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Federal Circuit Patent Bulletin: *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*

June 17, 2014

"[U]nexpected results do not per se defeat, or prevent, the finding that a modification to a lead compound will yield expected, beneficial properties. Rather, as secondary considerations of nonobviousness, they come into play in determining 'the ultimate question of patentability.'"

On June 12, 2014, in *Bristol-Myers Squibb Co. v. Teva Pharms. USA, Inc.*, the U.S. Court of Appeals for the Federal Circuit (Prost, Plager, Chen*) affirmed the district court's judgment that U.S. Patent No. 5,206,244, which related to a nucleoside analog including entecavir marketed as Baraclude® by BMS for treating hepatitis B, was invalid for obviousness under 35 U.S.C. § 103. The Federal Circuit stated:

Obviousness requires assessing (1) the "level of ordinary skill in the pertinent art," (2) the "scope and content of the prior art." (3) the "differences between the prior art and the claims at issue," and (4) "secondary considerations" of nonobviousness such as "commercial success, long-felt but unsolved needs, failure of others, etc." A party seeking to invalidate a patent as obvious must demonstrate "'by clear and convincing evidence that a skilled artisan would have been motivated to combine the teachings of the prior art references to achieve the claimed invention, and that the skilled artisan would have had a reasonable expectation of success from doing so.'" To establish obviousness in cases involving new chemical compounds, the accused infringer must identify some reason that would have led a chemist to modify a known compound. Generally, an obviousness inquiry concerning such "known compounds" focuses on the identity of a "lead compound." A lead compound is a compound in the prior

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art that would be "a natural choice for further development efforts." The motivation to modify that lead compound can come from any number of sources and need not necessarily be explicit in the art. "[I]t is sufficient to show that the claimed and prior art compounds possess a 'sufficiently close relationship . . . to create an expectation,' in light of the totality of the prior art, that the new compound will have 'similar properties' to the old." Whether a lead compound and a claimed compound have a sufficiently close relationship frequently turns on their "structural similarities and differences." . . .

BMS attacks the lower court's obviousness determination by contending that a skilled artisan would have had to make too many decisions to arrive at entecavir. Those decisions include selecting (1) the class of nucleoside analog compounds, (2) 2'-CDG as a lead compound from the class of carbocyclics, (3) the carbocyclic ring or guanine base of 2'-CDG for modification, (4) the 2' or 5' position on the carbocyclic ring, (5) the specific chemical element on the 5' position (carbon), and (6) the type of carbon to carbon bond (single or double). We conclude that the district court's analysis is well supported. . . .

Based on the record, we see no clear error in the district court's finding that the modification required to transform 2'-CDG into the structurally similar entecavir is a minor one: the addition of a single carbon atom to form an exocyclic methylene with the already-present carbon atom at the 5' position of the carbocyclic ring of 2'CDG to create entecavir. Upon selecting 2'-CDG as the lead compound, the steps of deciding which bond to modify and how to modify that bond "equate to a small, finite number of changes to try to [arrive at] the lead compound." . . . 2'-CDG and entecavir are very structurally similar, and it is well settled that structurally similar compounds often have similar properties. . . .

BMS also argues that a new chemical entity, as a matter of law, cannot be obvious when the claimed invention possesses unexpected properties. Specifically, BMS argues that the existence of unexpected properties forecloses a finding of a reasonable expectation of success. . . . Contrary to BMS's argument, unexpected results do not per se defeat, or prevent, the finding that a modification to a lead compound will yield expected, beneficial properties. Rather, as secondary considerations of nonobviousness, they come into play in determining "the ultimate question of patentability." Secondary considerations of nonobviousness "must always when present be considered," and can serve as an important check against hindsight bias. While secondary considerations must be taken into account, they do not necessarily control the obviousness determination. Here, the district court found evidence of some secondary considerations of nonobviousness, including commercial success, long-felt need, and unexpected results. On appeal, BMS focuses primarily on unexpected results.

To be particularly probative, evidence of unexpected results must establish that there is a difference between the results obtained and those of the closest prior art, and that the difference would not have been expected by one of ordinary skill in the art at the time of the invention. Unexpected properties, however, do not necessarily guarantee that a new compound is nonobvious. While a "marked superiority" in an expected property may be enough in some circumstances to render a compound patentable, a "mere difference in degree" is insufficient. And "differences in degree" of a known and expected property are not as persuasive in rebutting obviousness as differences in "kind"—i.e., a new property dissimilar to the known property. When assessing unexpected properties, therefore, we must evaluate the significance and "kind" of expected results along with the unexpected results. . . .

We agree with the factual findings on secondary considerations and find no clear error. As stated previously, we also agree with the district court's finding that the record demonstrates strong evidence of obviousness. After considering all of the findings for and against obviousness, as well as Teva's burden of proof, we see no basis to disturb the district court's ultimate legal conclusion, and we affirm the judgment that claim 8 of the '244 patent is invalid as obvious.