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Merck Challenges PTAB's Non-Obviousness Decision of Wyeth's Patent

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Earlier this month, a panel of the U.S. Court of Appeals for the Federal Circuit consisting of Chief Judge Sharon Prost and Judges Timothy Dyk and Evan Wallach heard arguments in *Merck Sharp & Dohme Corp. v. Wyeth LLC*[1].

Merck petitioned and the U.S. Patent Trial and Appeal Board (PTAB) instituted two *inter partes* reviews (IPRs) of Wyeth's U.S. Patent 8,562,999 on the basis of alleged obviousness.[2] Merck prevailed in showing all claims obvious except dependent claim 18. Merck appealed the sparing of claim 18 to the Federal Circuit, asserting that the PTAB had erred (1) in its assessment of the evidence; (2) in the legal test it applied; and (3) in violating the Administrative Procedure Act's (APA) requirement for reasoned decision-making.

The sole claim at issue — claim 18 of the '999 patent — depends from claim 1, which recites a formulation which inhibits aggregation induced by a siliconized container. Claim 1 reads:

> 1. A formulation comprising (i) a pH buffered saline solution, wherein the buffer has a pKa of about 3.5 to about 7.5, (ii) an aluminum salt and (iii) one or more polysaccharide-protein conjugates, wherein the formulation is comprised in a siliconized container means and inhibits aggregation induced by the siliconized container means.

[1] *Merck Sharp & Dohme Corp. v. Wyeth LLC*, (2018-2133, -2134) (U.S. Court of Appeals for the Federal Circuit)
[2] *Merck Sharp & Dohme Corp. v. Wyeth LLC*, (IPR2017-00378) and (IPR2018-00380) (U.S. Patent and Trademark Office Patent Trial and Appeal Board)

Claim 18 specifies the one or more polysaccharide-protein conjugates as 13 particular pneumococcal polysaccharide conjugates, each of which comprises the CRM197 polypeptide, a genetically detoxified form of diphtheria toxin. Claim 18 reads:

> 18. The formulation of claim 1, wherein the one or more polysaccharide-protein conjugate comprises an *S. pneumoniae* serotype 4 polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 6B polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 9V polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 14 polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 18C polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 19F polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 23F polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 1 polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 3 polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 5 polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 6A polysaccharide conjugated to a CRM197 polypeptide, an *S. pneumoniae* serotype 7F polysaccharide conjugated to a CRM197 polypeptide and an *S. pneumoniae* serotype 19A polysaccharide conjugated to a CRM197 polypeptide.

For much of the Nov. 7 oral arguments, the panel seemed to be chasing down the basis for the PTAB's holding that claim 18 was not proven to be obvious. The judges repeatedly asked both Merck and Wyeth if it was obvious to select the particular 13 polysaccharides. Merck said that it did not think that was the basis of the Board's decision to hold claim 18 not proven obvious, because one of the cited references, Peña, specifically taught the 13 polysaccharides recited in claim 18. Indeed, the PTAB's final written decisions appear to acknowledge that the Peña reference taught the same 13 polysaccharides, and instead relied on the failure of Peña to teach whether and to what those 13 polysaccharides were conjugated.

In its final written decisions, the PTAB rejected an argument from Merck that a person of skill in the art would have been motivated to go from the prior art seven-valent, nine-valent, and 11-valent vaccines to the 13-valent vaccine of claim 18 by a "natural progression." Merck explained the phrase during oral arguments as just another way of saying it would have been obvious. Chief Judge Prost noted that an explanation of motivation was needed to avoid use of improper hindsight. Wyeth countered Merck's "natural progression" argument by noting that the prior art nine-valent vaccine was not in a buffer as required in the recited

formulation and the prior art 11-valent vaccine used multiple carrier proteins, contrary to the disputed claim's recitation of a single carrier protein—CRM197—conjugated to all 13 polysaccharides. As Wyeth argued in its brief, the prior art failed to teach a 13-valent *conjugate* vaccine.

Throughout the hearing, the panel repeatedly asked the parties to point to portions of the IPR records where an expert witness interpreted the prior art in the manner that supported their assertions.

Judge Dyk to Merck: Did you have expert evidence that said that?

Chief Judge Prost to Merck: Where's your expert testimony?

Judge Dyk to Merck: Show us what and where your expert says that.

Judge Dyk to Merck: What you need is some expert testimony.

Chief Judge Prost to Wyeth: Did you have an expert testifying to that?

Judge Dyk to Wyeth: Did you have an expert say that?

Judge Dyk to Wyeth: Did your expert say that?

This drumbeat of questions reflects the appellate court's need to assess whether substantial evidence supported the PTAB's underlying factual determinations of its non-obviousness decision.

The court again focused on record evidence in response to Merck's urging that the PTAB's final written decision was defective under the APA. Judge Wallach noted that Merck's problem [in making this argument] may be that although the opinion failed to specifically point to evidence to support its holding, nonetheless the record is full of evidence to support its holding.

In its rebuttal time, Merck tried to cast Wyeth's '999 patent as an improper attempt at "evergreening" its protection for its commercial product, Prevenar 13. Merck asserted that Wyeth already had protection for an effective 13-valent vaccine. Wyeth's attempt to protect its formulation, Merck said, was merely an attempt to extend its initial protection of the vaccine by one year. The existence of a prior patent has been considered relevant to objective indicia of non-obviousness by the Federal Circuit; however, the PTAB did not reach the objective indicia of non-obviousness in its decision.

Merck asserted in its brief that the PTAB used the wrong test to analyze motivation to combine. It asserted legal error in the PTAB formulating the obviousness inquiry as whether a person of skill in the art would have been motivated to *modify* one reference with another, rather than whether a person of skill in the art would have understood that the teaching of

the first reference could be *applied* to the second reference, citing *Belden v. Berk-Tek*.[3] Merck urged that the Federal Circuit in *Belden* reversed the PTAB because it wrongly used a motivation-to-modify test rather than a motivation-to-apply test. Merck did not make this argument at the oral hearing.

The oral hearing focused on the PTAB's assessment of evidence of obviousness, rather than Merck's other asserted issues of using an erroneous legal standard and improper administrative agency decision-making. The panel's insistent refrain of asking for citations to the evidentiary record highlights the Federal Circuit's view of its role — to review the factual determinations underlying the obviousness determination to ascertain if the PTAB's based its determination of non-obviousness on substantial evidence.

Click here to listen to the arguments in *Merck Sharp & Dohme Corp. v. Wyeth LLC*.

[3] *Belden Inc. v. Berk-Tek LLC*, 805 F.3d 1064 (Fed. Cir. 2015)