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Federal Circuit Agrees "Pharmaceutical Composition" May Be Toxic

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The claim construction determinations in *Mayne Pharma International Pty. Ltd. V. Merck Sharp & Dohme Corp*. may leave stakeholders in the pharmaceutical space scratching their heads, and highlights that it's rarely possible to anticipate and avoid every claim construction issue that may be raised in a patent challenge. Indeed, a district court had agreed with the patent owner that the term "pharmaceutical composition" excluded toxic compositions and that the claimed pharmacokinetic profiles are achieved in humans. Nevertheless, both the USPTO Patent Trial and Appeal Board (PTAB) and the Federal Circuit construed the claims more broadly.

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The Patent At Issue

The patent at issue was Mayne's U.S. Patent 6,881,745, directed to "Pharmaceutical compositions for poorly soluble drugs." The court treated claim 9 as representative:

9. A pharmaceutical composition, consisting essentially of:
about 100 mg of an azole antifungal drug; and
one or more polymer having acidic functional groups; and
optionally one or more additional ingredients selected from the group consisting of a disintegrant, a diluent, a filler, an inert solid carrier, an inert solid matrix, a lubricant, a glidant, a colouring agent, a pigment, a flavour, water, ammonia, an alkaline agent, and methylene chloride,
wherein in vivo the composition provides a mean CMAX of at least 100 ng/ml, after administration in the fasted state.

In parallel district court litigation, Mayne asserted that Merck's Noxafil® tablets, having posaconazole as an active ingredient, infringed the patent. Merck petitioned for Inter Partes Review of certain claims of the '745 patent, and the PTAB found claims 2, 6, and 9–14 invalid over prior art.

The Federal Circuit Decision

The Federal Circuit decision was authored by Judge Lourie and joined by Judges Dyk and O'Malley.

The primary reference asserted in the IPR proceeding was an article by Kai that "discloses a solid dispersion technique for improving the bioavailability of a triazole antifungal agent, MFB-1041," and reports results of a pharmacokinetic study conducted in dogs. To distinguish this prior art, Mayne argued that the claims should be construed (i) as limited to nontoxic compositions (because MFB-1041 was known to be toxic) that (ii) produce the claimed pharmacokinetic profile in humans. In support of these positions, Mayne pointed to the terms "azole antifungal ***drug***" and "***pharmaceutical*** composition," and the ***human*** clinical trial reported in the specification that supported the recited pharmacokinetic profile.

The Federal Circuit decision also addresses interesting "real party in interest" issues that will not be discussed here.

The PTAB had construed the claims under the "broadest reasonable interpretation" standard. In the parallel district court proceedings, the court had adopted a narrower construction consistent with Mayne's arguments.

However, as the Federal Circuit noted in its decision, citing its 2015 decision in *Power Integrations*, the PTAB "is not generally bound by a prior judicial construction of a claim term."

On the first claim construction issue, the Federal Circuit found that the definition for "drug" provided in the specification did not exclude toxic agents:

The term "drug" will be widely understood and denotes a compound having beneficial prophylactic and/or therapeutic properties when administered to, for example, humans.

The court reasoned that this definition "indicates that the claimed 'pharmaceutical composition' … has at least some beneficial therapeutic properties," but does not rule out "adverse effects or toxicity." The court also credited Merck's arguments based on the specification's disclosure of saperconazole as an example of an azole antifungal drug. Since that agent was known to be toxic and yet is mentioned as an example of an azole antifungal drug, there was "no basis" for importing a "nontoxic" limitation into the claim.

On the second claim construction issue, the court found that the definition for "in vivo" provided in the specification supported a broad construction:

The term 'in vivo' in general means in the living body of a plant or animal, whereas the term "in vitro" generally means outside the body and in an artificial environment.

In particular, the court noted that "animals are expressly recited by the definition of in vivo," and thus concluded, "a person of skill would understand the claims to include animals."

Because Mayne did not dispute anticipation or obviousness under the PTAB's claim constructions, the court affirmed the PTAB decision invalidating claims 2, 6, and 9–14.

Anticipating Prior Art

I find it interesting that the Kai reference is discussed in the background section of the patent and was made of record during prosecution. Although the examiner cited Kai against (different) claims pursued in the (abandoned) parent application, he never cited it in this case. That a known reference can be found to be anticipating highlights the difficulty of anticipating claim construction and invalidity positions that may be raised in a patent challenge.