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Patent-eligible Subject Matter in the Life Sciences in the United States

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【Abstract】 The concept of "patent eligible subject matter"-whether an invention fits into a category of subject matter recognized as eligible for patenting-has become an increasingly important factor in recent years when determining validity of life sciences claims in the United States, both in the courts and in the United States Patent and Trademark Office (USPTO). The Supreme Court of the United States formulated in 2012 a two-step test for patent eligibility that the lower courts and the USPTO have struggled to interpret and apply. Analysis of various court opinions in the years since 2012 provides some indication of what types of claims are or are not considered to pass this test, and the USPTO periodically issues guidance documents (most recently in January 2019) to help patent examiners understand how to apply the test when examining claims. Widespread unhappiness with the evolving standards for patent eligibility has led many in the life sciences industry to call for legislation resetting the standards to something less vague, subjective, and onerous to patentees. Meanwhile, careful claim drafting is essential to maximize the likelihood of obtaining patent-eligible claims.

【Keywords】 § 101 patent-eligible subject matter life sciences methods compositions

1. Introduction

When the Supreme Court of the United States (Supreme Court) issued a series of decisions in 2012-2014 interpreting what categories of inventions are eligible for patenting in the United States, the results dramatically reshaped the patent landscape for a number of technologies, particularly life sciences and computer software. The impact of these decisions has made it far more difficult to obtain valid claims covering, for example, diagnostic methods and naturally occurring biomolecules, and presumably has rendered many such previously-granted claims invalid.

This article begins by summarizing the basic statutory framework defining what is patentable in the United States. We then trace how the courts' views regarding patent-eligible subject matter in the life sciences field have evolved over the years. We describe approaches the USPTO has taken to apply the court-made patent-eligibility standards when examining applications. Our article then discusses some legislative solutions proposed by various organizations in recent years, solutions intended to set new statutory standards for what constitutes patent-eligible subject matter and thereby address the perceived ambiguity of the court-made standards as well as the undue impact the standards have had on an entire industry. The ar-

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ticle concludes with practice tips for minimizing patent-ineligibility problems when drafting claims.

2. The Statutory Framework

In order to obtain a patent in the United States, a patent applicant must comply with several statutory provisions. For example, a patentable claim must be drawn to a novel and non-obvious invention ; the language of the claim must be definite ; the patent application must provide a description of the invention sufficient to show that the applicant was in possession of the claimed invention ; and the application must teach the skilled person how to make and use the claimed invention. In addition to these requirements, a threshold inquiry is whether the claimed invention is within a category of subject matter considered to be eligible for patenting in the United States. Section 101 of Title 35 of the United States Code defines four categories of inventions that are patent-eligible : processes/methods, machines, manufactures, and compositions of matter. Despite this broadly permissive statutory language, United States courts have, over the years, interpreted § 101 to exclude laws of nature, physical phenomena, and abstract ideas. Recent Supreme Court decisions further elaborating on these judicially-created exclusions have significantly affected how lower courts and the USPTO determine what inventions are patent-eligible subject matter.

3. Recent Jurisprudence Regarding § 101

In the last few years, United States courts have issued some significant opinions interpreting § 101 in the life sciences. These are discussed below in the context of different categories of claims : diagnostic method claims, method of treatment claims, process claims, and claims drawn to compositions of matter.

3.1. Diagnostic Method Claims

The Supreme Court addressed patent-eligibility in the context of diagnostic claims in *Mayo Collaborative Servs. v. Prometheus Labs., Inc.,* 566 U.S. 66 (2012). Prometheus claimed methods of selecting a dose of a thiopurine drug that would optimize therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder. Doctors had previously been treating autoimmune diseases with thiopurine drugs, but had difficulty determining the ideal dose that balanced efficacy and potential side effects, because patients metabolize the drugs differently. Prometheus identified correlations between thiopurine metabolite levels in the blood and the efficacy and side effects of the treatment. Prometheus' patent claimed methods of administering thiopurine drugs and then determining the levels of thiopurine metabolites in the patient's blood. The claim concluded with a "wherein" clause describing how metabolite concentration correlated with efficacy and side effects, but did not specify any particular action to be taken based on that information.

The *Mayo* Court introduced a new two-step test for determining patent eligibility of method claims. Under the *Mayo* test, a court must first determine whether a claim is directed to a patent-ineligible concept, i.e., a law of nature, natural phenomenon, or abstract idea. If so, the court must then search for an "inventive concept" by determining whether additional elements of the claim "transform the nature of the claim" into a patent-eligible *application* of the law of nature/natural phenomenon/abstract idea.

The *Mayo* Court decided that Prometheus' claims did not pass this new eligibility test. Under the first step of the test, the Court found that the claims were directed to a law of nature : the correlation between concentrations of certain metabolites in the blood and the likelihood that a given dosage of a thiopurine drug will prove ineffective or cause harm. In step two, the Court found that the recited "administering," "determining," and "wherein" elements were not "sufficient to transform the nature of the claim." According to

the Court, the administering step "simply refers to the relevant audience, namely doctors who treat patients with certain diseases with thiopurine drugs," and the "wherein" clause, at most, added a suggestion that those doctors consider the test results when making their treatment decisions.

Following the *Mayo* decision, the lower courts were left with the unenviable task of interpreting and applying the vague test set forth by the Supreme Court. In all five diagnostic method cases considered by the Court of Appeals for the Federal Circuit (CAFC) since then, the CAFC found the claims to be patent-ineligible.

The first of these five cases was *In re BRCA1- and BRCA2- Hereditary Cancer Test Patent Litigation*, 774 F.3d 755 (Fed. Cir. 2014), which involved both claims drawn to compositions of matter (discussed below in section 3.4) and methods of identifying a mutation in a patient's *BRCA1* gene by comparing the patient's *BRCA1* DNA sequences with wild-type *BRCA1* sequences. The latter claims required that the comparison be accomplished either by amplifying the subject's *BRCA1* gene using a set of primers and then sequencing, or by using a probe to detect certain alleles in the patient. The court found the claims ineligible as directed to an abstract idea under the *Mayo* test. Applying the first *Mayo* step, the CAFC found that the method claims were "directed to the patent-ineligible abstract idea of comparing BRCA sequences and determining the existence of alterations." In the second *Mayo* step, the court found that the elements describing the way in which the sequences are compared (via probe or via amplification and sequencing) "set forth well-understood, routine and conventional activity engaged in by scientists at the time of Myriad's patent applications" and did not add enough to make the claims patent eligible.

The patent at issue in *Ariosa Diagnostics, Inc. v. Sequenom, Inc*., 788 F.3d 1371 (Fed. Cir. 2015), involved Sequenom's discovery that maternal blood plasma harbored a small amount of cell-free fetal DNA (cffDNA) that the fetus inherited from its father, and that could be used to determine a fetus's gender and identify genetic defects. Sequenom's patent claimed methods of using cffDNA that included the steps of amplifying the cffDNA contained in a sample of plasma from a pregnant female and detecting the paternally inherited cffDNA. Despite acknowledging that the invention was a valuable contribution in that it permitted analyzing the fetus's genome without the risk of obtaining cells directly from the fetus, the CAFC held that the claims were not patent eligible because they were directed to a naturally occurring phenomenon (existence of cffDNA in maternal blood), and their remaining steps (preparing, amplifying, and detecting DNA, including PCR techniques) were merely "conventional."

In *Genetic Technologies Ltd. v. Merial LLC*, 818 F.3d 1369 (Fed. Cir. 2016), the invention stemmed from the discovery that, instead of detecting an allele of a particular gene by looking at the coding region of the gene, one could detect the allele indirectly by amplifying and analyzing non-coding regions linked to the coding region. The claims at issue required amplifying non-coding region DNA known to be linked to a coding region and analyzing the amplified DNA to determine if it correlated to the allele of interest. The CAFC held that the claims were drawn to ineligible subject matter because they were directed to a "law of nature" : the linkage between non-coding and coding sequences and the tendency of such non-coding sequences to be representative of the linked coding sequences. The court also noted that the steps of amplifying DNA and analyzing the amplified sequence were well known in the art at the time of filing and did not constitute an "inventive concept" under step two of the *Mayo* test.

The claims in *The Cleveland Clinic Foundation et al. v. True Health Diagnostics, LLC*, 859 F.3d 1352 (Fed. Cir. 2017), recited methods for characterizing a subject's risk for cardiovascular disease by determining the level of myeloperoxidase (MPO) in a sample from the patient and comparing that with the MPO levels in control subjects not having cardiovascular disease. De-

pendent claims limited the way MPO is detected (such as by flow cytometry) and how the MPO values in the control subjects are evaluated. The court found the claims to be directed to a naturally occurring phenomenon (correlation of the level of MPO in a biological sample to the presence of cardiovascular disease), and opined that the process steps merely described the correlations and did not recite any new detection or analytical techniques.

More recently, the CAFC in *Roche Molecular Systems, Inc. v. Cepheid*, 905 F. 3d 1363 (Fed. Cir. 2018), addressed claims that were directed to a method for detecting *Mycobacterium tuberculosis* (MTB) in a biological sample, as well as composition of matter claims we discuss in section 3.4 below. Roche's scientists had discovered eleven position-specific "signature nucleotides" diagnostic for MTB. The method claims required amplifying DNA segments using PCR primers customized for the signature nucleotides and detecting the presence or absence of the amplification product to determine if MTB is present. The CAFC held that the claims were directed to a natural phenomenon (correlating the presence of these signature nucleotides with the presence of MTB), and found that, since the PCR step was well-known and the determining step was merely a mental process, there was no inventive concept, and thus the claims were patent-ineligible.

The above cases lead to a view that, after *Mayo*, the CAFC is categorically unwilling to uphold any method of diagnosis claims that simply recite a natural correlation (regardless of how novel it is) and employ routine methods to detect it. The courts seem to be demanding that the claims specify a novel way of measuring something, or some other detail that they can latch onto as providing an "inventive concept" in Step 2 of the *Mayo* test. Since many innovations in the diagnostic industry involve discovery of a new correlation, and not a new detection tool, it has become very difficult to find a path forward to patent-eligibility for diagnostic method claims.

3.2. Method of Treatment Claims

The Supreme Court has not spoken on the patent eligibility of method of treatment claims, other than to provide a remark in *Mayo* indirectly implying that, unlike the diagnostic methods claimed by Prometheus, methods of treatment with drugs will generally qualify as patent eligible : "[u]nlike, say, a typical patent on a new drug or a new way of using an existing drug, the [Prometheus] patent claims do not confine their reach to particular applications of those laws."

The CAFC recently had occasion to consider that dictum from *Mayo* when evaluating the method of treatment claimed in *Vanda Pharmaceuticals Inc. v. West-Ward Laboratories, Inc.,* 887 F.3d 1117 (Fed. Cir. 2018). Vanda's claim was drawn to a method of treating schizophrenia that involved determining the patient's CYP2D6 metabolizer genotype and administering iloperidone in a dose range that varied in a particular way depending on the patient's CYP2D6 genotype. The CAFC concluded that the claim was patent-eligible under the first step of the *Mayo* test, holding that the claims were directed to a method of using iloperidone to treat schizophrenia, and not to a correlation or other natural law. However, despite this hopeful clue that claims drawn to methods of treatment may be spared the wholesale invalidation we have seen applied to diagnostic method claims, it is important to note that only two of the three judges on the *Vanda* panel agreed with the decision. It remains to be seen what other CAFC panels will say about patent eligibility of other treatment claims, or whether the Supreme Court will eventually weigh in with a definitive ruling on this subject.

3.3. Process Claims

The CAFC applied the *Mayo* test to process claims in *Rapid Litigation Mgmt, Ltd. v. CellzDirect, Inc*., 827 F.3d 1042 (Fed. Cir. 2016), ultimately finding the claims to be patent-eligible. The patent at issue in that case involved a process for cryopreserving hepatocytes in a manner that produced cells able to survive multiple

free-thaw cycles. The conventional wisdom was that hepatocytes could be frozen only once, making it difficult to pool hepatocytes collected from multiple donors over time. The patentee obtained claims directed to a method of producing a preparation of cryopreserved hepatocytes that included steps of subjecting hepatocytes that had been previously frozen and thawed to density gradient fractionation to separate viable cells from non-viable cells, and refreezing the collected viable cells. In analyzing the claims under step one of the *Mayo* test, the court considered the defendant's position that the claims were directed to a natural phenomenon, but determined they were not. The court reasoned that the claims were directed to a better way of preserving hepatocytes, not to the inherent ability of some hepatocytes to survive multiple free-thaw cycles. The court noted that the end result of the claimed method was not simply an observation or detection of the ability of hepatocytes to survive multiple freeze-thaw cycles, but rather was a new and useful method of preserving hepatocyte cells—a useful application of the discovery. The court went on to say that step two of the *Mayo* test did not need to be reached in this case, but added that, even if the second step were considered, it would also result in a finding of patent-eligibility. According to the court, while the individual steps of freezing and thawing were well known and routine if viewed in isolation, the claimed combination of steps, taken as a whole, was far from routine or conventional.

3.4. Composition Claims

Important Supreme Court cases assessing patent eligibility of composition claims in the life sciences date back at least to 1948. In *Funk Brothers Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127 (1948), the Court considered a claim drawn to an inoculant for leguminous plants comprising a plurality of selected "mutually non-inhibitive strains" of different bacterial species of the genus *Rhizobium*, and found the claim was not patent-eligible as it encompassed what the Court interpreted to be a product of nature. Though the claimed mixture did not occur in nature, each individual strain of bacteria did. And though discovering the particular strains that were "mutually non-inhibitive" when combined required effort and was not predictable, the Court dismissed these facts, saying "The combination of species produces no new bacteria, no change in the six species of bacteria, and no enlargement of the range of their utility. Each species has the same effect it always had. The bacteria perform in their natural way. Their use in combination does not improve in any way their natural functioning. They serve the ends nature originally provided, and act quite independently of any effort of the patentee."

In 1980, the Supreme Court decided another significant case pertaining to biological compositions : *Diamond v. Chakrabarty*, 447 U.S. 303 (1980). The patentee had identified four plasmids encoding enzymes capable of degrading four different oil components. These plasmids could be transferred to a *Pseudomonas* bacterium, which itself has no ability to degrade oil, converting that bacterium into a genetically engineered organism potentially useful for the treatment of oil spills. The issue in this case was whether a composition claim drawn to the genetically engineered bacterium was patent-eligible. The Court said it was, stating that "the patentee had produced a new bacterium with markedly different characteristics from any found in nature and one having the potential for significant utility. His discovery is not nature's handiwork, but his own ; accordingly it is patentable subject matter."

Thirty-three years later, the Supreme Court revisited the patent eligibility of compositions of matter in *Ass'n for Molecular Pathology v. Myriad Genetics, Inc.*, 569 U.S. 576 (2013). Myriad had discovered the location and nucleic acid sequences of the *BRCA1* and *BRCA2* genes that, when mutated, are associated with predisposition to breast and ovarian cancers. The Supreme Court was asked to decide whether claims directed to "isolated" DNA encoding BRCA1 or BRCA2, or alternatively to isolated *complementary* DNA (cDNA)

encoding BRCA1 or BRCA2, were patent eligible subject matter.

The Court held that a segment of a naturally occurring DNA is a product of nature and does not become patent eligible under § 101 merely because it has been "isolated" from the surrounding genetic material. In contrast, the Court found Myriad's *cDNA* claims to be patent eligible, reasoning that BRCA1 and BRCA2 cDNAs lack the introns present in their genomic counterparts, and so do not exist in nature. In the Court's view, a patentee "unquestionably creates something new when cDNA is made" (at least when the corresponding genomic sequence contains introns).

The Court's decision finding claims to "isolated DNA" ineligible under § 101 disrupted decades of unquestioned acceptance of such claims by both the USPTO and the courts. It instantly rendered an untold number of issued claims invalid.

The first post-*Myriad* case in which the CAFC considered patent eligibility of composition claims was *In re Roslin Institute (Edinburgh)*, 750 F.3d 1333 (Fed. Cir. 2014), which related to the famous "Dolly the Sheep" : the first mammal ever cloned from an adult somatic cell. The claims sought by Roslin, but rejected by the USPTO, were directed to a live-born clone of a pre-existing, non-embryonic, donor mammal, where the mammal was selected from cattle, sheep, pigs, and goats. The court's central inquiry was whether the claimed subject matter possessed "markedly different characteristics" from any animal found in nature. The court found that Roslin's chief innovation was the preservation of the donor DNA such that the clone is an exact copy of the mammal from which the somatic cell was taken. As Dolly herself was said to be an exact genetic replica of another sheep, that led to the court's conclusion that the claimed clones were ineligible under § 101 because they did not possess characteristics "markedly different" from those of farm animals found in nature.

The CAFC's *In re BRCA1- and BRCA2- Hereditary Cancer Test Patent Litigation* opinion discussed above in the context of diagnostic assay claims also dealt with composition claims challenged on patent eligibility grounds. The composition claims were directed to pairs of single stranded DNA primers used to detect mutant BRCA1 and BRCA2 genes in a sample. The court stated that a DNA molecule with a function similar to that found in nature can be patent-eligible as a composition of matter only if it has a unique structure, different from anything found in nature. It held the claimed primer pairs ineligible under this standard because they necessarily have sequences identical to a portion (sense or antisense) of the naturally occurring BRCA1 or BRCA2 genomic sequence and are structurally identical to the ends of DNA strands found in nature. The court rejected the argument that the fact that the primer pairs were synthetically created meant they were patent eligible. It also rejected arguments that the primer pairs were not naturally occurring because single-stranded DNA cannot be found in the human body, explaining that (as held in *Myriad*) separating DNA from its surrounding genetic material is not an act of invention. It further rejected Myriad's position that the primers have a fundamentally different function than the same sequences incorporated into a naturally occurring genomic DNA strand, noting that the natural DNA would similarly function to bind to complementary nucleotide sequences.

A subsequent CAFC case that similarly involved consideration of DNA primer claims along with diagnostic assay claims is the *Roche Molecular Systems, Inc. v. Cepheid* case described above. Roche argued that the claimed primers, which hybridize to a particular MTB gene at a particular site, were chemically and structurally distinct from any nucleic acid that occurs in nature because the primers have a 3' end and a 3' hydroxyl group, which are absent in the circular chromosome that constitutes the naturally-occurring MTB genome. The court dismissed this argument as not a sufficient distinction from the naturally occurring DNA, and declared the primer claims to be invalid as drawn to patent-ineligible subject matter.

4. Section 101 Guidance from the United States Patent and Trademark Office

Applying the *Mayo* test in a consistent manner across technologies has proven to be difficult and created significant uncertainty for all interested parties. The USPTO's approach employs three steps, labeled Step 1, Step 2A, and Step 2B. Step 1 requires the examiner to confirm whether the claim is directed to a category of invention recognized under the statute as patent-eligible, i.e., is the claim drawn to a process, machine, manufacture or composition of matter? If the claim clears that low bar, then the examiner must proceed to Step 2A (corresponding to the first step of the *Mayo* test), determining whether the claim is "directed to" a "judicially recognized exception," i.e., a law of nature, a natural phenomenon (e.g., product of nature), or an abstract idea. If it is not directed to one of those exceptions, the claim satisfies § 101, and there is no need to go on to Step 2B. But if the claim is directed to one of those exceptions, the examiner must next determine under Step 2B (i.e., the second *Mayo* step) whether the claim provides an inventive concept by reciting "additional elements that amount to significantly more than the judicial exception." For the above analysis, the examiner is asked to construe the claim under its broadest reasonable interpretation and to analyze the claim as a whole, rather than limitation-by-limitation.

As the standards to be applied at each of Steps 2A and 2B are determinative of whether a given claim passes muster under those steps, the USPTO has been trying to digest the Supreme Court and CAFC case law to guide patent examiners and administrative patent judges of the Patent Trial and Appeal Board (PTAB) in how to apply the *Mayo* test in a way that produces reasonably consistent and predictable results across all technologies. To that end, the USPTO periodically issues updated "guidance" documents discussing new case law as it comes out and attempting to integrate it into a coherent approach. Most recently, the USPTO issued its "2019 Revised Patent Subject Matter Eligibility Guidance" in January 2019[1]. In its 2019 guidance, the USPTO has refined the analysis under Step 2A in two ways.

The first change in the 2019 guidance pertains to how examiners are to ascertain whether a claim recites an "abstract idea" type of judicial exception. The previous approach directed examiners to rely on analogy to the wording of claims held by a court to recite an abstract idea ; under the new guidance, examiners are instead to determine whether the limitation in question falls within any of the following subject matter groupings of abstract ideas :

mathematical concepts—mathematical relationships, mathematical formulas or equations, mathematical calculations ;

certain methods of organizing human activity—fundamental economic principles or practices (including hedging, insurance, mitigating risk) ; commercial or legal interactions (including agreements in the form of contracts ; legal obligations ; advertising, marketing or sales activities or behaviors ; business relations) ; managing personal behavior or relationships or interactions between people (including social activities, teaching, and following rules or instructions) ; and

mental processes—concepts performed in the human mind (including an observation, evaluation, judgment, opinion).

The above change to how examiners are to define "abstract idea" does not affect the other broad categories of judicial exceptions that are more often at issue for life sciences inventions : "law of nature and "natural phenomenon." However, the *second* change to Step 2A introduced by the 2019 guidance is likely to have a major effect in applicants' favor on how the USPTO weighs patent eligibility of *all* types of claims under *all* of the categories of judicial exceptions, resulting in many fewer rejections under § 101.

This important second change to the eligibility anal-

ysis draws a distinction between a claim that merely *recites* a judicial exception and one that is "*directed to*" a judicial exception, with the latter being the critical factor under the USPTO's revised Step 2A. Under the new framework, merely reciting a judicial exception does not equate to being "directed to" that exception. Instead, if a claim recites a judicial exception, it must then be analyzed to determine whether the claim integrates that recited judicial exception into a *practical application* of that exception. If it does so, the claim is not "directed to" a judicial exception, and the eligibility analysis ends there, at Step 2A, with a conclusion that the claim is patent-eligible. If the claim does not integrate that recited judicial exception into a practical application, then it is deemed to be "directed to" that judicial exception under Step 2A, and the examiner must move on to Step 2B in order to make the final determination of patent eligibility by determining if there is some "inventive concept" in the claim, other than the judicial exception.

The 2019 guidance directs examiners to assess "integration into a practical application" by : (a) identifying whether there are any additional elements recited in the claim beyond the judicial exception ; and (b) evaluating those additional elements individually and in combination to determine whether they integrate the exception into a practical application. Importantly, the examiner is explicitly told not to take into consideration whether the additional elements are "routine" or "conventional" or "well-known," instead reserving that consideration for Step 2B, if reaching Step 2B is necessary. And reaching Step 2B is necessary only if the claim fails Step 2A, i.e., fails to integrate the judicial exception into any practical application.

This change to how Step 2A is applied has had a noticeable effect already on patent prosecution, with examiners increasingly willing to withdraw prior rejections under § 101. However, the USPTO's guidance are merely guidance for examiners, and do not have the force of law. They may be withdrawn or modified at any time. And whether the courts will agree with the USPTO's new analysis remains to be seen.

5. Legislative Solutions

The recent jurisprudence redefining entire categories of inventions as "patent-ineligible" is based on ambiguous standards that appear nowhere in the statute, have retroactively invalidated whole categories of life sciences patents, and are difficult to apply consistently. These problems have led many in the life sciences industry to call for a legislative fix. At least three major intellectual property organizations have responded by proposing amendments to the statutory language of § 101 : Intellectual Property Owners Association (IPO)[2], American Intellectual Property Law Association (AIPLA)[3], and American Bar Association/ Intellectual Property Law Section (ABA/IPL)[4]. All three proposed amendments attempt to clarify the standards for patent eligibility by including in the statute a new subsection (b) that specifies what would constitute exceptions to eligibility, essentially overruling the Supreme Court's vaguely stated judicial exceptions and, in the process, permitting more inventions to qualify as patent-eligible. The IPO and AIPLA proposals both say that a claimed invention is patent-ineligible *only if* the claimed invention, as a whole, exists in nature independently of and prior to any human activity, or exists solely (or can be performed solely) in the human mind, and both of these proposals characterize these two specified exceptions as the "sole exceptions" to make it clear to the courts that they are not free to make up additional ones. By insisting that the claimed invention be assessed "as a whole," these proposals reject the current propensity of the courts to focus the eligibility analysis on what the court deems to be the "gist" of the claim, which can be embodied in a single limitation or even not recited in the claim at all.

The ABA/IPL proposal takes a different approach to defining what constitutes an exception to eligibility, focusing on whether the claim "preempts" all practical

applications of a law of nature, natural phenomenon, or abstract idea. According to this proposed amendment, when a claim does preempt all practical applications of a law of nature, natural phenomenon, or abstract idea, the claim "may be denied eligibility" (though the proposed language apparently does not *require* that it be denied eligibility). Furthermore, the proposed amendment takes care to say that, if the subject matter of the claim, taking into account all limitations of the claim as a whole, is a practical application of a law of nature, natural phenomenon, or abstract idea, the claim's patent eligibility "shall not be negated." The ABA/IPL proposal does not seem otherwise to address the existing jurisprudence regarding patent eligibility, and it is not clear from the awkward wording of the proposed amendment what effect if any it would have on reining in the courts' freedom to create new exceptions in the future.

All three proposals address another significant issue pertaining to much of the jurisprudence regarding patent eligibility : the courts' tendency to bring into the § 101 analysis questions regarding topics that should not have any bearing on patent eligibility : novelty, obviousness, and scope of enablement. This issue typically comes into play when a court is attempting to assess whether a claim that includes a limitation deemed to be a "natural phenomenon" or "abstract idea" is an attempt to patent that exception, or instead has other limitations constituting "something more" or an "inventive concept" that could make the claim patent-eligible subject matter. A limitation deemed to be "well-known" or "routine" is typically simply dismissed by the court as not qualifying as the essential "something more" or "inventive concept." This unfortunate confusion of prior art issues with patent eligibility issues has been heavily criticized by many United States patent attorneys, and would be forbidden by all three proposed amendments to § 101.

Although there is much support in the life sciences industry and among United States patent attorneys to overhaul § 101 in order to fix the perceived problems created by the Supreme Court, many in the fields of software and computers would resist any changes to the status quo, as they appreciate having a quick route to invalidating the patents of the non-practicing entities (often disparaged as so-called "patent trolls") that bring a significant percentage of infringement suits in the software and computer industries. To begin the conversation, the United States Senate called a closed-door hearing in December 2018 to take testimony from invited parties from various industries on the subject of whether § 101 should be revamped, and if so, how. We therefore may see some movement on this topic in 2019.

6. Tips for Dealing with § 101 Problems in Prosecution

Unless and until there is a legislative fix, one must deal with § 101 issues on a claim-by-claim basis. A few general strategies one might employ in different situations are described below. It is generally a good idea to prosecute a number of different independent claims that employ different strategies, as just because the USPTO decides that a given claim is patent-eligible does not mean a court evaluating that claim in litigation will agree.

6.1. Claiming Natural Products

If the invention is a biological molecule, think carefully about whether it could be construed to cover something known to occur in nature, and if so, add some structural limitation to exclude that possibility. The limitation "isolated" or "purified" can no longer be relied upon to do that job. So, if the invention is the discovery of a naturally occurring polypeptide, one might claim the polypeptide attached to something, such as an IgG Fc moiety or other heterologous polypeptide, a detectable label, or PEG, or perhaps instead claim a mixture of the polypeptide with something that is either non-naturally occurring or that alters the function of the polypeptide compared to how it func-

tions in nature. Claiming a method of manufacturing the polypeptide synthetically or recombinantly and then enforcing that method claim under 35 U.S.C. § 271(g) of the infringement statute is another strategy to get around the problem.

If the invention is a naturally occurring polynucleotide, or a portion thereof, one could claim it incorporated into an expression vector, or, if it is intended to function as a probe, claim a radiolabeled version. Claims to vectors, recombinant cells, and methods of expressing the polynucleotide can be other ways to capture the invention without claiming a naturally occurring molecule *per se*.

6.2. Claiming Diagnostic Assays

For diagnostic assay inventions, we look for ways to word the claim that minimize the abstract idea/law of nature/natural phenomenon aspects and emphasize physical steps. Ideally the claim would lack any limitation that appears to recite an abstract idea, law of nature or natural phenomenon, such as a mental step or a correlation between a measurement and a disease, and instead recite only the physical steps of the assay. This may be impossible for many diagnostic assay claims, where the invention is the correlation and not a new assay technique. In such a case, another idea is to follow the USPTO's new 2019 guidance and ensure that the claim recites not only the judicial exception, but also other limitations that either integrate that judicial exception into a practical application (e.g., a specific treatment step that follows from the diagnosis), or are not routine or conventional (e.g., a rarely used assay technique). The patent-eligible claim at issue in the *Vanda* case discussed above was styled as a method of treatment, but in fact included both an assay step (determining the patient's CYP2D6 metabolizer genotype) and a treatment step with a dosage that was determined based on what was found in the assay—i.e., a practical application of the correlation recited at the end of the claim. In some situations, adding a treatment step to a diagnostic assay claim may not be acceptable, as it raises an issue of divided infringement, i.e., whether a single party would ever infringe all steps of such a claim. However, thoughtful claim drafting can sometimes mitigate the divided infringement issue.

6.3. Claiming Methods of Treatment

If the invention is a method of treatment, we generally avoid including in the claim an explicit description of a natural phenomenon, such as the drug's mechanism of action. The *Vanda* decision discussed above suggests that, if the method is claimed with some degree of specificity (e.g., the particular disease, patient population, drug, and/or dosage), that would be beneficial for patent-eligibility. However, there are situations where the invention has broad applicability that can be expressed in the claim only by reciting a natural phenomenon (e.g., an IL-2 inhibitor useful for treating *any* disease characterized by over-expression of IL-2), and does not lend itself to the specificity that characterized the *Vanda* claim. In such a case, one can try relying on the fact that the claim includes a treatment step that integrates the natural phenomenon into a practical application, per the USPTO's 2019 guidance, and point to both the *Vanda* holding and to other indications (albeit only *dicta*) in the case law that methods of treatment are generally patent-eligible.

7. Conclusion

Recent jurisprudence in the United States has expanded the types of subject matter that are deemed ineligible for patenting, thereby invalidating many issued patents and making it increasingly difficult to obtain allowance of claims to certain kinds of life sciences inventions. The USPTO's 2019 guidance attempts both to provide more clarity to how the USPTO will examine claims for patent-eligibility, and to relax to some degree the very strict standards previously applied by the USPTO during prosecution. However, that guidance is not law and will not dictate how the

courts view the subject. Until there is a legislative change to the statute, we must rely on careful claim drafting with a view to both the case law and the USPTO guidance in order to maximize the likelihood of obtaining patent-eligible claims.

References
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