21st century medicine

Introduction

The Coalition for 21st Century Medicine (the "Coalition") gratefully acknowledges the opportunity to comment on the most recently issued update to the Interim Eligibility Guidance[1] (the "2015 Update" or the "Update") issued by the United States Patent and Trademark Office (the "Office"). We confine our comments to Section IV: Requirements of a *Prima Facie* Case, found on pages 6 and 7 of the 2015 Update.

The Coalition has serious concerns about the 2015 Update's stance on the role of "evidence" in the *prima facie* case under 35 U.S.C. §101. By focusing on arcane nuances in the legal meaning of the word "evidence," the 2015 Update tells non-lawyer examiners that no objective support beyond a conclusory allegation is required to satisfy their *prima facie* burden. In an area of patent examination in desperate need of analytical rigor and objectivity, the 2015 Update allows examiners to evaluate subject matter eligibility in the absence of both.

The 2015 Update summarizes what the Office believes is (and is not) necessary to satisfy the *prima facie* burden under §101 as follows:

> This rationale may rely, where appropriate, on the knowledge generally available to those in the art, on the case law precedent, on applicant's own disclosure, or on evidence. […]
>
> The courts consider the determination of whether a claim is eligible (which involves identifying whether an exception such as an abstract idea is being claimed) to be a question of law. Accordingly, courts do not rely on evidence that a claimed concept is a judicial exception, and in most cases resolve the ultimate legal conclusion on eligibility without making any factual findings.

2015 Update, page 6.

Our concerns with this statement and the rest of this section of the 2015 Update are discussed in a fair amount of detail below. But ultimately the Coalition believes that a relatively simple fix could resolve most of these problems: We propose that in any case where any element of the §101 rejection relies on an examiner's characterization of "the knowledge generally available to those in the art," the examiner must be required to cite objective support for the proposition in the form of journal articles, textbooks, and the like.

[1] The July 2015 Update: Subject Matter Eligibility, available at http://www.uspto.gov/sites/default/files/documents/ieg-july-2015-update.pdf, last accessed October 12, 2015.

Courts Treat Eligibility as a Question of Fact that Is "Rife with Underlying Factual Issues"

It is technically true that eligibility is a question of law, but saying so without any qualification or explanation is misleading, especially in a document directed to an examining corps largely lacking formal legal training. Nor is it accurate to say "courts *do not rely* on evidence," which wrongly implies they *never* rely on *any type* of evidence. And the statement "*most* cases resolve the ultimate legal conclusion on eligibility without making *any* factual findings" implies the Office has actually surveyed all relevant cases and found that *more than half* make *zero* factual findings, which is very unlikely.

In contrast to these misstatements of the legal framework for patent eligibility, consider the following from the Federal Circuit:

> [T]he analysis under §101, while ultimately a legal determination, is *rife with underlying factual issues*. For example, while members of this court have used varying formulations for the precise test, there is no doubt the §101 inquiry requires a search for limitations in the claims that narrow or tie the claims to specific applications of an otherwise abstract concept. *CLS Bank,* 707 F.3d at 1298–1302 (meaningful limitations). Further, factual issues may underlie determining whether the patent embraces a scientific principle or abstract idea. *Id.* (opinion of Lourie, J.) ('The underlying notion is that a scientific principle ... reveals a relationship that has always existed.')). If the question is whether 'genuine human contribution' is required, and that requires 'more than a trivial appendix to the underlying abstract idea,' and were not at the time of filing 'routine, well-understood, or conventional,' *factual inquiries likely abound*. *Id.* at 1283–85. *Almost by definition, analyzing whether something was 'conventional' or 'routine' involves analyzing facts*. *Id.* at 1284–85.

Ultramercial, Inc. v. Hulu, LLC, 722 F.3d 1335, 1339 (Fed. Cir. 2013) (emphasis added; internal citations omitted).

As another example, the district court's opinion in the *Mayo* case clearly relied on evidence in the form of testimony from plaintiff's expert to find that the claimed correlations were natural phenomena:

> This Court finds that there can be little doubt that the claimed correlations are "natural phenomena." According to Plaintiff's own expert, Dr. Bloomfield, "the key therapeutic aspect of such thiopurine drugs is that they are converted ***naturally*** by enzymes within the patient's body to form an agent that is therapeutically active."

Prometheus Laboratories, Inc., v. Mayo Collaborative Services, 86 U.S.P.Q.2D (BNA) 1705, 2008 U.S. Dist. LEXIS 25062, *10 (emphasis added).

Finally, positions taken by the Supreme Court when addressing questions of law are equally informed by factual determinations, as illustrated by citations to the specification and prior art cited therein:

> [a]t the time the discoveries embodied in the patents were made, scientists already understood that the levels in a patient's blood of certain metabolites, including, in particular, 6-thioguanine and its nucleotides (6-TG) and 6-methyl-mercaptopurine (6-MMP), were correlated with the likelihood that a particular dosage of a thiopurine drug could cause harm or prove ineffective. *See* U.S. Patent No. 6,355,623, col. 8, ll. 37-40, 2 App. 10. ("Previous studies suggested that measurement of 6-MP metabolite levels can be used to predict clinical efficacy and tolerance to azathioprine or 6-MP"[…]). But those in the field did not know the precise correlations between metabolite levels and likely harm or ineffectiveness. The patent claims at issue here set forth processes embodying researchers' findings that identified these correlations with some precision.

Mayo Collaborative Services, DBA Mayo Medical Laboratories, et al., v. Prometheus Laboratories, Inc., 566 U.S. __, 132 S. Ct. 1289, 1295 (2012).

The Guidance Should Make Clear that Objective Support Must Always be Cited to Satisfy the *Prima Facie* Burden Under §101

Ultimately this issue hinges upon an important semantic distinction: while the 2015 Update discusses "evidence" solely as that word is understood in very specific legal contexts (*e.g.*, expert testimony, factual records in litigation), as discussed above, non-lawyer examiners are far more likely to interpret statements that this *type* of evidence is not required to mean they need *no* evidence of *any type* whatsoever. For this reason, the Guidance should clearly state that examiners must cite *objective support* (a looser definition of "evidence") for the core elements of any §101 rejection (*i.e.*, that the claim is directed to a judicial exception and that any other elements are purely routine and conventional). With respect to explaining what kind of "objective support" is necessary, the 2015 Update already offers some guidance: "[A rejection] may rely, where appropriate, on the knowledge generally available to those in the art, on the case law precedent, on applicant's own disclosure, or on evidence." *2015 Update*, page 6.

Applicant's own disclosure: The disclosure is a valuable source of facts ("evidence") to support (or refute) a §101 rejection. After all, the specification defines what is claimed and what is not, a clear understanding of which is essential to properly deciding whether a judicial exception is claimed. Importantly, statements in the specification about certain details being well-known to those skilled in the art must be read in the full context of the specification rather than isolated and used to summarily reject under step 2 of *Mayo*.

Case law precedent: Prior precedent is probably the second best source of material to support or refute a §101 rejection. Examiners should look to see whether a claim they are examining is directed to subject matter very similar to what courts have already excluded, but cases finding particular subject matter ineligible must be interpreted narrowly. The Guidance should clearly warn examiners against analogizing too loosely. If there is no very close analogy, then the strong presumption should be that the claimed subject matter is eligible.

Knowledge generally available to those in the art: This is arguably the most sensitive issue in §101 rejections and the primary reason the Coalition is submitting these comments. Including this catch-all in the 2015 Update only reinforces what has been discussed above (*i.e.*, the implicit message to examiners that no objective support is required for §101 rejections) and legitimizes the very low quality rejections applicants currently must deal with.

If "general knowledge" is to be a meaningful factor in a §101 rejection, then the examiner must cite some objective source to substantiate this general knowledge. Here again the 2015 Update appears to encourage low quality rejections by suggesting that textbooks or non-prior art references are somehow inappropriate or inadequate sources for § 101 rejections while undefined "general knowledge" is sufficient. The Update makes much of the fact courts have cited sources that were not prior art as supposed support for the Office's claim that no evidence is necessary. *See, e.g.*, *2015 Update*, page 6 ("In Bilski, […] the Supreme Court cited […] modern day *textbooks* (that were *not prior art*)"; "In *Alice Corp.*, the documents were *textbooks* and an article (*only one* of which *qualified as prior art*)" (emphasis added)). Far from proving no evidence is required, this in fact proves the opposite—*i.e.*, evidence is required and, in the right context, non-prior art evidence may be sufficient.

This problem of "general knowledge" is related to the 2015 Update's erroneous and confusing treatment of judicial notice:

> Courts have not identified a situation in which evidence was required to support a finding that the additional elements were well-understood, routine or conventional, but rather treat the issue as a matter appropriate for judicial notice. As such, a rejection should only be made if an examiner relying on his or her expertise in the art can readily conclude in the Step 2B inquiry that the additional elements do not amount to significantly more (Step 2B: NO). If the elements or functions are beyond those recognized in the art or by the courts as being well-understood, routine or conventional, then the elements or functions will in most cases amount to significantly more (Step 2B: YES).

2015 Update, page 7. As discussed below, this relieves examiners of their *prima facie* burden because: (1) examiners are unlikely to understand the nuances of the legal concept of "judicial notice" and (2) are instead likely to interpret this part of the Update as license to base §101 rejections on their own subjective sense that something is routine and conventional. Once again the Update confuses matters by drawing a formal distinction between "judicial notice" and "evidence" without explaining the narrow legal context in which each term is being used.

This discussion suggests that judicial notice is a loose mechanism by which courts (and examiners) can simply convert their own subjective impressions into irrefutable facts.

Judicial notice requires some basis or support, the classic example being a court relying on an almanac to take judicial notice of the fact a particular night had a full moon. Judicial notice is not the court arbitrarily and unilaterally declaring that a particular night had a full moon or even relying on the judge's memory if a party disputes this. Examiners may not, by waving the wand of judicial notice, solely "rely[] on his or her expertise in the art [to] conclude in the Step 2B inquiry that the additional elements do not amount to significantly more." They must cite some form of objective support for one of only two core inquiries under §101.

The 2015 Update Effectively Relieves Examiners of their *Prima Facie* Burden

Relieving the examining corps of the requirement to base rejections on evidence, and instead encouraging them to base rejections "on the knowledge generally available to those in the art," runs counter to long-standing PTO practice allocating the burden of proof during examination. When the *prima facie* burden falls on examiners under every substantive basis for examination,[2] why should the threshold inquiry of eligibility be treated differently? In other words, why should an applicant be more readily barred at Judge Rich's front door to the patent system than at later stages? And how exactly is an applicant to overcome a rejection under §101 based on an examiner's subjective, unsupported sense of what is routine and conventional? Applicants may have considerable difficulty rebutting such a *prima facie* case, as it essentially requires them to prove a negative.

The Coalition believes that relieving the examining corps of the requirement to provide evidence in support of a *prima facie* case of subject matter ineligibility under 35 U.S.C. §101 will impede rather than advance the Office's stated goal of improving the record and clarifying that "the initial burden is on the examiner to explain why a claim or claims are unpatentable clearly and specifically, so that applicant has sufficient notice and is able to effectively respond." The Office's approach as set forth in the 2015 Update will only make the current state of affairs worse by encouraging examiners to engage in arbitrary, Potter Stewart-esque analysis ("I know it when I see it") to identify putative laws of nature and determine whether additional elements are routine, conventional, and well-understood in the art.

[2] As the Manual of Patent Examining Procedure makes clear, the initial burden rests with the examiner to establish: (1) a *prima facie* case of anticipation under 35 U.S.C. §102 (MPEP §2121 ("When the reference relied on expressly anticipates or makes obvious all of the elements of the claimed invention, the reference is presumed to be operable. Once such a reference is found, the burden is on applicant to provide facts rebutting the presumption of operability")); (2) a *prima facie* case of obviousness under 35 U.S.C. §103 (MPEP §2142 ("The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness.")); (3) a *prima facie* case of lack of written description under 35 U.S.C. §112 (MPEP §2163.04 ("A description as filed is presumed to be adequate, unless or until sufficient evidence or reasoning to the contrary has been presented by the examiner to rebut the presumption. … The examiner has the initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the claims.")); and (4) a *prima facie* case of lack of enablement under 35 U.S.C. §112 (MPEP §2164.04 ("In order to make a rejection, the examiner has the initial burden to establish a reasonable basis to question the enablement provided for the claimed invention.")).

Consider, for example, a recent case involving the following claim (some details genericized to provide anonymity to the applicant and the examiner):

> *A method for predicting therapeutic efficacy or response to an anticancer drug in a subject having [Cancer A], said method comprising:*
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> *(a) determining the phosphorylation level of a panel of signal transduction pathway biomarkers comprising [Marker A], [Marker B], and [Marker C] in a cellular extract produced from a cancer cell isolated from said subject to obtain a marker profile;*
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> *(b) comparing said marker profile obtained in step (a) with known marker profiles for [Cancer A] cell lines comprising [Cell Line A], [Cell Line B], [Cell Line C], [Cell Line D], [Cell Line E], [Cell Line F], [Cell Line G], and [Cell Line H] to identify similarities and/or differences between the phosphorylation level of the panel of signal transduction pathway biomarkers in the cellular extract and in the [Cancer A] cell lines; and*
>
> *(c) predicting therapeutic efficacy or response to an anticancer drug based on similarities between said marker profile obtained in step (a) for the cellular extract and said known marker profile for one of the [Cancer A] cell lines, wherein the [Cancer A] of said subject is predicted to respond to the same anticancer drug that produces a response in the [Cancer A] cell line having the similar marker profile.*

The examiner's rejection consisted, in its entirety, of the following:

> *Claims [X, Y & Z] are rejected under 35 USC 101 because the claimed invention is directed to judicial exceptions without significantly more. Claims [X, Y & Z] are directed to methods of predicting therapeutic efficacy or response to an anticancer drug in a subject based upon the phosphorylation level of biomarkers within a sample taken from said subject. Instant claims [X, Y & Z] involve a judicial exception, that is the correlation between (a) a marker profile produce by comparing the phosphorylation level of biomarkers from a sample from a subject to the phosphorylation levels of said biomarkers in a cancer cell line and (b) the therapeutic efficacy or response to an anticancer drug in said subject, which is a natural principle. The claims do not include additional elements that are sufficient to amount to significantly more than the judicial exception. The claims do not include additional elements that are sufficient to amount to significantly more than the judicial exception.*
>
> *Moreover, all method steps of the claims are set forth at a high level of generality such that substantially all practical applications of the judicial*

exception(s) are covered. Therefore, the claims are deemed to be patent ineligible.

Several things are worth noting. First, the examiner finds that the claims fail step 1 of *Mayo* merely because they "involve" a judicial exception, rather than limiting rejections to claims "directed to" a judicial exception. The Coalition's concern about the December 2014 Guidance's change from "involving" to "directed to" having little practical effect[3] appears to have been well-founded. Second, even assuming the claim is "directed to" the correlation identified by the examiner, there is no explanation how any human-derived statistical correlation between the laboratory detection of biomolecules in a sample extracted from a patient to generate a profile and a clinical prediction (i.e., approximation) of therapeutic response is a natural principle. This is just stated as an indisputable fact as if by the Office's inaccurate version of judicial notice. Third, the examiner's *prima facie* case (one that at this point should still be supported by evidence) appears to rely entirely on the superficial use of eligibility catch-phrases like "a high level of generality" and "all practical applications of the judicial exception(s) are covered" without any explanation or analysis.

Finally, the examiner summarily states, without any analysis and without any objective support, that "[t]he claims do not include additional elements that are sufficient to amount to significantly more than the judicial exception." Again assuming the claim may properly be dissected into the correlation (the supposed natural principle) on one hand and everything else on the other, the examiner has not provided any analysis of everything else. Was determining the phosphorylation levels of these specific markers routine and conventional in this specific cancer type at the time of filing? Was generating a profile specific for that panel of markers? Was it routine and conventional to compare the phosphorylation levels of these specific markers (or the profile derived therefrom) in a sample from a patient having [Cancer A] to the levels of these markers (or a profile derived therefrom) in the specific recited cell lines?

This cursory level of "analysis" is not the exception but the current rule in TC1600. Coalition members can point to dozens of examples just like this, where patenting of potentially life-saving diagnostics has ground to a halt. And the 2015 Update's discussion of the *prima facie* case will only make things worse.

Given the conclusory nature of the §101 rejections already being issued by the Office, rather than making it easier for the examining corps to reject applications under §101, it would seem more sensible to require examiners to satisfy their burden by: (1) making their analysis express and detailed, including a showing that the claims at issue have truly been considered "as a whole" as required by *Diamond v. Diehr*[4]; (2) writing a detailed rejection with more than cursory recitation of catch-phrases like "the subject matter of the claim is considered a law of

[3] *See*, Coalition for 21st Century Medicine Comments on December 2014 Guidance, page 3, *available at* http://www.uspto.gov/sites/default/files/documents/2014ig_a_21st_2015mar16.pdf (last visited October 14, 2015).

[4] 450 U.S. 175, 188-189 (1981).

nature"; and (3) providing objective support beyond a conclusory assertion that a claim element is "routine, conventional, and well-understood" in the art.

Conclusion

Ultimately the Coalition believes that a relatively simple fix could resolve this issue. Rather than referring to "evidence" in a narrow legal sense and noting a few examples where this narrow conception of evidence was not strictly required by courts, the Office should clarify that in any case where an element of the §101 rejection relies on an examiner's characterization of "the knowledge generally available to those in the art", the examiner must cite objective support for the proposition in the form of journal articles, textbooks, and the like. Absent such clarification, non-lawyer examiners will understand a statement that they don't need "evidence" for a *prima facie* case to mean they need not cite any support at all for their rejection.