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Spring Has Sprung Obviousness Trends from the Federal Circuit

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There have been only a few precedential decisions from the Federal Circuit related to obviousness since spring sprung. While these decisions have produced mixed results for the lower courts, clinical study protocols have held up to appellate scrutiny both in the context of motivation to combine and reasonable expectation of success.

Reversed and Remanded to the Bench

At the beginning of the month, in *Janssen Pharmaceuticals, Inc. v. Teva Pharmaceuticals USA, Inc.* (No. 22-1258), a Federal Circuit panel told U.S. District Judge Claire C. Cecchi (New Jersey) that she erred in finding claims to a schizophrenia drug nonobvious.

Janssen markets and sells Invega Sustenna®, which, according to the website, is an extended-release injectable suspension of paliperidone palmitate used to treat schizophrenia in adults. Prior to Invega Sustenna, the conventional approach for dosing of antipsychotic drugs was to "start low and go slow." The dosing regimens for Invega Sustenna® and claimed in U.S. Patent No. 9,439,906 are contrary to this conventional approach in that injections of high, rather than low, loading doses are used to begin treatment.

When Janssen sued Teva for allegedly infringing claims of the ?906 patent, Teva tried to convince Judge Cecchi in a bench trial that the claims of the ?906 patent are invalid as obvious based on a clinical study protocol describing an interventional Phase III clinical trial, which hypothesized that three fixed doses of paliperidone palmitate would be more efficacious than a placebo in treating subjects with schizophrenia, U.S. Patent No. 6,555,544, which describes the composition used in the claim of the '906 patent, and International Publication No. WO 2006/114384, which describes preparation of aseptic crystalline paliperidone palmitate.

On appeal, the Federal Circuit first took issue with the lower court's finding that Teva failed to show that it would be obvious to use the claimed dosing regimen for the general population of patients because the clinical study protocol did not show that the drug had generalized safety and efficacy. In this regard, the panel explained that, since the ?906 patent describes a dosing regimen for "a psychiatric patient" being treated for schizophrenia, and "nothing in the claims requires that the

[dosing] regimen be used for — let alone be ideal for — the patient population generally," an analysis based on a general population of patients was improperly framed. The lower court was told that it instead should have focused its reasonable expectation of success analysis on a single schizophrenia patent.

In addition, the Federal Circuit found fault with the lower court's failure to give adequate weight to the perspective and creativity of a person of ordinary skill in the art when deciding whether the dosing regimen claimed in the ?906 patent would have been obvious based on the prior art combination. In this regard, the panel explained that the lower court erred by focusing on the clinical study protocol's lack of results rather than considering what the protocol would fairly suggest to a person of ordinary skill in the art. In fact, the panel concluded that a person of ordinary skill in the art would still have ascribed "significance … to the Phase III status of the protocol" and the knowledge that paliperidone palmitate was already marketed for schizophrenia. In this regard, the appellate panel deemed the lower court to have taken a "seemingly siloed and inflexible approach."

Moreover, the panel explained that, while identifying a recognized problem or need in the prior art is one way to demonstrate motivation, there was no requirement for Teva to show that the clinical study protocol was flawed for a person of ordinary skill in the art to be motivated to modify it. Rather, the opinion reminds us that:

[a] motivation 'may be found explicitly or implicitly in market forces; design incentives; the interrelated teachings of multiple patents; any need or problem known in the field of endeavor at the time of invention and addressed by the patent; and the background knowledge, creativity, and common sense of the person of ordinary skill.'

Suffice it to say, the Federal Circuit found that the lower court's obviousness analysis "ran afoul of KSR's basic mandate in a number of ways." In any event, Teva now has the renewed opportunity to prove that the ?906 patent is invalid. With almost $3 billion in sales in 2023 and the ?906 patent being the last remaining Orange Book patent for Invega Sustenna, Janssen has a lot at stake.

Applause to the Bench

In mid-April in *Salix Pharmaceuticals, LTD. et al v. Norwich Pharmaceuticals, Inc.*(22-2153), a divided panel of the Federal Circuit affirmed a District of Delaware ruling invalidating certain claims of Salix's U.S. Patent Nos. 8,309,569 (claim 2), 10,765,667 (claim 3), 7,612,199 (claim 4), and 7,902,206 (claim 36) invalid as obvious. This family of patents protected the composition and use of Xifaxan®, which is used to treat IBS-D.

After a bench trial, Judge Richard G. Andrews held that the claims were invalid as obvious based on a clinical study protocol published on the clinicaltrials.gov website describing a Phase II study and a journal article. The protocol does not include any efficacy or safety data or the claimed dose of 1,650 mg/day or thrice-daily dosing (550 mg/dose), but does provide an outline of a planned Phase II clinical trial evaluating twice-daily doses (1,100 mg/day and 2,200 mg/day) for the treatment of IBS-D. The journal article teaches a 400mg dose administered three times a day for the treatment of IBS, but also mentioned that optimal dosing may be higher. Based on these separate teachings, the lower court found that the protocol and journal article disclose each and every limitation of the claims-at-issue, and then concluded that a person of ordinary skill in the art would have been motivated to combine the protocol and journal article to arrive at the claims with a reasonable expectation of success.

On appeal, Salix argued that, even if the protocol and journal article in combination discloses the claimed dosage, there was insufficient evidence to support a finding of a reasonable expectation of success in using that particular dosage amount. In this vein, amici argued in support of Salix that disclosure of clinical trials are not sufficient to inform a skilled artisan about the reasonable likelihood of success in the future and that there is a very low success rate of clinical trials. However, the majority found no error in the district court's holding that a person of ordinary skill in the art would have considered the combination of the two references (not just the protocol) and possessed a reasonable expectation of success in using the 550mg/dose from the protocol (after noting from the journal article that the optimal dosage for IBS may be higher than 400mg TID) since "certainty and absolute predictability are not required to establish a reasonable expectation of success."

What Says the High Court on Clinical Study Protocols?

If the recent denial of cert in *Vanda Pharmaceuticals Inc., Petitioner v. Teva Pharmaceuticals USA, Inc.* is any indication, it does not seem like the justices are particularly interested in reviewing the Federal Circuit's obviousness test (at least when clinical study protocols are in the mix). Vanda had argued that the "reasonable expectation of success" test when combining prior art in the obviousness review used by the Federal Circuit was wrong and counter to Supreme Court precedent from 2007 requiring "predictable results."

The Vanda appeal stemmed from a 2022 bench trial in the District of Delaware where U.S. District Judge Colm Connolly found Vanda's patents covering Hetlioz®, which is used to treat certain sleep disorders, invalid as obvious. Briefly, two different combinations of prior art, both of which include references discussing Phase II or Phase II clinical trials, were determined to render the claims obvious. The Federal Circuit affirmed the lower court's finding of obviousness and noted that the use of ongoing clinical trials as one piece of evidence, combined with other prior art references, to support a finding of reasonable expectation of success is not error.

Vanda argued to the high court that the Federal Circuit's test would make "the mere existence of a clinical trial" part of a reasonable expectation of success in the obviousness analysis, which would make "experimentation unpatentable, no matter how innovative or unpredictable the results." Vanda's petition was denied cert without further explanation.

So, What's the Takeaway?

We know that generally, when the obviousness test involves combining references, a person of ordinary skill in the art (1) must have been motivated to make such a combination, and (2) have had a reasonable expectation of success in arriving at the claimed invention. In the context of clinical study protocols, we also know that the lack of safety and efficacy data does justify discounting a protocol in either (1) or (2). Rather, with respect to reasonable expectation of success, the Salix majority did caution that:

[a]lthough we have rejected the idea that 'efficacy data [are] always required for a reasonable expectation of success,' *OSI Pharms., LLC v. Apotex Inc.*, 939 F.3d 1375, 1385 (Fed. Cir. 2019), we are hesitant to conclude as a general matter that the disclosure of a Phase II clinical trial plan, standing alone, provides an expectation of success sufficient to render obvious a dosage that was not included within the planned clinical trial.

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