

ATTORNEY REVIEW

The Obviousness Standard in a Post-KSR World

By: Clifford M. Davidson, Esq.

On April 30, 2007, the Supreme Court sent shock waves throughout the world of patents with its holding in *KSR International v. Teleflex Inc.*, 127 S.Ct. 1727 (April 30, 2007). Suffice it to say that in this decision, the Supreme Court held that the Federal Circuit had been applying a flawed analysis with respect to the obviousness inquiry. In doing so, the Supreme Court called into question the motivation to combine references when undertaking an obviousness analysis, and further apparently resurrected “obvious-to-try” as a useful standard for determining obviousness of a patent claim. More detail is found in my previous article in the June issue of this publication. Now, the dust has settled somewhat, and the following will examine the fall-out of the KSR decision.

THE USPTO’S VIEW

Shortly after the issuance of the KSR decision, the deputy commissioner for patent operations at the USPTO (Margaret A. Focarino) issued a memorandum to the patent examiners. The Focarino memo included some important messages. First, she noted that the Graham factors for obviousness under 35 U.S.C. §103(a) are still in force. The Graham factors instruct one to determine the following: (1) the scope and content of the prior art; (2) the differences between the claims and the prior art; (3) the level of ordinary skill in the prior art; (4) secondary considerations, if any, of non-obviousness. It further noted that the Supreme Court did not completely reject the TSM test (teaching, suggestion, or motivation) for making a determination of obviousness. Instead, the Supreme Court rejected a rigid application of the TSM test, which would require an explicit showing of a teaching, suggestion, or motivation to combine prior art before holding a claim to be obvious.¹ The Focarino memo instructed the examiners to provide explicit analysis to explain the reason why multiple prior art references are combinable in the manner prescribed by the examiner. The full text of the PTO memo is found at <http://pub.bna.com/ptcj/PTOMay3memo.pdf>.

HOW HAVE THE COURTS BEEN AFFECTED BY THE KSR DECISION?

Just 1 week after the KSR decision, the Court of Appeals for the Federal Circuit (CAFC) had already adapted itself to the KSR decision and applied a “common sense” obviousness analysis in place of its previously rigid “explicit” TSM test. See *Leapfrog Enterprises, Inc. v. Fisher-Price, Inc.*, No. 06-1402 Fed. Cir. (May 9, 2007).

But how does the KSR decision affect pharmaceutical patent litigation? Although it is very early in the game since KSR was decided, there have been a number of recent decisions that provide us with some guidance.

THE COURT OF APPEALS FOR THE FEDERAL CIRCUIT

The Federal Circuit has considered the effect of the KSR decision on an obviousness determination in a recent case involving the blockbuster diabetes drug ACTOS®. The case was on appeal from the United States District Court for the Southern District of New York, where a bench trial solely on the issues of validity and enforceability of the API patent covering ACTOS (U.S. Patent No. 4,687,777) was not shown to be invalid under 35 U.S.C. § 103 [*Takeda Chem Indus., Ltd. v. Mylan Labs.*, 417 F.Supp.2d 341 (S.D.N.Y. 2006)]. The District Court decision had been entered prior to the KSR decision. The Federal Circuit’s reasoned analysis in the *Takeda* decision is instructive as to how the Federal Circuit views the interaction between the KSR decision, its own body of work, and the *Graham* test.

The ‘777 patent claimed the active ingredient by virtue of its chemical structure. With respect to structurally similar compounds, the Court stated that “in order to find a prima facie case of unpatentability in such instances, a showing that the ‘prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention’ was also required” [*Takeda Chem Indus., Ltd. v. AlphaPharm Pty. Ltd. and Genpharm, Inc.* . . . F.d (Fed. Cir. 2007)]. The Federal Circuit then went on to discuss the fact that while the Supreme

Court in KSR rejected a rigid application of the TSM test in an obviousness inquiry, the Court did indicate there is no necessary inconsistency between the idea underlining the TSM test and the *Graham* analysis. Rather, the Supreme Court had acknowledged the importance of identifying “a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does” in an obviousness determination. KSR at 1731. The Federal Circuit concluded that in cases involving new chemical compounds, it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.” Id. at page 6.

A closer look at the prior art and the reasoning behind the decision is warranted. The closest prior art to the active compound in ACTOS (pioglitazone) was compound b, which was one of 54 compounds synthesized in a prior art Takeda patent (U.S. Patent No. 4,287,200). The parties did not dispute that compound b was the closest prior art compound, and compound b was in fact characterized in the prosecution history of the ‘777 patent as being “especially important.” The District Court, however, disagreed. It considered compounds identified in a published article (Sodha II) to be closer art. Therein, three specific similar compounds were deemed most favorable in terms of toxicity and activity, and compound b was singled out as causing undesirable side effects (eg, causing an increase in body weight). To arrive at pioglitazone, one would have to make two changes to compound b: replacing the methyl group with an ethyl group (homologation) and moving the ethyl substituent to another position on the ring (“ring walking”).

The Federal Circuit considered the aforementioned information and concluded the following:

... rather than identify predictable solutions for anti-diabetic treatment, the prior art disclosed a broad selection of compounds, any one of which could have been selected as a lead compound for further investigation. Significantly, the closest prior art compound (compound b, the 6-methyl) exhibited negative properties that would have directed one of ordinary skill in the art away from that compound. Thus, this case fails to present the type of situation contemplated by the court when it stated that an invention may be deemed obvious if it was obvious-to-try. The evidence showed that it was not obvious-to-try.

The Federal Circuit decision in the Norvasc® litigation was rendered months before the KSR decision. However, comments by certain judges in a Federal Circuit Decision not to rehear the case en banc did touch upon the KSR decision. More particularly, in *Pfizer, Inc. v. Apotex, Inc.* 480 F.3d 1438 (Fed. Cir. 2007), the Federal Circuit held that the patent claiming Pfizer’s amlodipine besylate (active ingredient in Norvasc®) was invalid because a skilled artisan would have been motivated to combine prior art references to achieve the claimed invention and would have had a reasonable expectation of success, and further that it would have been obvious to optimize acid

addition salt formulation for an active pharmaceutical ingredient in a hypertension drug (amlodipine besylate instead of amlodipine maleate).

In his dissent from the denial of rehearing en banc, Judge Lourie of the Federal Circuit stated the following:

These issues are of exceptional importance. Chemical and pharmaceutical compounds often can be found to be prima facie obvious because they are based on prior work that could reasonably suggest them, See KSR . . . but commercialization of such compounds may depend on their possession of unexpected properties. Such properties may be biological or physical. A failure to recognize all such properties that may be relevant to the value of such a compound may doom the compound to being poured down the drain rather than becoming an important therapeutic. General public, innovative companies, and ultimately generic companies depend upon faithful adherence to this principle. In addition, our cases hold that unexpected properties make for non-obviousness. . . , and this decision disdains such properties if they are not biological. That is a conflict with our precedent that needs resolution.

The issue to which Judge Lourie was speaking, that the panel mistakenly determined that the superior properties of the besylate did not overcome a prima facie case of obviousness because they showed no superior therapeutic (biological) value, was furthered by the dissent of Judge Rader.

IN THE U.S. DISTRICT COURTS

Two weeks after the KSR decision, a judge in the U.S. District Court for the District of Maryland gave jury instructions in a biotech case that advised the jury that it could find the disputed patent invalid for obviousness under the obvious-to-try standard that was given a fresh breath of life in KSR. In that case, which involved a genetically engineered enzyme for cloning DNA, the jury nevertheless held the patents’ validity. It was particularly noteworthy that the judge agreed to stress in his instructions that the jury should not use hindsight to find the invention was obvious-to-try, and that such a finding would only be proper if that which was considered to be obvious-to-try was ultimately successful, noting in his instructions that arts, such as biotechnology, are not generally predictable [*Invitrogen Corp. v. Clontex Laboratories, Inc.*, D.Md. No. AW-96-4080 (May 16, 2007)].

The KSR decision also came into play in the end of ANDA litigation concerning Pepcid® Complete, an OTC acid indigestion product. In that case, McNeil asserted its U.S. Patent No. 5,817,340 covering the combination of famotidine and antacids, and the use of an impermeable coating against the generic product. Following a 9-day bench trial, Judge Pauley of the U.S. District Court for the Southern District of New York found that the ‘340 patent was invalid for obviousness. Judge Pauley concluded that all of the relevant limitations in the claims of the ‘340 patent were found in the prior art,

and that the '340 patent had done nothing more than combine the predictable results of two prior art references (regarding a chewable tablet) with the predictable results of two other patents (regarding taste-masking). The judge cited KSR frequently in his decision, while stating that it did not change the result of his analysis in this case. In view of the strong showing of obviousness, the judge also held that the secondary considerations patentability, such as commercial success, could not overcome the invalidity of the claims.

In *Abbott Laboratories v. Sandoz, Inc.*, slip opinion, 2007 WL 1549498 (N.D.Ill.), Sandoz asked the Court to stay enforcement of a preliminary injunction it had issued shortly prior to the KSR decision. At issue here is the ANDA filing by Sandoz for Biaxin® XL. Abbot's U.S. Patent No. 6,010,718 included claims directed, eg, to an extended-release erythromycin derivative in the gastrointestinal environment, comprising the erythromycin derivative and 5% to 50% polymer, so that when ingested orally, the composition induces statistically significant lower mean fluctuation index in the plasma than an immediate-release version of the drug, while maintaining substantially equivalent bioavailability.

The gist of the Sandoz position was that the KSR decision rendered the preliminary injunction order reversible. The Sandoz position centered around the combination of a patent that disclosed the use of an alginic acid polymer in making sustained-release formulations (including Clarithromycin) and a patent publication disclosing sustained-release formulations of azithromycin in general (and including the use of HPMC as a polymer). Sandoz argued that the combination of these references along with the FDA definition of a term "bioequivalence" would have motivated a person of ordinary skill in the art to combine these sources of information to arrive at an extended-release clarithromycin product (solving a known problem).

The Court disagreed before the KSR decision (by granted the preliminary injunction) and after the motion for stay of enforcement of the preliminary injunction after the KSR decision. The Court found that Sandoz had not produced evidence indicating that the pharmacokinetic limitations were disclosed in the prior art or were inherent to the structural limitations of the prior art compositions. After a thorough discussion of the KSR decision, the Court stated that "the need to demonstrate the presence of all claim limitations in the prior art (when the legal theory is based on obviousness due to the combination of prior art teachings) has not been obviated" by the KSR decision. A crucial finding by the Court was that a person skilled in the art would not be motivated to interchange clarithromycin in one reference for azithromycin in the other reference because the prior art clarithromycin patent did not disclose the claimed PK profile.

WHERE DO THESE DECISIONS LEAVE US?

While it certainly does appear that the courts have duly noted the KSR decision, and have taken particular care in providing the bases for determining motivation to combine references in recent decisions, it does not appear that there will be any drastic change in the way

courts review patent claims. It does appear that the "unexpected result" basis for patentability remains a strong force in overcoming an argument of a motivation to combine prior art references. On the other hand, it is still too early to tell what effect the KSR decision will have on patent examiners at the USPTO. One may guess that experienced examiners will tend to continue to examine patent claims in the manner they have done so previously, but perhaps with more attention to the necessity to provide an explanation as to motivation to combine references. Less experienced patent examiners may jump on the KSR bandwagon and slow the already time-challenged review of patent applications to a crawl. ♦

REFERENCE

1. Indeed, there was never a requirement that a result of the TSM test required explicit teaching, suggestion, or motivation to combine prior art to make a determination of obviousness of a claim.

BIOGRAPHY



Clifford M. Davidson, Esq. is a founding partner at Davidson, Davidson & Kappel, LLC, an Intellectual Property law firm with offices in New York City and Frankfurt, Germany. He counsels pharmaceutical clients in pharmaceutical patent-related matters, including patent prosecution, freedom to operate and infringement opinions, due diligence

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