On March 20, 2012, the US Supreme Court issued an opinion in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.* (No. 10-1150) regarding the patent eligibility of method claims, finding the particular claims in Prometheus’ patents, relating to methods of treatment, *patent-ineligible* under 35 U.S.C. § 101. The Court also remanded the *Association for Molecular Pathology v. USPTO and Myriad Genetics, Inc.* (No. 11-725) case to the Federal Circuit for consideration in light of the decision in *Mayo v. Prometheus*. Both cases have been avidly followed by the life sciences industry for guidance on the standard for patent eligibility under Section 101.

### A. Background: The Lower Court Decisions in the *Mayo* Case

The patent claims in the *Mayo* case are directed to treating gastrointestinal disorders by optimizing the drug dose based on levels of certain metabolites. Below is a representative claim from the patents-in-suit, US Patent No. 6,355,623 and US Patent No. 6,680,302:

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

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

   (b) **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 $8 \times 10^8$ 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 $8 \times 10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

The Supreme Court’s decision in the *Mayo* case reinforces that, under Section 101, claims must not embody laws of nature. Also, importantly, the Supreme Court made it clear that such claims must not preempt essentially all uses of such laws of nature. The Court emphasized that a patentee must not monopolize an entire field (in this case a method of medical treatment) by broadly claiming a method that covers mental processes and natural phenomenon. Instead, the claims must be limited to the actual method the patentee invented which, by virtue of being useful, must be limited to a particular application of the natural phenomenon.

As we discuss further below, the Supreme Court’s decision differs from the Federal Circuit’s application of Section 101 in important respects; for example, placing greater emphasis on preemption. It remains to be seen if the Federal Circuit will follow suit, starting with the upcoming remand in *Myriad*.
Prometheus sold a diagnostic kit that embodied this process. The controversy arose when Mayo announced that it intended to begin using and selling its own test (using different metabolite levels to determine toxicity than in Prometheus’ test). The district court determined that Mayo’s test infringed, but found the above (and additional) claims unpatentable as claiming only correlations between thiopurine drug metabolite levels and therapeutic efficacy and toxicity. Prometheus Labs. v. Mayo Collaborative Services, No. 04-CV-1200 (S.D.Cal. 2008). The court found that the “administering” and “determining” steps were merely data-gathering steps and the “warning” step, embodied by the wherein clauses, was only a mental step that did not specify any actual step or change in dosage.

The Federal Circuit reversed and held the above (and additional) claims patentable, in large part because it considered the “administering” and “determining” steps as transformative under the “machine-or-transformation” test. Prometheus Labs. v. Mayo Collaborative Services, 628 F.3d 1347, 1352 (Fed. Cir. 2010). Even though the court held that the claims covered a “particular application of naturally occurring correlations, and accordingly did not preempt all uses of the recited correlations between metabolite levels and drug efficacy or toxicity,” id. at 1355, its opinion focused on the transformative steps that actively changed the patient or determined correlations and not on preemption (either generally or in the area of personalized medicine).

B. The Supreme Court’s Decision in the Mayo Case
The Supreme Court, in a unanimous opinion delivered by Justice Breyer, reversed the Federal Circuit, stating, “Prometheus’ patents set forth laws of nature … namely, relationships between concentrations of certain metabolites in the blood and the likelihood that a dosage of a thiopurine drug will prove ineffective or cause harm.” Mayo Collaborative Services v. Prometheus Labs, Inc., No. 10-1150, at 8 (March 20, 2012) (emphasis added). The Court noted that, “[w]hile it takes a human action (the administration of a thiopurine drug) to trigger a manifestation of this relation in a particular person, the relation itself exists in principle apart from any human action.” Id. Essentially, in the Court’s opinion, the claims did not have statements that “apply natural law”; instead, they merely embodied natural relationships between metabolite levels and therapeutic efficacy or toxicity. Id.

The Court explained that the “administering” step refers to the relevant audience (the doctors), and that simply limiting abstract ideas to application in a particular technological environment would not be enough to impart patentability. Id. at 9. Next, the “determining” step simply instructs doctors to determine metabolite levels, regardless of the process used. Id. at 10. These processes, which the patent stated were well known in the art, could not be used to impart patentability. Id. Also, the wherein clauses simply “tell a doctor about the relevant natural laws, at most adding a suggestion that he should take those laws into account when treating his patient.” Id. at 9. Lastly, the combination of these steps added nothing to the laws of nature that each embodied separately. Id. at 10.

One of the Court’s major concerns was the potential inhibition of further discovery by allowing patents that might preempt future and unpredicted directions in technology (here methods of treatment in the area of personalized medicine). For example, the Court rejected Prometheus’ argument that the claims were sufficiently narrow to have limited applications or threaten preemption of a broad area of technology. Narrow or not, the Court expressed concern that such claims “threaten to inhibit the development of more refined treatment recommendations … that combine Prometheus’ correlations with later discovered features of the metabolites, human physiology or individual patient characteristics.” Id. at 18. The Court also noted that the “‘determining’ step [was] set forth in highly general language covering all processes that make use of the correlations after measuring metabolites, including later discovered processes that measure metabolite levels in new ways.” Id.

C. What Can We Do in Light of Mayo?
The Federal Circuit on remand in the Myriad case may shed more light on what level of articulation a method-of-treatment claim must contain and to what extent it will synchronize its view of Section 101 in the life sciences field with that of the Supreme Court. Importantly, it remains to be seen if preemption will figure prominently in the Federal Circuit’s view of patent eligibility. Also, the Supreme Court did not place much stock in the transformative nature of process steps, which was important to the Federal Circuit’s ultimate conclusion of patent eligibility. One factor that may influence the outcome is that, while the Prometheus claims were directed to a method, the claims in Myriad call for a composition.
Similarly, in *Myriad*, the only claims found patentable by the Federal Circuit contained a number of transformative steps. *Association for Molecular Pathology v. U.S.P.T.O. and Myriad Genetics, Inc.*, 653 F.3d 1329 (Fed. Cir. 2011) (finding the transformative steps of “growing” cells in the presence or absence of a test compound, followed by “determining” the rate of grow and finally “comparing” the growth rates in the presence and absence of the test compound as imparting patentability).

Presently, in light of the *Mayo* case, the requirement broadly appears to be that, to be patent-eligible, a process must articulate clear steps that go beyond those that are “obvious, already in use, or purely conventional.” *Id.* at 12.

Thus practitioners should continue to stress, if applicable, that their diagnostic applications, e.g., correlations of drug level and efficacy/toxicity, are poorly understood and not routine, conventional activity engaged in by the scientific community.

In applying the decision in *Mayo* however, it would also be prudent to include specific steps that impart novelty and neutralize concerns of preemption of future improvements. For example, if one discovers a natural phenomenon, e.g. that a mutation causes a particular disease, certain diagnostic applications of this phenomenon should be patentable. However, drafting a claim to include simply detecting the mutation and correlating it with the disease may not be enough. To be patent-eligible, the claim may have to articulate more specific steps. While it remains unclear what the “more” needs to be, it would likely include adding therapeutic (or method of treating) steps based on the diagnostic information, rather than simply detecting or considering natural phenomenon, for example, steps for treating the patient based on this information. Bottom line, including at least one specific physical or biological claim element that is not “conventional” (see PTO memo below) would presently appear to be a good approach for addressing the issue presented in *Mayo* when drafting claims to biological or chemical processes.

Examiners must continue to ensure that claims, particularly process claims, are not directed to an exception to eligibility such that the claim amounts to a monopoly on the law of nature, natural phenomenon, or abstract idea itself. In addition, to be patent-eligible, a claim that includes an exception should include other elements or combination of elements such that, in practice, the claimed product or process amounts to significantly more than a law of nature, a natural phenomenon, or an abstract idea with conventional steps specified at a high level of generality appended thereto.

The *Mayo* decision may be applied narrowly, such as to claims that are broad, like the ones at issue in the case, or where there is a threat of preemption. Also, it remains to be seen how the Federal Circuit will apply *Mayo*, both with respect to patent eligibility in the area of personalized medicine and diagnostic claims, and in articulating a standard under Section 101.

Disclaimer: Fish & Richardson P.C. represented Mayo in the above-referenced cases.
The FDA’s Recent Guidance on Biosimilars

On February 9, 2012, the US Food and Drug Administration (FDA) published the long-awaited guidance documents on the criteria for development of biosimilars, for which an abbreviated approval pathway is envisioned under the Biologics Price Competition and Innovation Act of 2009. The Act establishes two categories of generic biologics: biosimilars and “interchangeable” biologic products. The draft guidance addresses only the criteria for approval of a biosimilar product (which is defined as one that is “highly similar” to the pioneer product notwithstanding minor differences in clinically inactive components). Here we provide a brief summary of the recent guidance from the FDA.

The guidance lays out a “stepwise” approach to demonstrating biosimilarity, starting with extensive structural and functional characterization of the proposed and referenced product. This characterization is the foundation of a biosimilar development program and informs the type and extent of additional studies that the FDA will require.

According to the guidance documents, the structural characterization should use state-of-the-art technology comparing primary structure, higher-order structure, enzymatic post-translational modifications, and other potential variants and modifications. This characterization should be performed on several lots to determine any variability in the manufacturing process. The functional characterization involves comparing the proposed and reference product with regard to biologic activity and potency, as well as the mechanism of action, to demonstrate that there are no clinically meaningful differences.

The FDA guidance also proposes that applicants conduct animal studies, including animal toxicity studies. Animal toxicity studies are useful when uncertainties remain about the safety of the proposed product after the structural and functional characterization that should be addressed before embarking on clinical studies. The animal studies envisioned by the FDA will likely include pharmacokinetic (PK) and pharmacodynamic (PD) studies, which can be incorporated into a single animal toxicity study if appropriate. Animal immunogenicity studies will generally not be required, unless there is a concern of immunogenic reactions from impurities or excipients.

According to the guidance documents, clinical studies will also likely be required. The scope will depend upon uncertainty regarding biosimilarity between the proposed and reference product after structural and functional characterization and animal studies. The FDA has emphasized that human PK and PD studies, as well as immunogenicity comparisons, will generally be required. Additional clinical studies may be required to demonstrate safety and effectiveness. The FDA envisions discussing the type and extent of clinical studies with the applicant, depending upon what residual uncertainties remain about biosimilarity based on the foundational and animal studies.
The Patent Prosecution Highway 2.0 Program in the USPTO

On January 29, 2012, the USPTO instituted the Patent Prosecution Highway (PPH) 2.0 program. This article provides a summary of this program and the requirements for participation.

The PPH program is a work-sharing program based on agreements with other national and regional patent offices that allows examiners to leverage the search and examination results from patent offices in participating countries, thereby speeding up the examination process for counterpart applications. The PPH program expedites examination by making the application “special” and thus having it examined out of turn. It is important to remember, however, that under the PPH program, the fact that an application filed in a participating jurisdiction has allowable claims does not mean that similar claims in the corresponding application will be automatically allowed; examiners are still required to conduct their own search and examination based on the patent law of the office examining the patent application. The PPH program merely allows for an expedited examination.

There are three types of PPH programs. The first type is the “regular” PPH program, where an applicant receiving a ruling from the Office of First Filing (OFF) that at least one claim is patentable may request that the Office of Second Filing (OSF) expedite the examination of corresponding claims in the counterpart application filed in the OSF. The United States Patent and Trademark Office (USPTO) currently has PPH agreements with the following 20 jurisdictions: Australia, Austria, Canada, China, Denmark, European Patent Office, Finland, Germany, Hungary, Iceland, Israel, Japan, Korea, Mexico, Norway, Russia, Singapore, Spain, Taiwan, and the United Kingdom.

The second type of PPH program is the PCT-PPH program, where an applicant receiving a favorable Written Opinion or International Preliminary Report on Patentability from one of the participating offices acting as an international authority may request that a corresponding national phase entry or a national application filed at the USPTO be expedited. The USPTO currently has PCT-PPH agreements with the following 11 jurisdictions: Australia, Austria, Canada, European Patent Office, Finland, Japan, Korea, Norway, Russia, Spain, and Sweden.

The third type of program is the PPH 2.0 program, which is a new version of the PPH MOTTAINAI pilot program that began on July 15, 2011, and attempts to simplify PPH requirements and procedures. The PPH 2.0 program commenced on January 29, 2012, and will run for a trial period of one year ending on January 28, 2013 (but may be terminated earlier if participation exceeds a manageable level for the participating offices). The PPH 2.0 program is not available for plant applications, design applications, reissue applications, reexamination proceedings, and applications subject to a secrecy order. The USPTO and PPH 2.0 participating offices will evaluate the results of the PPH 2.0 program to determine whether and how the program should be implemented after the trial period. The USPTO currently has PPH 2.0 agreements with the following eight jurisdictions: Australia, Canada, European Patent Office, Finland, Japan, Russia, Spain, and the United Kingdom.

The PPH 2.0 program applies to PPH requests filed in the USPTO on or after January 29, 2012, based on claims that have been allowed by one of the above-listed PPH 2.0 participating offices in a counterpart application filed in that office. Thus, until January 28, 2013, the “regular” PPH program will be available only for US applications relying on allowable claims from Austria, China, Denmark, Germany, Hungary, Iceland, Israel, Korea, Mexico, Norway, Singapore, and Taiwan.
Unlike the regular PPH program, which uses an OFF and OSF framework (as described above), the PPH 2.0 program uses an Office of Earlier Examination (OEE) and Office of Later Examination (OLE) framework. Under the PPH 2.0 program, participation in the PPH may be requested on the basis of an allowance from any patent family application from any participating office, regardless of whether the participating office was the office of first filing. To be eligible to participate in the PPH 2.0 program at the USPTO, applicants must meet the following four requirements:

1. At least one claim in a patent application must have been determined to be allowable/patentable by one of the PPH 2.0 participating offices.

2. The US application and the corresponding application filed in the PPH 2.0 participating office that has at least one allowable/patentable claim must have the same priority or filing date (examples are provided in the annex to the USPTO’s notice on the PPH 2.0 program referenced at the end of this article).

3. All the claims in the US application, as originally filed or amended, must “sufficiently correspond” to one or more of the allowable/patentable claims in the application filed in the PPH 2.0 participating office. A claim is considered to “sufficiently correspond” where, accounting for differences due to translations and claim format, the claim in the US application is of the **same or similar scope** as a claim indicated as allowable in the application filed in the PPH 2.0 participating office. A claim in the US application which is **narrower in scope** than the claims indicated as allowable in the application filed in the PPH 2.0 participating office will also sufficiently correspond **if presented** as a claim **dependent** upon a claim which is of the same or similar scope as a claim indicated as allowable in the application filed in the PPH 2.0 participating office.

4. Substantive examination of the US application must not have begun. The issuance of a restriction requirement in the US application does not constitute the beginning of substantive examination. As long as the examiner has not started working on the first action on the merits, an applicant can still request participation in the PPH 2.0 program. If the examiner has started work on the first action on the merits, one can file a continuing application and file a request for participation in the PPH 2.0 program in the continuing application.

If all four of the above requirements are met, in order to apply for the PPH 2.0 program an applicant will need to:

1. Submit a request for participation in the PPH program (Form PTO/SB/20). The request forms are jurisdiction specific and can be found on the USPTO PPH web page (one of the references at the end of this article links to a sample request).

2. Submit a copy of the latest office action prior to issuance of the Decision to Grant a Patent in the application from the PPH 2.0 participating office if the application was not allowed in a first office action. If the office action is not in English, an English translation (which may be a machine translation) must be submitted. There is no need to provide a statement that the English translation is accurate. In addition, there is no need to submit a copy of the Decision to Grant a Patent or a copy of the allowable claims.

3. Submit an information disclosure statement (IDS) listing the documents cited in all the office actions from the PPH 2.0 participating office and copies of the cited documents in the IDS, unless such an IDS has already been filed in the counterpart US application.

4. Fill in a claims correspondence table in the request or in a separate table. The claims correspondence table must indicate how **all** the claims in the US application correspond to the allowable/patentable claims in the application filed in the PPH 2.0 participating office.

5. The request and all supporting documents must be submitted to the USPTO via EFS-Web and indexed with the document description “Petition to make special under Patent Pros Hwy.” Any preliminary amendment or IDS submitted with the PPH 2.0 documents must be separately indexed as a preliminary amendment and an IDS, respectively.

A petition fee is not required.
If the request does not meet all the requirements of the PPH 2.0 program or provide the required documents listed above, the applicant will be notified and any defect(s) identified. The applicant is then given one opportunity to cure the defect(s) by filing a renewed request. If the request is not perfected, the applicant will be notified and the application will await action in its regular turn. Note that during the period when the applicant is notified of any defect(s), the USPTO will not suspend action on the application. Thus, if a first substantive action is issued during the period between when an applicant is notified of any defect(s) with the initially filed request and the filing of a renewed request, the renewed request will be dismissed.

Once a proper request is filed, the request is generally decided within two months of its filing. If the PPH is granted, the examiner will generally examine the application in two to three months from the grant of the PPH request, provided the application has completed all its pre-exam processing and is ready for examination. An application that has been given special status remains under special status during the entire prosecution.

After the request has been granted, any claims added or amended during prosecution must continue to “sufficiently correspond” to one or more allowable claims in the application filed in the PPH 2.0 participating office. A claim in the US application that introduces a category of claims different from those indicated as allowable in the application filed in the PPH 2.0 participating office (e.g., adding claims drawn to a process of manufacturing a product when only product claims have been allowed) is not considered to sufficiently correspond even if the new claims are dependent on claims which sufficiently correspond to allowable claims in the application filed in the PPH 2.0 participating office. Any amendments to the claims must include a statement certifying that sufficient correspondence is maintained. If the certification is omitted, the amendment will not be entered.

A request for participation in the PPH 2.0 program carries over to a request for continued examination but does not carry over to a continuing application.

According to the USPTO, the benefits of the PPH programs include accelerated examination, a higher allowance rate (90% for PPH cases vs. 50% for non-PPH cases), fewer actions per disposal when compared to non-PPH cases, and reduced pendency. PPH 2.0 and other PPH programs are worth considering alongside accelerated examination and prioritized Track I procedures as ways of expediting examination of a patent application.

Useful Links:
1. USPTO PPH web page (includes FAQs, PPH brochure, PPH video, and forms): http://www.uspto.gov/patents/init_events/pph/index.jsp
2. PPH information portal site with statistics and information from all participating offices: http://www.jpo.go.jp/cgi/linke.cgi?url=/ppph-portal/index.htm
3. USPTO notice titled “Revised Requirements for the Patent Prosecution Highway (PPH) Program to Implement PPH 2.0 with Participating Offices” http://www.uspto.gov/web/offices/com/sol/og/2012/week10/TOC.htm#ref15
4. Sample request for PPH 2.0: http://www.uspto.gov/forms/sb0020jp.pdf
America Invents Act – Stay Up to Date

The America Invents Act (AIA), enacted on September 16, 2011, changes the landscape for those seeking to challenge the validity of an issued patent outside of litigation. The AIA introduces several new mechanisms for levying challenges to the validity of a granted patent at the United States Patent and Trademark Office (USPTO), namely ex parte examination, inter partes reexamination, post-grant review, inter partes review, and supplemental examination.

Fish & Richardson has recently hosted a series of webinars discussing these mechanisms. More information, including archived presentations and audio, is available at www.fr.com/post-grant-webinar-series/

Articles contributed by:
Gauri M. Dhavan (Boston), Irene E. Hudson (NY), Joseph Koipally (Boston), S. Peter Ludwig (NY)

For more information, please contact:

Gwilym J.O. Attwell, Delaware
302-778-8458
attwell@fr.com

Steven C. Carlson, Silicon Valley
650-839-5197
steven.carlson@fr.com

Teresa A. Lavoie
Southern California/Twin Cities
858-678-4307, 612-766-2006
lavoe@fr.com

S. Peter Ludwig, New York
212-641-2320
ludwig@fr.com

Gauri M. Dhavan, Boston
617-521-7057
dhavan@fr.com

Irene E. Hudson, New York
212-641-2325
hudson@fr.com

Terry G. Mahn, Washington, DC
202-626-6421
mahn@fr.com

To subscribe to any of our Life Sciences newsletters, visit: www.fr.com/subscriptions

Fish & Richardson is one of the largest law firms in the United States practicing exclusively in the areas of intellectual property, litigation, and technology law. Well recognized as a leader in intellectual property, the firm handles more patent litigation than any other firm in the world and has successfully litigated biologic and other patent cases for leading pharmaceutical and life sciences companies. Our experienced patent litigators work closely with our patent prosecutors and regulatory attorneys to provide solutions that maximize the return on our clients’ significant investments in research and development.