting effort designed

¹⁵¹*Mayo*, 132 S. Ct. at 1298.

¹⁵²*Mayo*, 132 S. Ct. at 1298.

¹⁵³*Mayo*, 132 S. Ct. at 1293 (quoting *Diamond v. Diehr*, 450 U.S. 175, 185 (1981)).

¹⁵⁴*Mayo*, 132 S. Ct. at 1295.

¹⁵⁵*Mayo*, 132 S. Ct. at 1296.

¹⁵⁶*See supra* §3.02[E][2][a] (“*Prometheus v. Mayo* (Fed. Cir. 2012)”) (quoting representative claim 1 of Prometheus’s U.S. Patent No. 6,355,623). The “wherein” clauses of claim 1 recite as follows:

wherein the level of 6-thioguanine less than about 230 pmol per 8×10^8 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and

wherein the level of 6-thioguanine greater than about 400 pmol per 8×10^8 red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

¹⁵⁷*Mayo*, 132 S. Ct. at 1297.

¹⁵⁸*Mayo*, 132 S. Ct. at 1297.

¹⁵⁹*Mayo*, 132 S. Ct. at 1297.

¹⁶⁰*Mayo*, 132 S. Ct. at 1302.

¹⁶¹*Mayo*, 132 S. Ct. at 1294.

to monopolize the law of nature itself. A patent, for example, could not simply recite a law of nature and then add the instruction “apply the law.”¹⁶²

In the case at bar, the “administering” and “determining” steps did not themselves recite laws of nature, but “neither [were] they sufficient to transform the nature of the claim.”¹⁶³ Both steps were known in the art and represented “well-understood, routine, conventional activity” to scientists in the relevant technology.¹⁶⁴ Taken together with the “wherein” clauses, all the method steps in combination “add[ed] nothing to the laws of nature that is not already present when the steps are considered separately.”¹⁶⁵ In the Court’s view, the claimed series of steps “simply tell doctors to gather data from which they may draw an inference in light of the correlations.”¹⁶⁶

The Court supported its decision denying patent-eligibility in *Mayo* with citation to precedent and policy. It identified the precedent “most directly on point” as its earlier decisions in *Diamond v. Diehr*¹⁶⁷ and *Parker v. Flook*.¹⁶⁸ As detailed earlier in this chapter, *Diehr* and *Flook* both involved the application of mathematical formulae in computer programs used to control industrial processes. The *Mayo* court characterized Prometheus’s method claims as “present[ing] a case for patentability that is weaker than the (patent-eligible) claim in *Diehr* and no stronger than the (unpatentable) claim in *Flook*.”¹⁶⁹ The *Mayo* Court’s characterization of the claimed inventions in *Diehr* and *Flook* as “processes that embodied *the equivalent of natural laws*”¹⁷⁰ demonstrates the wide-ranging applicability of the *Mayo* holding, potentially reaching far beyond

¹⁶²*Mayo*, 132 S. Ct. at 1297.

¹⁶³*Mayo*, 132 S. Ct. at 1297.

¹⁶⁴*Mayo*, 132 S. Ct. at 1298.

¹⁶⁵*Mayo*, 132 S. Ct. at 1298.

¹⁶⁶*Mayo*, 132 S. Ct. at 1298. The Court summarized that

the claims inform a relevant audience about certain laws of nature; any additional steps consist of well-understood, routine, conventional activity already engaged in by the scientific community; and those steps, when viewed as a whole, add nothing significant beyond the sum of their parts taken separately. For these reasons we believe that the steps are not sufficient to transform unpatentable natural correlations into patentable applications of those regularities.

Mayo, 132 S. Ct. at 1298.

¹⁶⁷450 U.S. 175 (1981). *Diehr* is discussed *supra* at 3.02[C] (“Computer-Implemented Processes”).

¹⁶⁸437 U.S. 584 (1978). *Flook* is discussed *supra* at 3.02[C] (“Computer-Implemented Processes”).

¹⁶⁹*Mayo*, 132 S. Ct. at 1299. The *Mayo* opinion also distinguished the patent-ineligible claims of Prometheus with the patentable process claimed in the English case, *Neilson v. Harford*, Webster’s Patent Cases 295 (1841). The *Neilson* process for operating a blast furnace applied the “law of nature” that “hot air promotes ignition better than cold air,” *Mayo*, 132 S. Ct. at 1300, but added to that principle “several unconventional steps (such as inserting the receptacle, applying heat to the receptacle externally, and blowing the air into the furnace) that confined the claims to a particular, useful application of the principle.” *Mayo*, 132 S. Ct. at 1300.

¹⁷⁰*Mayo*, 132 S. Ct. at 1298 (emphasis added).

medical diagnostic subject matter.

In *Diamond v. Diehr*, the Court observed that “the basic mathematical equation, like a law of nature, was not patentable.”¹⁷¹ The overall process claimed in *Diehr* was patent-eligible, however, because the combination of process steps in addition to the recited mathematical formula were not “in context obvious, already in use, or purely conventional.” Rather, the additional steps in *Diehr* “apparently added to the formula something that in terms of patent law's objectives had significance—they transformed the process into an inventive application of the formula.”¹⁷² In contrast, the process steps in *Parker v. Flook* that supplemented the recitation of a mathematical formula for updating alarm limits were “well known,” such that there “was no ‘inventive concept’ in the claimed application of the formula.”¹⁷³

The *Mayo* Court also supported its disqualification of Prometheus's method claims from patent-eligibility as furthering the policy that “patent law [should] not inhibit further discovery by improperly tying up the future use of laws of nature.”¹⁷⁴ Although the “laws of nature” encompassing Prometheus's correlations were “narrow” and of “limited application[,]” the method claims at issue nevertheless implicated this policy concern. By “tell[ing] a treating doctor to measure metabolite levels and to consider the resulting measurements in light of the statistical relationships they describe, [Prometheus's claims] tie up the doctor's subsequent treatment decision whether that treatment does, or does not, change in light of the inference he has drawn using the correlations.”¹⁷⁵ Moreover, the claims “threaten to inhibit the development of more refined treatment recommendations (like that embodied in [accused infringer] Mayo's test), that combine Prometheus' correlations with later discovered features of metabolites, human physiology or individual patient characteristics.”¹⁷⁶ The Court skirted arguments of Prometheus and several *amici* that treating the claimed processes as unpatentable “laws of nature” would significantly chill further medical diagnostic research, responding that it would defer to Congress on such issues.¹⁷⁷

¹⁷¹*Mayo*, 132 S. Ct. at 1298.

¹⁷²*Mayo*, 132 S. Ct. at 1299. The *Mayo* Court's use of the qualifying adjective “inventive” is a troubling regression to pre-1952 Patent Act terminology that circularly required that patentable inventions involve an ill-defined quality of “invention.” See *infra* §9.02[C] (“Replacing ‘Invention’ with Nonobviousness”).

¹⁷³*Mayo*, 132 S. Ct. at 1299 (quoting *Flook*, 437 U.S. at 594). Again, the Court's reliance on the quotation from *Flook* referring to an “inventive concept” as a criteria of §101 patent-eligibility is troubling. See *infra* §9.02[C] (“Replacing ‘Invention’ with Nonobviousness”).

¹⁷⁴*Mayo*, 132 S. Ct. at 1301.

¹⁷⁵*Mayo*, 132 S. Ct. at 1302.

¹⁷⁶*Mayo*, 132 S. Ct. at 1302.

¹⁷⁷See *Mayo*, 132 S. Ct. at 1305 (recognizing “the role of Congress in crafting more finely tailored rules where necessary [citing Plant Patent Act, 35 U.S.C. §§161–164],” and declining to “determine here whether, from a policy perspective, increased protection for discoveries of diagnostic laws of nature is desirable.”).

The Court also rejected the argument of *amicus* United States that the novelty, nonobviousness, and disclosure requirements of 35 U.S.C. §§102, 103, and 112 act as the primary screening tools for patentability. According to the Court, “[t]his approach ... would make the ‘law of nature’ exception to §101 patentability a dead letter.” *Mayo*, 132 S. Ct. at 1303. The Court opined, without citation to

[c] Unintended Consequences of *Mayo*

The Supreme Court's sweeping 2012 decision in *Mayo Collaborative Servs. v. Prometheus Labs., Inc.*¹⁸² was soon to impact the medical diagnostics research community beyond the parties in *Mayo*. In the view of this author, the *Mayo* framework created the potential for (presumably) unintended negative consequences that may chill future medical diagnostic research (an issue raised by Prometheus and various *amici* in *Mayo*). The Federal Circuit's June 2015 decision in *Ariosa Diagnostics, Inc. v. Sequenom, Inc.*,¹⁸³ aptly illustrates the concern. Compelled by the Supreme Court's broad language defining the second step of the *Mayo* framework, the Federal Circuit in *Ariosa* affirmed the invalidation under §101 of a groundbreaking patent on prenatal testing.

More particularly, declaratory judgment defendant Sequenom's U.S. Patent No. 6,258,540 ('540 patent) was directed to certain non-invasive methods of prenatal diagnosis of fetal DNA. Advantageously, the new methods avoided the risks of prior methods involving sampling from the fetus or placenta. In 1997, Drs. Dennis Lo and James Wainscoat discovered the presence in maternal plasma and serum of cell-free fetal DNA ("cffDNA"), a non-cellular fetal DNA that circulates freely in the blood stream of pregnant women. Previously, other researchers had discarded the plasma and serum in maternal blood samples as medical waste. Drs. Lo and Wainscoat developed a method for detecting the small fraction of *paternally* inherited cffDNA in the maternal plasma or serum that could be used to determine fetal characteristics such as gender and genetic defects. The '540 patent owner, Sequenom, commercialized the invention as the MaterniT21 test, which was the first marketed non-invasive prenatal diagnostic test for fetal aneuploidies such as Down's syndrome.¹⁸⁴ The Lo and Wainscoat invention was lauded as a "paradigm shift in non-invasive prenatal diagnosis" and the inventors' article describing the invention was cited more than a thousand times.¹⁸⁵

Although the Federal Circuit in *Ariosa* agreed that the Lo and Wainscoat invention "revolutionized prenatal care,"¹⁸⁶ the court nevertheless held the asserted claims of the '540 patent invalid as directed to a patent-ineligible method under 35 U.S.C. §101 of using a natural phenomenon. While the court did "not disagree that detecting cffDNA in maternal plasma or serum that before was discarded as waste material is a positive and valuable contribution to science," it concluded that "even such valuable contributions can fall short of statutory patentable subject matter, as it does here."¹⁸⁷

Applying step one of the *Mayo* framework (i.e., determining whether the claims at issue are directed to a patent-ineligible concept), the Federal Circuit in *Ariosa* first noted that Sequenom's asserted claims "begin[] and end[]" with natural phenomena. Representative claim 1 of the '540 patent recited:

authority, that "to shift the patent-eligibility inquiry entirely to these later sections risks creating significantly greater legal uncertainty, while assuming that those sections can do work that they are not equipped to do." *Mayo*, 132 S. Ct. at 1304. The Court "decline[d] the Government's invitation to substitute §§102, 103, and 112 inquiries for the better established inquiry under §101." *Mayo*, 132 S. Ct. at 1304. The Court did not explain why, in its view, the §101 inquiry is "better established" than the analysis under §§102, 103, and 112.

¹⁸² 132 S. Ct. 1289 (2012).

¹⁸³ Nos. 2014-1139, 2014-1144, 2015 WL 3634649 (Fed. Cir. June 12, 2015).

¹⁸⁴ See *Ariosa*, 2015 WL 3634649, at *9 (Linn, J., concurring).

¹⁸⁵ *Ariosa*, 2015 WL 3634649, at *9 (Linn, J., concurring).

¹⁸⁶ See *Ariosa*, 2015 WL 3634649, at *8.

¹⁸⁷ *Ariosa*, 2015 WL 3634649, at *8.

1. A method for detecting a paternally inherited nucleic acid of fetal origin performed on a maternal serum or plasma sample from a pregnant female, which method comprises

amplifying a paternally inherited nucleic acid from the serum or plasma sample and

detecting the presence of a paternally inherited nucleic acid of fetal origin in the sample.

As elaborated in the written description of the '540 patent, the claimed method started with obtaining the cffDNA in maternal blood, and then used known amplification tools such as polymerase chain reaction (PCR) to provide a usable sample of paternally inherited cffDNA. According, the Federal Circuit concluded that the claims were directed to naturally-occurring subject matter or phenomena, satisfying step one of the *Mayo* framework.

The Federal Circuit in *Ariosa* next explained that the second step of the *Mayo* framework considers whether “additional elements ‘transform the nature of the claim’ into a patent-eligible application.”¹⁸⁸ The Supreme Court described the second *Mayo* step as a “search for an ‘inventive concept’—i.e., an element or combination of elements that is ‘sufficient to ensure that the patent in practice amounts to significantly more than a patent upon the [ineligible concept] itself.’”¹⁸⁹ A claim that recites a natural phenomenon “must include ‘additional features’ to ensure ‘that the [claim] is more than a drafting effort designed to monopolize the [natural phenomenon].’”¹⁹⁰

Critically to the case at bar, the Federal Circuit read the Supreme Court’s guidance regarding *Mayo* step two to mean that “[f]or process claims that encompass natural phenomenon, *the process steps are the additional features that must be new and useful.*”¹⁹¹ The Circuit determined that, like those in *Mayo*, the process steps in Sequenom’s claims were *not* new and useful:

Using methods like PCR to amplify and detect cffDNA was well-understood, routine, and conventional activity in 1997. The method at issue here amounts to a general instruction to doctors to apply routine, conventional techniques when seeking to detect cffDNA. *Because the method steps were well-understood, conventional and routine, the method of detecting paternally inherited cffDNA is not new and useful.* The only subject matter new and useful as of the date of the application was the discovery of the presence of cffDNA in maternal plasma or serum.¹⁹²

In the view of this author, the Federal Circuit’s conclusion in *Ariosa* that Sequenom’s patent claims were not patent eligible was fundamentally flawed. The Circuit erroneously dissected the '540 patent claims rather than considering the patent eligibility of the method *as a whole*. The heart of the

¹⁸⁸ *Ariosa*, 2015 WL 3634649, at *3 (quoting *Mayo*, 132 S. Ct. at 1298).

¹⁸⁹ *Ariosa*, 2015 WL 3634649, at *3 (quoting *Mayo*, 132 S. Ct. at 1294).

¹⁹⁰ *Ariosa*, 2015 WL 3634649, at *5 (quoting *Mayo*, 132 S. Ct. at 1297).

¹⁹¹ *Ariosa*, 2015 WL 3634649, at *5 (citing *Parker v. Flook*, 437 U.S. 584, 591 (1978) (“The process itself, not merely the mathematical algorithm, must be new and useful.”)).

¹⁹² *Ariosa*, 2015 WL 3634649, at *5 (emphasis added).

court's error was to narrowly view the novelty of the individual "detection" and "amplification" process steps divorced from the subject matter on which they operated, cffDNA. As convincingly explained by in a concurring opinion by Judge Linn, before the claimed invention "*no one* was amplifying and detecting paternally-inherited cffDNA using the plasma or serum of pregnant mothers."¹⁹³ In contrast, the process steps of *Mayo* "were the very steps that doctors were already doing—administering the [thiopurine] drug at issue, measuring metabolite levels, and adjusting dosing based on the metabolite levels. . . ."

In his concurring opinion, Judge Linn grudgingly joined the *Ariosa* court's opinion (invalidating the asserted '540 patent claims under §101) because he felt "bound" to do so "by the sweeping language of the test set out in *Mayo*" In Judge Linn's view, "the breadth of the second part of the test was unnecessary to the decision reached in *Mayo*." The *Mayo* Court "discounted, *seemingly without qualification*, any 'post-solution activity that is purely conventional or obvious.'"¹⁹⁴ To do so effectively ignored the Supreme Court's earlier instruction in its landmark 1981 decision *Diamond v. Diehr*¹⁹⁵ that "'a new combination of steps in a process may be patentable even though *all* the constituents of the combination were well-known and in common use before the combination was made.'"¹⁹⁶

Judge Linn convincingly contrasted the facts of *Mayo* with those of *Ariosa*. In *Mayo*, the "conventional activity" recited in the process steps (i.e., administering a readily-available drug, measuring metabolite levels, and adjusting dosage accordingly) was already well-known at the time of the invention. In contrast, in *Ariosa* "the amplification and detection of cffDNA had never before been done."¹⁹⁷ In Judge Linn's view, Sequenom's '540 patent claimed "a new method that should be patent eligible."¹⁹⁸ Its invention was "nothing like the invention at issue in *Mayo*."¹⁹⁹ Sequenom had "'effecuate[d] a practical result and benefit not previously attained,'" such that under traditional principles its patent should have been upheld.²⁰⁰ Unfortunately, Judge Linn concluded, the Supreme Court's "blanket dismissal of

¹⁹³ *Ariosa*, 2015 WL 3634649, at *9 (Linn, J., concurring) (emphasis in original).

¹⁹⁴ *Ariosa*, 2015 WL 3634649, at *9 (Linn, J., concurring) (quoting *Mayo*, 132 S. Ct. at 1299 (original alterations omitted)) (emphasis added).

¹⁹⁵ 450 U.S. 175 (1981). *Diehr* is further examined *supra* §3.02[C].

¹⁹⁶ *Ariosa*, 2015 WL 3634649, at *9 (Linn, J., concurring) (quoting *Diamond v. Diehr*, 450 U.S. 175, 188 (1981)) (emphasis added).

¹⁹⁷ *Ariosa*, 2015 WL 3634649, at *9 (Linn, J., concurring) (emphasis added).

¹⁹⁸ *Ariosa*, 2015 WL 3634649, at *9 (Linn, J., concurring).

¹⁹⁹ *Ariosa*, 2015 WL 3634649, at *10 (Linn, J., concurring).

²⁰⁰ *Ariosa*, 2015 WL 3634649, at *10 (Linn, J., concurring) (quoting *Le Roy v. Tatham*, 63 U.S. 132, 135-136 (1859); citing generally Jeffrey A. Lefstin, *Inventive Application: a History*, 67 FLA. L.REV. 565 (2015), available at SSRN: <http://ssrn.com/abstract=2398696> or <http://dx.doi.org/10.2139/ssrn.2398696>) (analyzing traditional notions of patent eligibility of newly discovered laws of nature). Professor Lefstin, author of the law review article cited by Judge Linn in his concurrence, also commented in the PATENTLYO blog:

[T]he *Ariosa* opinion appears to endorse dissection of the claim to a degree not only contrary to *Diehr*, but beyond that suggested by *Flook* itself. While *Flook* explained that "the process itself" must be new and useful, *Ariosa* suggests that the individual steps of the process must be new and useful, and identifies the discovery of cffDNA as "[t]he only subject matter new and useful as of the date of the application." Given that most inventions consist of rearrangements of old

conventional post-solution steps leaves no room to distinguish *Mayo* from this case.”²⁰¹

Another troubling aspect of the Federal Circuit’s decision in *Ariosa* is its cramped and conclusory analysis of the role of preemption concerns in the §101 patent-eligibility inquiry. The appellate court observed that “[t]he Supreme Court has made clear that the principle of preemption is the basis for the judicial exceptions to patentability.”²⁰² Thus, in the Circuit’s view, “questions on preemption are *inherent* in and resolved by the § 101 analysis.”²⁰³ When a patent’s claims are deemed to recite patent-ineligible subject matter under *Mayo*, “as they are in this case, preemption concerns are *fully addressed and made moot*.”²⁰⁴ The Circuit also refused to distinguish between partial and complete preemption, rejecting Sequenom’s arguments that its ‘540 patent claimed a narrow and specific application of using cffDNA that did not encompass numerous other uses of cffDNA. In the court’s view, “[w]hile preemption may signal patent ineligible subject matter, *the absence of complete preemption does not demonstrate patent eligibility*.”²⁰⁵

elements, it is difficult to understand how the court can refrain from addressing the claim steps as an ordered whole, as mandated by *Mayo* itself.

And that highlights what is perhaps the most puzzling (or disturbing) aspect of *Ariosa*. According to Judge Linn’s concurrence, the steps of the method *were* new: at the time of the invention, no one was amplifying paternally-inherited sequences from maternal serum or plasma, because no one thought that those fractions contained significant amounts of fetal DNA. That contrasts with *Mayo*, where the acts recited in the method were identical to those performed in the prior art. . . .

If the step of amplifying paternally inherited DNA from serum or plasma was new, by what analysis could the court could regard it as “well-understood, routine, and conventional activity”? One way would be to sub-dissect that step into the conventional step of obtaining a cell-free fraction, and the conventional step of amplifying a sample containing DNA. That approach seems to lead to the *reductio ad absurdum* that most biotechnology processes are patent-ineligible, because they consist of the conventional steps of transferring drops of fluid from one tube to another. . . .

Jeffrey A. Lefstin, *Ariosa v. Sequenom and the Path Ahead for Subject-Matter Eligibility*, PATENTLYO (June 14, 2015), <http://patentlyo.com/patent/2015/06/sequenom-subject-eligibility.html>. Another excellent and thoughtful analysis of *Ariosa* and the “natural products” debate is Leslie Fischer, *Guest Post -- On Ariosa and Natural Products*, PATENT DOCS (Sept. 27, 2015), <http://www.patentdocs.org/2015/09/guest-post-on-ariosa-and-natural-products.html>.

²⁰¹ *Ariosa*, 2015 WL 3634649, at *9 (Linn, J., concurring).

²⁰² *Ariosa*, 2015 WL 3634649, at *7 (citing *Alice Corp. v. CLS Bank Int’l*, 134 S.Ct. 2347, 2354 (2014) (“We have described the concern that drives this exclusionary principal as one of pre-emption”)).

²⁰³ *Ariosa*, 2015 WL 3634649, at *7 (emphasis added).

²⁰⁴ *Ariosa*, 2015 WL 3634649, at *7 (emphasis added).

²⁰⁵ *Ariosa*, 2015 WL 3634649, at *7 (emphasis added). See also Jeffrey A. Lefstin, *Ariosa v. Sequenom and the Path Ahead for Subject-Matter Eligibility*, PATENTLYO (June 14, 2015), <http://patentlyo.com/patent/2015/06/sequenom-subject-eligibility.html> (commenting that “the Federal

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Circuit seems to be suggesting that arguments regarding preemption can be taxed against the patentee in the § 101 inquiry, but not counted in the patentee's favor.”).